



Acute pancreatitis: It can be the first sign of silent gallstones

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ABSTRACT

Objective: The management of asymptomatic cholelithiasis is controversial. Silent gallstones are generally assumed to cause complications after at least one episode of biliary colic. The ratio of those silent stones that had initially caused, -or were diagnosed as the etiological agent of- acute pancreatitis has not been reported in the literature yet. Our study was designed to investigate the ratio of asymptomatic cholelithiasis in acute biliary pancreatitis cases.

Material and Methods: One hundred and seventy-one patients of 305 cases, who were followed up with the diagnosis of acute biliary pancreatitis, were identified retrospectively. Demographic specifications, laboratory findings and clinical progressions of the patients were inspected. Clinical histories were detailed by phone calls. Gallstones were radiologically detected in 85 out of 171 cases. Those patients were divided as symptomatic and asymptomatic. Clinical findings and follow-ups were evaluated by "Chi-square" test.

Results: In the study group, 80% of the patients were asymptomatic (n= 68) and 16.47% of the patients (n= 14) had complicated pancreatitis. Regarding the severity of the clinical course, being symptomatic or not was not identified as a significant factor (p= 0.108). In regard of creating symptoms, the size of the stone was not significant (p= 0.561) and obtained no prediction about the clinical severity of the pancreatitis (p= 0.728).

Conclusion: Asymptomatic cholelithiasis patients had a major percentage in acute biliary pancreatitis cases. The "wait and see" approach should be re-evaluated for silent gallstones in prospective trials.

Keywords: Acute biliary pancreatitis, asymptomatic cholelithiasis, silent gallstones

INTRODUCTION

The management of asymptomatic gallbladder stones is still a matter of debate. Gallstones that are noticed during routine abdominal ultrasonography performed for other reasons and that do not cause any symptoms and/or complications associated with gallstones are called asymptomatic gallstones. Although dyspeptic complaints are thought to be due to gallstones in the absence of typical biliary symptoms, this issue is controversial (1,2).

Since the occurrence of gallbladder stones in the population is clearly higher than the rate of cholecystectomy cases, the management of asymptomatic disease needs even further analysis (1,3).

In a study focusing on the natural course of the gallstones, no remarkable complications have been noted in any of the patients enrolled in the study before the occurrence of typical symptoms of gallstone disease (GSD) (4).

On the other hand, it has been previously reported that 10-year cumulative complication rate for asymptomatic and symptomatic patients are 3% and 7%, respectively (5). This latter study has shown that silent gallstones might not stay uneventful in the long term.

Acute biliary pancreatitis (ABP) is one of the most severe complications of GSD.

There are numerous factors that determine the clinical severity of pancreatitis. Recognizing and differentiating these clinically and therapeutically important factors significantly affect the morbidity and mortality of this disease (6-10). Although most of the patients with ABP have self-limiting mild disease with excellent prognosis, severe ABP with multi-organ failure might occur in 10-15% of the patients and bears a considerable risk for mortality (11).

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In this study, we aimed to investigate the incidence and role of asymptomatic gallstones in ABP, and clinical features of patients with asymptomatic gallstone who had been diagnosed with ABP. At the same time, the effect of the gallstone size on the development of symptoms and whether stone size or the presence of symptoms are related to the severity of pancreatitis were also examined.

