ARAŞTIRMA / RESEARCH

Evaluation of esophageal motor functions in patients diagnosed with primary biliary cholangitis, primary sclerosing cholangitis and autoimmune hepatitis

Primer biliyer kolanjit, primer sklerozan kolanjit ve otoimmün hepatit tanısı alan hastalarda özofagus motor fonksiyonlarının değerlendirilmesi

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Abstract

Purpose: The aim of this study was to evaluate the relationship between autoimmune liver diseases and esophageal motor disorders (EMD).

Materials and Methods: 63 patients diagnosed with primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC) and autoimmune hepatitis (AIH) and followed up in our hospital were included in the study. The control group consisted of 33 patients. Upper gastrointestinal endoscopy, esophageal motility study and pH meter tests were performed on all participants.

Results: Of the 63 patients included in the study 49.2% of the patients, EMD was detected while 31.7% of them had pathology in the pH meter. The rates of EMD of patients with PBC, PSC and AIH were 50%, 63.6%, and 42.9%, respectively while the pathology rates of the pH meter were found as 25%, 54.5%, and 28.6%, respectively. Statistically significant difference was found between autoimmune liver disease and control group in terms of esophageal motor diseases. As a result of manometric examination, median lower esophageal sphincter resting pressure was significantly lower in autoimmune liver patients compared to the control group.

Conclusion: Our study presents that EMD is common in patients with PBC, PSC, and AIH, and that the presence of cirrhosis has no impact on the development of EMD.

Keywords: Primary biliary cholangitis, primary sclerosing cholangitis, autoimmune hepatitis, esophageal motility disorder

Öz

Amaç: Bu çalışmada otoimmün karaciğer hastalıkları ile özofagus motor bozuklukları (EMD) arasındaki ilişkisinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya Primer biliyer kolanjit (PBC), primer sklerozan kolanjit (PSC) ve otoimmün hepatit (AIH) tanısı konan hastanızı takip edilen 63 hasta dahil edildi. Kontrol grubu 33 hastadan oluşturuldu. Çalışmaya dahil edilen tüm hastalıklarla üst gastrointestinal endoskopisi, özofagus motilite çalışması ve pH metre testleri yapıldı.

Bulgular: Çalışmaya dahil edilen 63 hastanın %49,2’sinde EMD, %31,7’sinde pH metreden patoloji saptandi. PBC, PSC ve AIH hastalarının EMD oranları sırasıyla %50, %63,6 ve %42,9 iken pH metrenin patoloji oranları sırasıyla %25, %54,5 ve %28,6 olarak bulundu. Otoimmün karaciğer hastalığı ile kontrol grubu arasında özofagus motor hastalıkları açısından istatistiksel olarak anlamlı fark bulundu. Manometrik incelene sonucunda otoimmün karaciğer hastalarında kontrol grubuna göre alt özofagus sfinkter dinlenme basınç anlamlı olarak daha düştü.

Sonuç: Çalışmamız, PBC, PSC ve AIHli hastalarda EMD’nin yaygın olduğunu ve sırızo varlığının EMD gelişimi üzerinde hiçbir etkisi olmadığını ortaya koymaktadır.

Anahtar kelimeler: Primer biliyer kolanjit, primer sklerozan kolanjit, otoimmün hepatit, özofagus motilite bozukluğu

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INTRODUCTION

Among the diseases considered to have an autoimmune etiology in the liver, the most common ones are primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), and autoimmune hepatitis (AIH)\(^1\). PBC is an autoimmune disease that leads to inflammation in intralobular bile ducts\(^3\). On the other hand, PSC is a chronic cholestatic disease characterized by inflammation, fibrosis and abnormal narrowing of intrahepatic and extrahepatic bile ducts\(^4\). Toxins, ischemia, infection, genetic and autoimmune factors are considered responsible for the etiopathogenesis of the disease\(^5\). AIH is an inflammatory disease that mainly covers hepatocytes and it occurs as a result of the immune response to normal liver cell membrane protein and antigenic determinants on the membrane\(^6\). Comorbidity of PBC, PSC and AIH with other autoimmune diseases such as systemic lupus erythematosus (SLE), systemic scleroderma, type 1 diabetes mellitus, Sjögren's syndrome, celiac disease, autoimmune hemolytic anemia, rheumatoid arthritis (RA), autoimmune thyroiditis, Graves' disease and ulcerative colitis has been shown\(^7\).

