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Investigation of Amyloid Accumulation in Postoperative Gallbladder Material

Postoperatif Safra Kesesi Materyalinde Amiloid Birikiminin Araştırılması

Ali Osman AVCI [1*], Emre AKARSU [2], Hesna Müzeyyen ASTARCI [2]

[1] Department of Internal Medicine, Lokman Hekim University, Ankara, Türkiye

[2] Department of Pathology, Lokman Hekim University, Ankara, Türkiye

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Abstract

Objective: Amyloid deposition in the gallbladder and biliary tract is a relatively underexplored area in the medical literature. The frequency of amyloid deposition in gallbladders after cholecystectomy remains unclear. The present study aims to address this gap in knowledge by investigating amyloid deposition in postoperative gallbladder materials.

Materials and Methods: The study comprised adult patients over the age of 18 who had undergone cholecystectomy for gallstones. Tissue samples taken from the fundus, corpus, and neck regions of the postoperative gallbladder were cut into 5-micron thicknesses for routine examination, stained with hematoxylin-eosin, and then stained with Congo red to search for amyloid deposits under a polarized light.

Results: The study involved 100 patients (57 females, 43 males). The average age of female patients was 46.49 ± 16.20 years, and for male patients, it was 49.58 ± 14.91 years. No amyloid deposition was observed in any gallbladder tissue sample.

Conclusion: It was concluded that it is not necessary to look for amyloid deposits in gallbladder material after cholecystectomy, regardless of the patient's age, gender, concomitant diseases, duration and composition of gallstones.

Keywords: Cholecystectomy, Gallbladder, Amyloidosis

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Öz

Amaç: Safra kesesi ve safra yollarında amiloid birikimi, tıbbi literatürde nispeten az araştırılmış bir alandır. Kolesistektomi sonrası safra kesesinde amiloid birikiminin sıklığı halen belirsizdir. Bu çalışma, postoperatif safra kesesi materyallerinde amiloid birikimi sıklığını araştırarak bu bilgi boşluğunu gidermeyi amaçlamıştır.

Gereç ve Yöntemler: Çalışma, safra kesesi taşı nedeniyle kolesistektomi geçiren 18 yaş üstü yetişkin hastaları kapsamaktadır. Postoperatif safra kesesinin fundus, korpus ve boyun bölgelerinden alınan doku örnekleri rutin inceleme için 5 mikron kalınlığında kesilerek hematoksilen-eozin ile boyanmış, daha sonra Kongo kırmızısı ile boyanarak polarize ışık altında amiloid birikimi aranmıştır.

Bulgular: Çalışmaya 100 hasta (57 kadın, 43 erkek) katılmıştır. Kadın hastaların ortalama yaşı 46,49 ± 16,20 yıl, erkek hastaların ise 49,58 ± 14,91 yıldı. Hiçbir safra kesesi doku örneğinde amiloid birikimi gözlenmedi.

Sonuç: Hastanın yaşı, cinsiyeti, eşlik eden diğer hastalıkları, safra kesesi taşlarının süresi ve bileşiminden bağımsız olarak kolesistektomi sonrası safra kesesi materyalinde amiloid birikimi aramanın gerekli olmadığı sonucuna varılmıştır.

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[*]**Sorumlu Yazar (Corresponding Author):** Ali Osman Avcı, **e-mail**: aliosman.avci@lokmanhekim.edu.tr

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Introduction

Gallbladder stones (cholecystolithiasis) are a common condition, affecting up to 20% of the global population (1, 2). While 80% of individuals with gallstones remain asymptomatic, the remaining 20% experience symptoms such as abdominal and back pain (3,4). Among symptomatic patients, 20-25% eventually undergo cholecystectomy. Although many patients experience pain relief post-surgery, 20-30% continue to experience postoperative discomfort (5, 6).

The pathophysiology of gallbladder stones and chronic cholecystitis involves the accumulation of amyloid in the gallbladder or biliary tract, with amyloid deposition being a well-documented phenomenon that can affect multiple organs. The literature contains a limited number of case reports on this subject (7–12). Additionally, a case of cholangitis due to amyloid deposition in the biliary tract has been reported (13), although the frequency of this condition remains poorly understood.

Amyloid deposition, known as amyloidosis, results from serum amyloid A (SAA), which is a prominent acute-phase reactant. In healthy individuals, SAA is present in concentrations of less than 3 mg/L (0.3 mg/dL). However, during the acute-phase inflammatory response, SAA levels can increase exponentially, reaching up to 1000 times baseline levels within 24 hours in response to proinflammatory cytokine stimulation (14). Persistently elevated SAA levels, along with low-grade inflammation, have been associated with life-threatening complications, including secondary amyloidosis and coronary heart disease (15, 16). Elevated SAA levels also serve as markers of subclinical inflammation and potential amyloidosis risk (15, 16).

This study aimed to investigate amyloid deposition in postoperative gallbladder tissue.

Materials and Methods

This prospective study was conducted at a university hospital, examining postoperative gallbladder samples from 100 adult patients who underwent cholecystectomy for gallstones. Demographic characteristics, family history, body mass index (BMI), and other concomitant diseases were analyzed. Inclusion criteria: Adult patients (over 18 years old) undergoing cholecystectomy for gallstones. Exclusion criteria: Patients under 18 years of age, or those with familial Mediterranean fever or gout, or those using colchicine.

Gallbladder tissue samples were obtained from the fundus, corpus, and neck of the gallbladder as part of the routine procedure. Five-micron-thick sections were extracted from paraffin blocks and stained with hematoxylin and eosin. Samples were processed using paraffin embedding, cut into 5-micron-thick sections, and stained with hematoxylin and eosin. No amyloid deposits were detected during the routine examination.