MATERIAL and METHODS

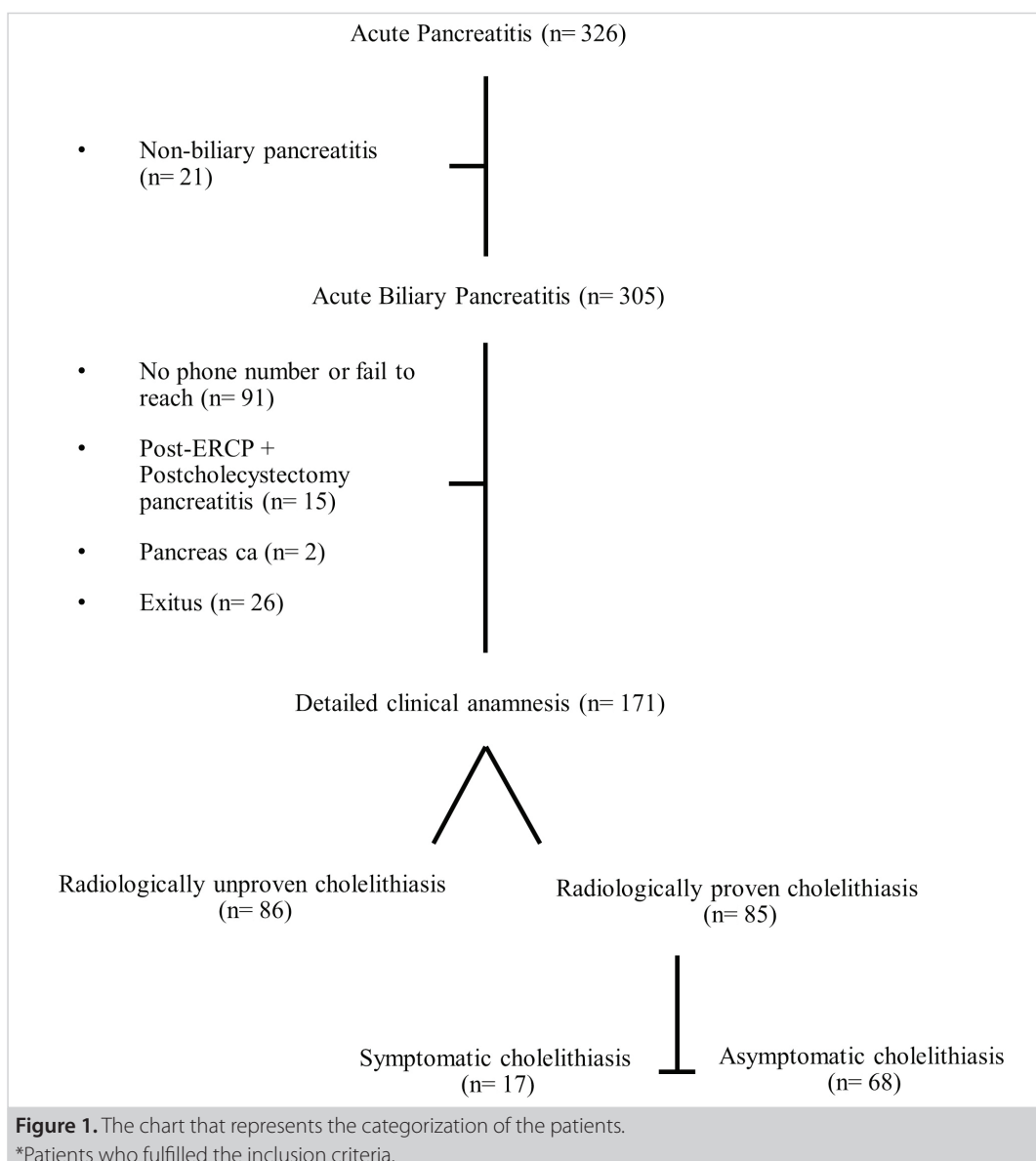
Study Design

Eighty-five eligible cases according to the inclusion criteria out of 326 patients admitted to the outpatient clinic of the surgical emergency unit in İstanbul University Cerrahpaşa Medical Faculty between January 2005-March 2013 and had been diagnosed with acute pancreatitis were included in this retrospective study (Figure 1).

Demographic features, laboratory findings and clinical outcomes of the patients were collected from the patients' files. Medical histories of the patients were detailed by telephone interviews.

Exclusion Criteria

Patients who had been diagnosed with acute pancreatitis due to other causes rather than acute biliary pancreatitis, and whose detailed histories were not accessible from the patient file archive system or who did not respond to phone calls, and patients with no radiologically proven gallstones, deceased patients, patients with performed ERCP, patients who had undergone cholecystectomy and patients with pancreas cancer history were excluded.



Inclusion Criteria

Eighty-five patients with radiologically proven cholelithiasis were included in this study and divided into two groups; Group 1: symptomatic cholelithiasis (n= 17), Group 2: asymptomatic cholelithiasis (n= 68) (Figure 1).

