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ARTICLE**Evaluation of the effect of pre-surgical transaminase enzyme disorder on early outcomes of laparoscopic cholecystectomy**Saeed Safari<sup>1</sup>, Mahdi Alamrajabi<sup>2</sup>, Jalal Vahedian Ardakani<sup>1</sup>, Masoud Baghaei<sup>1</sup>, Farhad Zamani<sup>3</sup>, Mohammad Hossein Sobhkhizi<sup>1</sup>✉<sup>1</sup> Department General Surgery, Firoozgar Clinical Research Development Center (FCRDC), Iran University of Medical Sciences, Tehran, Iran<sup>2</sup> Colorectal Surgeon/Laparoscopist, Firoozgar Clinical Research Development Center (FCRDC), Iran University of Medical Sciences, Tehran, Iran<sup>3</sup> Department of Gastroenterology and Hepatology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

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**Abstract****Introduction:** Gallbladder removal surgery is performed in two ways: open, or laparoscopic. Compared with open surgery, laparoscopic surgery has a shorter admission period, less cost of treatment, and the patient's faster return to work and daily activities. This study aims to investigate the effect of the disorder of transaminase enzymes before surgery on laparoscopic cholecystectomy outcomes.**Methods:** The present study is a cross-sectional analysis conducted during the period of 2015-2016 on all patients with a diagnosis of acute cholecystitis admitted to the surgical ward of Firoozgar Hospital in Tehran. These patients, based on the level of disorder of the alanine aminotransferase (ALT) and aspartate aminotransferase (AST) enzymes, were divided into two groups: enzymatic disorder less than 2 times normal and normal, and enzymatic disorder higher than 2 times normal up to a maximum of 10 times normal. Data were collected by the researcher using a checklist containing the variables under study and analyzed in SPSS-22.**Results:** The results of the study showed that of 89 patients with acute cholecystitis, 59.6% were female and the rest were male. The mean and standard deviation of the age of the patients was  $48.6 \pm 18.71$ . The analytical results showed that there was no significant relationship between elevated liver enzymes SAT and ALT and variables such as incidence of hemorrhage during surgery, change of surgical method (laparoscopic to open), surgical difficulty report by the surgeon, changes in anesthesia after surgery, and duration of hospitalization ( $P > 0.05$ ).**Conclusions:** The results of this study showed that laparoscopy is possible for acute cholecystitis, even with the presence of elevated liver enzymes, and it depends largely on the experience of the surgeon and the anatomy of biliary duct.**Key Words:** Laparoscopic; Collosectomy; Cross-sectional Study; ALT; AST; Iran**Introduction**

Gallstone is one of the most common digestive

diseases in the world with different kinds of the outbreak in different parts of the world. The incidence of this disease in the adult population of

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the western societies is about 10-15% (1). In the United States, about 12 percent (30 million) of the people suffer from gallbladder stones, and about 700,000 cases of cholecystectomy occur annually (2). The disease can be symptomatic or asymptomatic. Symptoms appear in a relatively specific way, such as alternate pains in the upper abdominal region or in a non-specific manner such as nausea and vomiting (3).

Gallbladder removal surgery is the only treatment for a gallstone, and until 1986 this procedure was performed solely by surgery and by splitting the abdominal wall: they removed the gallbladder and there were no complications of the stone being remained in the body. However, there were some complications and discomforts caused by the open surgical removal of the gallbladder, which was due to damage to the abdominal wall. In order to reduce these complications, in 1987 for the first time Philip Moore carried out this surgery by laparoscopy with video optics technology, which, due to its popularity, quickly became popular, so that today, except in limited cases, there is no need to open the abdomen anymore. This method can also be used for acute cases of gallbladder inflammation and even for patients with a hernia, abdominal ascites, and pregnancy (4, 5). This surgery, in comparison with open surgery, has a shorter hospitalization time, less cost of treatment, and faster return to work and daily activities (6). Although the complications and problems of using anesthetic in this operation is not significantly different with that of the open surgery of gallbladder removal, and although increased loss and bile duct stenosis are still the complications of its performing, almost all doctors believe that laparoscopic surgery is the preferred method for patients with symptomatic gallbladder stone (7, 8).