Subsequently, the histochemical examination phase was initiated, with 8-micron-thick sections obtained from the paraffin blocks and subjected to Congo red staining (18). A total of 600 Congo red-stained gallbladder sections from 300 paraffin blocks were examined under polarized light to detect amyloid deposits, characterized by apple-green birefringence. During this examination, skin biopsies with amyloid deposits detected with Congo red were used as positive controls.

Statistical Analysis

Data were analyzed using SPSS (version 27). Descriptive statistics, including means, standard deviations, and percentages, were calculated. The Kolmogorov-Smirnov test was used to check for normal distribution. Kolmogorov-Smirnov tests were used for normality checks, and the Mann-Whitney U test was used to compare variables. A p-value of less than 0.05 was considered significant.

This study was approved by the University Scientific Research Ethics Committee (meeting date: 08.08.2023, approval number: 2023/129). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, and informed consent was obtained from all patients.

Results

The study sample included 100 patients, 57 females and 43 males. The age range for females was 21-90 years, with a mean age of 46.49 ± 16.20 years, while for males it was 23-88 years with a mean age of 49.58 ± 14.91 years. The mean BMI of female patients was 28.75 ± 5.17, while that of male patients was 28.34 ± 4.50 (Table 1).

Family history of gallstones was reported in 33 (57.89%) female patients and 23 (53.48%) male patients. Concomitant chronic diseases, such as diabetes, hypertension, and hypothyroidism, were observed in 36 (63.15%) females and 20 (46.51%) males. After cholecystectomy, 7% of patients (4 females and 3 males) reported persistent symptoms at 3 and 6 months post-surgery (Table 1).

Table 1.

Demographic Characteristics of Patients

	N (%)	Age (Year)	BMI	Family Story	Comorbidity	SAC
Total	100	47.82±15.65	28.58±4.87	56 (56%)	56 (56%)	7 (7%)
Female	57	46.49±16.20	28.75±5.17	33 (57.89%)	36 (63.15%)	4 (7.01%)
Male	43	49.58±14.91	28.34±4.50	23 (53.48%)	20 (46.51%)	3 (6.97%)

BMI: Body Mass Index, **SAC**: Symptomatic after cholecystectomy

A statistically significant discrepancy was not identified when male and female patients were compared in terms of age, BMI, family history, comorbidity, and the persistence of postcholecystectomy symptoms (Table2).

Table 2.

Comparison of Results

	Female (n:57)				Male (n:43)				
	Min	Max	Mean	SD	Min	Max	Mean	SD	P Value
Age (year)	21	90	46.49	16.20	23	88	49.58	14.91	0.345
BMI	18.07	42.52	28.75	5.17	20.02	41.62	28.34	4.50	0.686
Family Story	33 (57.89%)				23 (53.48%)				0.610
Comorbidity	36 (63.15%)				20 (46.51%)				0.102
SAC	4 (7.01%)				3 (6.97%)				0.650

BMI: Body Mass Index, **SAC**: Symptomatic after cholecystectomy, **SD**: Standard deviation

Discussion

The present study found that 7% of patients continued to experience symptoms after cholecystectomy, a phenomenon with unclear aetiology. This suggests that the symptoms may not be related to gallbladder pathology, but rather to another, undiagnosed factor. This warrants further investigation into potential causes of postoperative symptoms.

Regarding amyloid deposition, while previous case reports suggest the possibility of amyloid in the gallbladder or biliary tract, the present study did not detect amyloid in any postoperative gallbladder tissue. This result aligns with the literature, where amyloid deposition in these tissues is rare. The absence of amyloid

deposits in our cohort further underscores the infrequency of this condition in patients undergoing cholecystectomy for gallstones (7-12).

Non-modifiable risk factors for gallstone development are often summarized by the mnemonic '5Fs' – 'fair, fat, female, forty, and family history' (19-21). In this study, 57% of patients were female, the average age exceeded 40 years, the mean BMI was above 27.5, and 56% had a family history of gallstones.

No significant differences were observed between male and female patients regarding age, BMI, family history, or postoperative symptoms. Most notably, amyloid deposits were not found in the gallbladder tissues across all patient demographics, ranging from 21 to 90 years of age, with varying family histories of gallstones and multiple comorbidities. This finding remained consistent even after re-examining the tissues with a different brand of Congo red dye.

The lack of amyloid deposition in the gallbladder tissues suggests that routine screening for amyloid in gallbladder specimens after cholecystectomy may not be necessary.

Limitations of the study: The two most important limitations of this study are the number of cases being 100 and the use of only Congo red for amyloid detection. Although positive control was used, more specific tests are available for amyloid accumulation in tissues. Since there was not enough budget for the study, more patients, SAA level measurement and other amyloid search methods could not be used. Our greatest wish is that it will lead to prospective studies in a larger patient group, by also checking SAA levels, and using amyloid search methods other than Congo red.

Conclusion

It was concluded that it is not necessary to look for amyloid deposits in gallbladder material after cholecystectomy, regardless of the patient's age, gender, concomitant diseases, duration and composition of gallstones. Further research is needed to investigate the possible causes of symptoms that persist after cholecystectomy and to clarify the role of amyloid deposits in the gallbladder and biliary tract.

Ethics Committee Approval: The study was approved by the Lokman Hekim University Scientific Research Ethics Committee (date: 08.08.2023 and approval number: 2023/129).

Informed Consent: Written consent was obtained from the participants.

Conflict of Interest: Authors declared no conflict of interest.

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