Statistical Analysis

Chi-square test was employed to analyze clinical findings and follow-ups of those two groups using IBM SPSS Statistics 20 for Windows (Illinois, USA).

RESULTS

Acute biliary pancreatitis was the first clinical presentation in 68 patients. Seventeen patients (20%) out of 85 declared to have symptoms of biliary colic prior to acute biliary pancreatitis, but the remaining 68 patients (80%) did not define any biliary symptoms prior to their admission to the emergency unit (Figure 1).

There were 85 patients (45 females, 40 males) with radiologically documented cholelithiasis. Mean age was 55.02 ± 17 years and 50.93 ± 16.70 years for female and male patients, respectively, and there was no significant difference ($p= 0.275$). Mean duration of complaints was four days, and hospitalization duration was eight. Median follow-up time was 34 months. In forty-six patients who had comorbidities, the leading cause was "cardiac complications" (Table 1).

Regarding patients with radiologically proven cholelithiasis, rate of comorbidity was higher in symptomatic cases ($p < 0.05$) (Table 2).

Fourteen patients (16%) were reported to have complicated pancreatitis according to the modified Atlanta classification,

Table 1. Clinical and demographic characteristics of the study population (n= 85)

Clinical and demographic characteristics of the patients	
	Value
Mean age (years) (n= 85)	53
Mean age (female, years) (n= 45, 52%)	55
Mean age (male, years) (n= 40, 48%)	51
Mean duration of hospitalization (days)	8.88
Mean duration of complaints (days)	4
Median value of follow-up time (months)	34
Smoking (number of patients)	15 (17.64%)
List of reported comorbidities* (n= 46)	
	Number of patients
Metabolic diseases	13 (15.29%)
Cardiac diseases	31 (36.47%)
Neurological diseases	3 (3.52%)
Gastrointestinal diseases	8 (9.41%)
Respiratory diseases	5 (5.88%)
Other	6 (7.05%)

*Patients with one or more comorbidities and who were radiologically proven to have gallstones.

and lack or existence of symptoms has no significant effect on the severity of pancreatitis ($p > 0.05$) (Table 3).

Detected gallstones were grouped according to their diameters as follows: <1 cm and ≥ 1 cm. There was no significant correlation between the diameter of the gallstones and the occurrence of complicated pancreatitis ($p > 0.05$) (Table 4).

Table 2. The relationship of comorbidities and symptom status (n= 85)

	Number of patients without comorbidities	Number of patients with comorbidities	p
Symptomatic patients (n= 17, 20%)	3	14	<0.05
Asymptomatic patients (n= 68, 80%)	33	35	

Table 3. Clinical classification of pancreatitis according to symptomatic status of patients before pancreatitis (n= 85)

	Symptomatic patients	Asymptomatic patients	p
Complicated pancreatitis*	5	9	>0.05
Non-complicated pancreatitis*	12	59	

*Clinical classification of pancreatitis according to modified Atlanta classification.

Table 4. Effect of gallstone diameter on clinical classification (n= 85)

	Gallstone diameter <1 cm	Gallstone diameter >1 cm	p
Complicated pancreatitis*	9	5	>0.05
Non-complicated pancreatitis*	49	22	

*According to modified Atlanta classification.

Table 5. Relation between gallstone diameter and symptom status of the patients (n= 85)

	Gallstone diameter <1 cm	Gallstone diameter >1 cm	p
Symptomatic patients	11	6	>0.05
Asymptomatic patients	47	21	

Table 6. Detailed anamnesis findings

	Symptomatic patients (n= 17)	Asymptomatic patients (n= 68)	p
Patients who were diagnosed with cholelithiasis	13 (76%)	7 (10%)	<0.05
How was the patient diagnosed for cholelithiasis?	12 R 1 C	7 In	N/A
Patients who are aware of risks of cholelithiasis	9	None	N/S
Doctor recommendations for the management of cholelithiasis	8 Op	3 Op	N/S
	4 P	1 P	N/S
	1 F	3 F	N/S

C: On checkup, F: Clinical follow-up, In: Incidentally, Op: Operation, P: Leaved to patient's decision, R: Radiological.