Esophageal motility disorders (EMD) are a group of diseases that present with dysphagia, regurgitation, and atypical non-cardiac chest pain\(^8\). The diagnosis of these diseases is made through radiological and manometric findings\(^9\). In autoimmune rheumatological diseases such as systemic lupus erythematosus (SLE), systemic sclerosis, Sjögren's syndrome, celiac disease, autoimmune hemolytic anemia, rheumatoid arthritis (RA), autoimmune thyroiditis, Graves' disease and ulcerative colitis has been shown\(^9\).

Even though the relationship between EMD and many other autoimmune diseases has been revealed, there is no study in the literature revealing any relationship between autoimmune liver diseases and EMD. The main objective of this study is to evaluate esophageal motor functions in patients diagnosed with primary biliary cholangitis, primary sclerosing cholangitis, and autoimmune hepatitis.

MATERIALS AND METHODS

Study population

Between November 2019-December 2020 in the gastroenterology outpatient clinic of our hospital, 63 patients who were previously diagnosed with PBC, AIH and PSC and 33 patients of the same age with functional dyspepsia diagnosed according to the Rome IV criteria\(^14\) (1. One or more of the following: a. Postprandial fullness (discomfort), b. Early satiety (discomfort), c. Epigastric pain (discomfort), d. Epigastric burning (discomfort) 2. There are no data for a structural disease to explain the symptoms. Upper gastrointestinal (GIS) system endoscopy should be normal. Symptoms started at least 6 months before diagnosis and diagnostic criteria should be present for the last three months.) were included in the study and served as the control group. Patients with any other autoimmune, neurogenic, myogenic or malignant diseases; those with diabetes mellitus and thyroid disease, those with structural anomalies in the esophagus (such as zenker's diverticulum); those with a previous diagnosis of EMD and those younger than 18 years of age and having missing data were excluded from the study.

The study was a prospective study and written consent was obtained from the patients. The study has been conducted following the ethical standards specified in the 1964 Helsinki Declaration. In our study, research and publication ethics and the rules were followed. Ethical approval for this study was obtained from the Ethics Committee of Ankara City Hospital, dated 10.28.2020 and numbered E1/1042/2020.

Data collection

The study was performed in the endoscopy and motility unit of the gastroenterology clinic of Ankara City Hospital. First of all, after the approval of the ethics committee of our hospital for the study, consent was obtained from the volunteer patients who participated in the study. Upper GI endoscopy, esophageal motility and pH meter procedures were performed in each patient. Patient data were recorded and analyzed.

Administration of manometry protocol

None of the patients were allowed to use medications that could change esophageal motor functions during the motility test. After 8 hours of fasting, the manometer catheter was administered nasally into the stomach using a conventional esophageal manometer (MMS Dentsleeve). Gastric baseline pressure was lowered. Subsequently, the lower esophageal sphincter location was determined by retracting the
Evaluation of esophageal motor functions in liver disease

catheter for intervals of 1 cm, with deep inspiration and/or dry swallows. Esophageal motor functions were evaluated through performing 10 wet swallows for 20-second intervals after the sleeve area of the catheter was placed in the lower esophagus.

The conventional classification of esophageal motility was used for the diagnosis of abnormal esophageal functions. The classification is summarized as follows 13: a) The hypotensive lower esophageal sphincter disorder; normal esophageal trunk functions and low lower esophageal sphincter pressure defined as less than 10 mmHg, b) Hypertensive lower esophageal sphincter disorder; lower sphincter pressure more than 45 mmHg, c) Non-specific esophageal motility disorder; i) Those with low esophageal trunk contraction amplitudes (<30 mmHg), ii) Those with normal lower sphincter functions and with a peristaltic trunk contraction more than 30%, iii) Those with more than 30% contractions that cannot be transmitted to the distal esophagus, iv) Those with normal esophageal body functions and less than 30% in complete relaxation in the lower esophageal sphincter

Administration of Ph Meter protocol

Esophageal manometry was performed after 8 hours of fasting by stopping the intake of medications that can affect the stomach pH of the patients 10 days in advance. The place of the lower esophageal sphincter was determined through a manometer. Then, the distal tip of the PHI15 / PHN15 (Sandhill) dual Ph catheter was deployed nasally 5 cm proximal to the lower esophageal sphincter. The patient’s 24-hour Ph meter was recorded and the presence of distal and proximal reflux was examined after the catheter was fixed to the nose.