Regarding symptomatic status of the patients, no significant difference was observed ($p > 0.05$) between the two groups according to gallstone size: gallstone diameter <1 cm (n= 58), gallstone diameter >1 cm (n= 27) (Table 5).

While detailing the patients' history, we recognized that sixty-one patients from the asymptomatic group and four patients from the symptomatic group were reported to be aware of cholelithiasis just after the diagnosis of pancreatitis. Only nine of them were aware of the clinical risks of cholelithiasis such as cholecystitis and pancreatitis (Table 6).

Recommendations by the physicians, in each group of patients, were as follows: to operate, to follow-up, leaving to patient's decision (Table 6).

DISCUSSION

This study demonstrated that pancreatitis was the first sign to clinically emerge in 68 patients (80%) with silent gallstones and revealed that asymptomatic gallstones play a significant role in ABP and they do not have a milder clinical course.

There is no prospective study in the literature that can offer a definitive therapeutic approach to asymptomatic gallstones. The literature on silent stones argues that clinical follow-up is sufficient (1,4,5,12). This leaves surgeons in a dilemma in terms of treatment approach for gallbladder stones that have never created symptoms. This study showed that the majority of our acute biliary pancreatitis cases were not previously aware that they had gallbladder stones. Innocent gallstones were discussed in studies which also include cost effectiveness data as a secondary goal. All those reality mentioned before have raised the idea that silent gallstones should be clinically re-questioned; to operate or not (13). Knowing the incidence of asymptomatic

cholelithiasis in acute biliary pancreatitis cases can make us reevaluate the decision to follow-up.

The clinical significance of asymptomatic gallstones is controversial. It has been reported that in patients with gallstones, the lifelong likelihood of having symptomatic GSD is 10-25% (12). It is evident that most of the gallbladder stones remain "silent" during early decades of life but they may cause severe symptoms or complications in 40% of the patients older than forty years (14). Once ABP occurs, the management might be challenging, and therefore, it is crucial to elucidate the risk factors that lead to ABP. This difficulty to assess the risk factors which may lead to complicated pancreatitis have led clinicians to search for some predictive values such as gallstone size and functional tests (7-10,15-22). While investigating the importance of silent gallstones in acute pancreatitis, we addressed the clinical progression of the cases together with these predictive values and focused on gallstones in this manner.

Few prospective studies have investigated the natural course of gallstones in the literature (23-25). Festi et al. have reported the results of their eight-year long prospective study on GSD (24). In this study, cholecystectomy rate has been found relatively high in asymptomatic cases (%41.3), thus it was not achievable to monitor potential long-term complications of silent GSD. Moreover, it was not evident how many complications had taken place in asymptomatic patients.

In another study, researchers investigated the patients whose GSD had been initially diagnosed with life-threatening complications or death related to the disease. Out of thirty mortality patients, only 20% had biliary colic pain and other symptoms, while the remaining 80% had no symptoms

associated with cholelithiasis. These surprising results reveal that silent GSD does not mean predictably a mild clinical course (26).

The results of our study showed that concomitant disease rate was higher in symptomatic GSD patients. Or vice versa, one may think that patients with concomitant disease may have higher rate of symptoms in comparison to asymptomatic patients.

In patients with acute biliary pancreatitis, we identified cardiac diseases as the most common comorbidity. Co-occurrence of pancreatitis and cardiac disease suggests cardiac problems in cholelithiasis as a risk factor for biliary pancreatitis. It is necessary to be aware that patients with asymptomatic cholelithiasis accompanying cardiac problems may carry a higher risk for biliary event.

In the literature, asymptomatic patients were previously classified as low-risk (gallstone diameter larger than 3 mm or smaller than 20 mm and no concomitant serious disease) and high-risk groups (gallstone diameter smaller than 3 mm or larger than 20 mm; biliary sludge) (12). In our study, we found that the gallstone size had no effect on the course of pancreatitis.

Moreover, it has been reported that there is no previous biliary colic pain in half of the patients with pancreatitis (27), which does not support the results of some other studies reporting that at least a biliary colic pain bout is expected before the manifestation of biliary complications (2,12).

The results of this study showed that asymptomatic gallstones can emerge with acute pancreatitis, which is one of the most important biliary complications, with a substantially high incidence. It also showed that the size of the gallstone is not important in terms of symptom development, and once pancreatitis occurs, the clinical course is not milder in asymptomatic patients compared to symptomatic ones.

According to detailed anamnesis data, most of the cholelithiasis patients in the symptomatic group had been diagnosed before admission. It was found that about half of them had not been aware of the clinical risks of cholelithiasis. A similar situation revealed that there is no biliary risk information among the cases diagnosed incidentally with cholelithiasis in the asymptomatic group. In both groups, there were uncertainties in doctor's evaluations, where the decisions of follow-up and surgery were left to the patient's own decision. This indicates that in clinical practice surgeons have difficulty in making definitive treatment decisions in cases of cholelithiasis.

CONCLUSION

In conclusion, according to the results obtained in this study, asymptomatic GSD may result in acute pancreatitis with a noteworthy incidence, and severity of pancreatitis in asymptom-

atic patients is similar to symptomatic cases. Also, the size of the gallstone is not a good predictor for the existence of biliary symptoms or to assess the severity of pancreatitis. Asymptomatic cholelithiasis patients have a major percentage in acute biliary pancreatitis cases. The "wait and see" approach for silent gallstones might be supported with prospective studies to build up a structured treatment algorithm.

The main limitation of this retrospective study is the way of data collection. Anamnesis detailing was completed with telephone interviews, which relied on patient's subjective memories about the incident. Retrospective design was chosen to analyze the unbiased approach of the clinicians about silent gallstones and ABP. On the other hand, this limitation provided us to see the if gallstone size really matters and to assess if silent gallstones were as innocent when left without adequate surgical intervention.

Ethics Committee Approval: This study was approved by İstanbul University Cerrahpaşa Faculty of Medicine Deanery Clinical Research Ethics Committee (Decision no: B.30.2.İST.0.30.90.00/29620, Date: 02.10.2013).

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**ORJİNAL ÇALIŞMA-ÖZET**

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Akut pankreatit: Sessiz safra taşlarının ilk bulgusu olabilir

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ÖZET

Giriş ve Amaç: Asemptomatik kolelitiazisin tedavisi tartışmalıdır. Sessiz safra kesesi taşlarının genellikle en az bir biliyer kolik atağından sonra komplikasyonlara neden olduğu varsayılır. Başlangıçta akut pankreatite neden olan veya etiyolojik etken olarak teşhis edilen sessiz taşların oranı literatürde henüz bildirilmemiştir. Çalışmamız akut biliyer pankreatit olgularında asemptomatik kolelitiazis oranını araştırmak için tasarlanmıştır.

Gereç ve Yöntem: Akut biliyer pankreatit tanısıyla takip edilen 305 olgunun 171'i geriye dönük olarak belirlendi. Hastaların demografik özellikleri, laboratuvar bulguları ve klinik ilerlemeleri incelendi. Klinik geçmişler telefon görüşmeleriyle detaylandırıldı. Yüz yetmiş bir vakanın 85'inde safra kesesi taşları radyolojik olarak tespit edildi. Bu hastalar semptomatik ve asemptomatik olarak ayrıldı. Klinik bulgular ve takipler "Ki-kare" testiyle değerlendirildi.

Bulgular: Çalışma grubunda hastaların %80'i asemptomatikti (n= 68) ve hastaların %16,47'sinde (n= 14) komplike pankreatit vardı. Klinik gidişatın şiddetine göre semptomatik olup olmaması anlamlı bir faktör olarak belirlenmedi (p= 0,108). Semptom oluşturma açısından taşın boyutu önemli değildi (p= 0,561) ve pankreatitin klinik şiddeti hakkında herhangi bir öngörü elde edilmedi (p= 0,728).

Sonuç: Asemptomatik kolelitiazis hastaları, akut biliyer pankreatit vakalarında majör bir yüzdeye sahipti. İleriye dönük çalışmalarda sessiz safra taşları için "bekle ve gör" yaklaşımı yeniden değerlendirilmelidir.

Anahtar Kelimeler: Akut biliyer pankreatit, asemptomatik kolelitiazis, sessiz safrataşı

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