The patient was considered to have distal pathological reflux if one of the following criteria is available: a) total reflux duration more than 5% in a 24-hour pH meter, b) outpatient reflux duration of more than 6.3%, c) inpatient reflux duration of more than 1.2%, d) reflux period longer than 9.2 minutes, e) a total number of reflux episodes more than 5, f) number of reflux episodes longer than five minutes more than three

The patient was considered to have proximal pathological reflux if one of the following criteria is available: a) total number of reflux in the proximal more than %1, b) number of outpatient reflux more than 6.3%, c) the longest reflux episode which is longer than 3 minutes, d) a total of reflux episodes more than 5

Statistical analysis

The statistical evaluation has been performed via the Statistical Software Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL). Of the numerical variables, those with normal distribution are presented as mean ± standard deviation while those that do not present normal distribution are shown as the median (min-max). The statistical differences in the demographic data between the groups were estimated by ANOVA test and in those in the pressures measured between the groups were estimated by the Mann-Whitney U test. The GPower analysis method was used, and type 1 error was accepted 5%. The sample size was determined as 55. The differences between two groups were evaluated by Student’s t test, and when the data distribution was not normal Mann–Whitney U test was used. Chi-square test and Fisher’s exact test were used to evaluate categorical and continuous variables, respectively. A p value < 0.05 was considered statistically significant.

RESULTS

Of the 63 patients included in the study, 53 were female (84.1%) and 10 were male (15.9%). The average age of patients was 55.2 (26-75). The median time of follow-up was 52.9 (3-128) months. Of the 63 patients, 28 were diagnosed with AIH (%44.4), 24 with PBC (38.1%), and 11 with PSC (17.5%). The average age of all three patient groups was similar. While PSC appears equally in both males and females, it has been observed that PBC and AIH are more common in female patients. While the average follow-up period of the PBC patients was 70 months, the average follow-up period in the other patient groups was about 40 months. The demographic characteristics of the patients are presented in Table 1.

There was no significant difference between mean age 55.2 ± 10.2 years vs 47 ± 13.4 years, p = 0.09 in patients in patients with autoimmune liver disease compared to the control group (table 2).

While most of the patients had no symptoms related to the stomach or esophagus, 9 of the patients had dyspepsia and 2 had reflux symptoms. None of them had dysphagia. According to the upper
gastrointestinal endoscopy results of the patients, lower esophageal sphincter laxity was found in 4 patients while Grade A esophagitis has been found in one patient following the Los Angeles classification.

Antral or pangastritis in 56 (89%) patients, alkaline reflux gastritis in 3 patients (5%), and peptic ulcer or erosions have been observed in 4 (6%) patients.

Table 1. Demographic characteristics of the patients

<table>
<thead>
<tr>
<th></th>
<th>PSC (n:11)</th>
<th>PBC (n:24)</th>
<th>AIH (n:28)</th>
<th>Total (n:63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n (%)</td>
<td>11 (%18)</td>
<td>24 (%38)</td>
<td>28 (%44)</td>
<td>63</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5 (%45.5)</td>
<td>23 (%95.8)</td>
<td>25 (%89.3)</td>
<td>53 (%84)</td>
</tr>
<tr>
<td>Male</td>
<td>6 (%54.5)</td>
<td>1 (%4.2)</td>
<td>3 (%10.7)</td>
<td>10 (%16)</td>
</tr>
<tr>
<td>Age, mean (min-max)</td>
<td>50 (35-64)</td>
<td>55.8 (39-68)</td>
<td>56.7 (26-71)</td>
<td>55.2 (26-75)</td>
</tr>
<tr>
<td>Duration of illness, n (min-max)</td>
<td>39.2 (6-84 m)</td>
<td>71 (14-121 m)</td>
<td>43.3 (3-128 m)</td>
<td>52.9 (3-128 m)</td>
</tr>
<tr>
<td>Endoscopic findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antral or pangastritis</td>
<td>9 (%81.8)</td>
<td>22 (%91.6)</td>
<td>25 (%89.3)</td>
<td>56 (%89)</td>
</tr>
<tr>
<td>Alkaline reflux gastritis</td>
<td>1 (%9.1)</td>
<td>1 (%4.2)</td>
<td>1 (%3.6)</td>
<td>3 (%5)</td>
</tr>
<tr>
<td>Peptic ulcer or erosions</td>
<td>1 (%9.1)</td>
<td>1 (%4.2)</td>
<td>2 (%7.1)</td>
<td>4 (%6)</td>
</tr>
</tbody>
</table>

PBC: Primary biliary cholangitis, PSC: primary sclerosing cholangitis, AIH: autoimmune hepatitis

The data of the patients on esophageal motility disorders are presented in figure 1. EMD has been detected in 12 (42.9%) of 28 patients diagnosed with AIH, in 12 (50%) of 24 patients diagnosed with PBC, and in 7 (63.6%) of 11 patients diagnosed with PSC. EMD has been observed in total 31 of the 63 patients we included in the study (%49.2). When evaluated in terms of esophageal motor disease, a statistically significant difference was found between autoimmune liver disease and the control group (p: 0.001). As for the manometric findings, the median lower esophageal sphincter resting pressure was significantly lower in autoimmune liver patients compared to the control group (p: 0.01). There was no significant difference in median esophageal contraction amplitude (p: 0.34) and simultaneous swallows 100% complete (p:0.128) in autoimmune liver patients compared to the control group (table 2).

Table 2. The comparison of manometric findings between ALD patients and control groups

<table>
<thead>
<tr>
<th></th>
<th>ALD (n:63)</th>
<th>Control Group(n:33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>0.098a</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>53 (84)</td>
<td>23 (70)</td>
<td></td>
</tr>
<tr>
<td>Male n (%)</td>
<td>10 (16)</td>
<td>10 (30)</td>
<td></td>
</tr>
<tr>
<td>Age, years (median ±SD)</td>
<td>55.2 (10.2)</td>
<td>47 (13.4)</td>
<td>0.09b</td>
</tr>
<tr>
<td>Esophageal motor disorders n (%)</td>
<td>31 (49.2)</td>
<td>2 (6)</td>
<td>0.001b</td>
</tr>
<tr>
<td>Contraction amplitude (mean) (Std. Deviation)</td>
<td>0.3333 (2.12)</td>
<td>0.6364 (1.91)</td>
<td>0.34c</td>
</tr>
<tr>
<td>LES resting pressure (mean) (Std. Deviation)</td>
<td>19.8 (12.2)</td>
<td>20.20 (7.09)</td>
<td>0.01c</td>
</tr>
<tr>
<td>Simultaneous swallows %100 complete n (%)</td>
<td>61 (97)</td>
<td>31 (94)</td>
<td>0.128b</td>
</tr>
</tbody>
</table>

ALD: autoimmune liver disease  LES: lower esophageal sphincter

In our study, pathological pH meters were not detected in any of the 33 patients with functional dyspepsia. Pathology was detected in pH meters in 20 (31.7%) of 63 patients with autoimmune liver disease; 11 were distal and 9 were both proximal and distal.

When the patient groups were examined, pathology was detected in 8 patients with AIH, 6 patients with PBC and 6 patients with PSC. The pH meter results of AIH, PBC and PSC patients are presented in figure 2.
In our study, 29 patients had a diagnosis of cirrhosis (46%). A total of 14 patients with cirrhosis were found to have EMD (48.3%) including nonspecific motor disorder (20.7%) in 6, hypotensive lower sphincter disorder in 4 (13.8%) and hypertensive lower sphincter disorder in 4 (13.8%) of them. No statistically significant difference has been observed in terms of EMD rates in cirrhotic and non-cirrhotic AIH, PBC and PSC patients (p:0.332). The data on this subject are presented in Table 3.

### Table 3- EMD in patients with cirrhotic and non-cirrhotic AIH, PBC and PSC

<table>
<thead>
<tr>
<th></th>
<th>Non-cirrhotic (n:34)</th>
<th>Cirrhotic (n:29)</th>
<th>p value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>17 (%50)</td>
<td>15 (%51.7)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Esophageal dysmotility</td>
<td>17 (%50)</td>
<td>14 (%48.3)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Non-specific</td>
<td>11 (%32.3)</td>
<td>6 (%20.7)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hypotensive lower esophageal sphincter</td>
<td>5 (%14.7)</td>
<td>4 (%13.8)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hypertensive lower esophageal sphincter</td>
<td>1 (%3)</td>
<td>4 (%13.8)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

PBC: Primary biliary cholangitis, PSC: primary sclerosing cholangitis, AIH: autoimmune hepatitis

\(^a\): Fisher exact test

**DISCUSSION**

Although the reason of the primary esophageal motor disorder is not known exactly, it is considered that immune-mediated mechanisms play an important role in etiopathogenesis. Even though esophageal motor diseases have been revealed to be associated with many autoimmune diseases, there is not enough data in the literature about the relationship between PBC, AIH and PSC diseases. In this study, it has been presented that PSC, PBC and AIH, which are among autoimmune liver diseases, is frequently comorbid with EMD, and esophageal dysmotility has no relationship between cirrhotic and non-cirrhotic patients.

In our study, it has been observed that female patients are more common. We strongly believe that this situation is due to the fact that the PBC and AIH
are more common for females\textsuperscript{13}. The average follow-up duration of the patients in our study was 52 months and that was sufficient. When the endoscopy results have been examined, pangastritis or antral gastritis has been observed in most of the patients. Even though EMD was common in patients, there was no apparent endoscopic result supporting this situation.

There are many studies in the literature examining the relationship between autoimmune liver diseases and other autoimmune conditions. Nevertheless, considering the gastrointestinal involvement of autoimmune liver diseases, it has been observed that it is particularly associated with celiac disease and inflammatory bowel diseases\textsuperscript{14}. No study directly discusses the relationship between autoimmune hepatitis or PSC and EMD, and it has been emphasized that only if these diseases are comorbid with scleroderma or CREST syndrome can be performed by EMD\textsuperscript{17,18}. Yet, these studies could not go beyond a case series. In our study, other autoimmune diseases (mainly scleroderma and CREST) that may be comorbid with autoimmune liver disease has not been included; the relationship between autoimmune liver diseases and EMD has been presented.

In our study, EMD has been observed in 49.2\% of the patients evaluated through the manometric examination. In the esophageal motility study conducted by Richter et al., they found the prevalence of esophageal dysmotility to 5\% in a normal population\textsuperscript{19}. In our study, the detection of EMD in approximately half of the patients and its incidence rate which is 10 times more than the normal population has led us to the idea that the rate of EMD in autoimmune liver diseases may be higher than we expected. The fact that EMD was detected in approximately half of the patients in our study, its incidence was 10 times higher than the normal population, and the statistically significant difference compared to patients with functional dyspepsia led us to the idea that the rate of EMD in autoimmune liver diseases may be higher than we expected.

In the study of Bektas et al. conducted with 37 PBC patients, esophageal motor disorders were compared with the same number of control groups with functional dyspepsia\textsuperscript{20}. Esophageal dysmotility was detected in 17 (45.9\%) of the patients and 10 of these patients had sjogren’s syndrome. In 43.8\% (7/16) of Sjogren’s negative patients, EMD was detected. There was no abnormality detected in any of the functional dyspepsia patients. Of these 17 PBC patients with EMD, 10 had a nonspecific esophageal motor impairment, 5 had esophageal hypomotility, 1 had nutracker esophagus and 1 had hypertensive lower esophageal sphincter. When these results examined, whilst it seems to be compatible with the results of our study, the absence of rheumatological and autoimmune diseases such as scleroderma, Sjogren’s, SLE and RA, which were associated with esophageal motility disorder, makes our study more significant.

Even though the rate of EMD was quite high in our PBC patients, most of these patients did not have any symptoms, which may make the diagnosis of EMD difficult in this patient group. Solely one patient with hypertensive lower sphincter had dyspepsia. Whilst pathology is obvious in 25\% of the patients in pH meter; no symptoms have been observed in these patients. Regarding these results we have obtained, we have observed that EMD could develop although there were no associated symptoms in patients with a diagnosis of PBC. Because of the absence of GERD and dyspepsia symptoms in these patients, an algorithm can be formed to request these tests routinely for the diagnosis of EMD and GERD in this patient group.

The comorbidity of PSC and scleroderma has been presented in the studies conducted\textsuperscript{21}. As it is well known, scleroderma is one of the important reasons for EMD. As a matter of fact that Powell et al. presented the comorbidity of CREST (calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia) syndrome and PSC on a case by case basis\textsuperscript{22}. In our study, EMD has been observed in 7 of 11 patients with PSC (63.6\%). In our PSC patients, a higher rate of EMD has been observed. We strongly believe that the reason for this situation could be as a result of affecting the esophagus just like in scleroderma although there is no scleroderma diagnosis in our patient group, the abnormal collagen storage and fibrosis condition in the bile duct epithelium present in PSC.

In our study, EMD has been observed in 12 of 28 patients with autoimmune hepatitis (42.8\%). In the case series conducted by Marie et al., they found the comorbidity of CREST syndrome with autoimmune hepatitis, and the development of EMD in the patients accordingly\textsuperscript{23}. Whether this situation emerged from a causal relationship or whether it occurred by chance is examined through this study. Since anti-centromere antibodies have been detected
in 13% of patients diagnosed with autoimmune hepatitis, it has been evaluated that autoimmune hepatitis may be partially associated with systemic sclerosis and may result in EMD due to dysfunction of humoral immunity. The patients in our study do not have rheumatological and autoimmune diseases such as CREST syndrome, but EMD has been observed in about half of AIH patients; we can say that AIH and EMD show frequent comorbidity through autoimmunity similar to the causal ideas of the aforementioned study.

It has been considered that progressive autoimmune diseases, PBC, PSC, and AIH, may result in secondary esophageal peristaltic abnormalities by causing neuromuscular disorders in the cirrhosis stage, and as a result, EMD may develop more frequently in cirrhosis patients. However, in our study, it has been observed that the development of cirrhosis does not have an impact on EMD. There was no difference between cirrhotic and non-cirrhotic patient groups regarding the development of EMD. As in the study of Chen et al., there was no significant difference in lower esophageal sphincter resting pressure between the cirrhotic and healthy control groups in our study.24

However, in the study of Chen et al., it was found that the amplitude of contraction decreased 10 cm higher than the sphincter, and the third waves in the esophageal body increased, resulting in EMD development in patients.24 We strongly believe that it is because all of the cirrhosis patients in the study carried out by Chen et al. had esophageal varices. None of the patients in our study has esophageal varices.

The most important limitation of our study is the small number of patients, yet there is no study conducted on this subject in the literature and this study can be regarded as a pilot study.

In literature studies, other rheumatological diseases frequently coexist. We believe that other autoimmune rheumatological diseases with motility disorder may develop in our patient group when patients have a longer follow-up, particularly because our follow-up period is about 1 year. Our present results may be reflected as a motility disorder in the early period being a precursor of future rheumatologic diseases. For this reason, with manometric studies in this patient group, it may be beneficial in terms of having the chance to make the early diagnosis of other rheumatological diseases in patients with motility disorder.

In conclusion, we have found that half of the patients diagnosed with PBC, PSC, and AIH were asymptomatic, but half of them had EMD. We have also demonstrated that the incidence of cirrhosis has no impact on the development of EMD. We strongly believe that early diagnosis of EMD, which is frequently comorbid with autoimmune liver diseases with an asymptomatic course by manometric studies may provide additional useful contributions in the diagnosis and follow-up process.

REFERENCES