There is still controversy about the use of laparoscopic cholecystectomy in the treatment of acute cholecystitis. It is imagined that in these cases, compared to chronic cholecystitis, the rate of the conversion of laparoscopic surgery to open surgery is 10 to 15% higher (9-11). Laparoscopic cholecystectomy has been used successfully in treating acute cholecystitis as the first surgical procedure in most of these patients; this is related to increased experience and development of available devices (12). Today, laparoscopic cholecystectomy surgery has become a standard treatment for symptomatic gallbladder stone. For patients with acute cholecystitis, surgery is not only recommended during the first 72 hours of the onset of symptoms, but it seems to be completely

safe and comfortable, but if the patient reaches the surgeon later or if for any reason, the surgery is not possible in the first 72 hours, it is recommended that surgery be delayed for 6 weeks due to adhesion and severe inflammation of surgical position (13).

Various risk factors have been proposed for the difficulty and malpractice of laparoscopic cholecystectomy surgery and its occasional conversion to open surgery. There is consensus on some of these factors- such as male gender and operation time-but, it is still not possible to conclusively comment on many other factors. One of these risk factors is the high level of liver enzymes (transaminases) which, based on traditional medical teachings, prevent the surgery from being performed (fear of exacerbation of liver failure due to mediators released during surgery or due to pneumoperitoneum during a laparoscopy). This can cause a patient who has been prematurely put under surgery to be deprived of surgery at the right time merely because of the high level of these enzymes, and as a result he has to nominate for delayed surgery. Therefore, considering the above description, the aim of this study is to investigate the effect of preoperative transaminase enzyme disorder on the outcomes of laparoscopic cholecystectomy.

## Methods

The present study is a cross-sectional analysis performed on all patients with a diagnosis of acute cholecystitis (with sonographic, clinical and laboratory signs of acute cholecystitis, without a history of biliary or recent or old ERSP) referred to the surgical ward of Firoozgar Hospital in Tehran. These patients were divided into two groups based on the degree of disorder of the alanine aminotransferase (ALT) and aspartate aminotransferase (AST) enzymes: the first group included patients with enzymatic disorder up to less than 2 times normal and normal, and the second group included patients with an enzymatic disorder higher than 2 times normal to maximum 10 times normal. Then, laparoscopic cholecystectomy was performed early (under 72 hours) for these patients. All the surgeries were performed by two full-time surgeons in the hospital, and the data before and after the surgery were collected by the researcher. The inclusion criteria for the study were a patient with acute cholecystitis before 72 hours; and the exclusion criteria included patients with acute cholecystitis for more than 4 days, any history of (chronic or acute) disease, preoperative interventions such as

ERCP, or any history of liver or biliary disease. The data collection tool was a questionnaire including demographic characteristics and variables related to the difficulty of surgery including the amount of intraoperative bleeding, duration of operation, conversion of surgery to open surgery, duration of hospitalization in the surgical ward (as the operative morbidity) as well as other related complications (exacerbation of enzyme disorders and the occurrence of liver failure, etc.). The data were entered in SPSS-22 and then analyzed descriptively.

## Results

In this study, of 280 patients with gallstones who were candidates for cholecystectomy, 89 patients with acute cholecystitis and elevated liver enzymes (ALT and AST) were entered into the study. Table 1 shows the demographic and descriptive characteristics of the subjects. As shown, of 89 patients with acute cholecystitis and elevated ALT and AST liver enzymes, 59.6% (54 cases) were female and the rest were male. The mean and standard deviation of the age of the patients was  $48.6 \pm 18.71$  and the minimum and maximum ages were 20 and 87 respectively. 68.5% and 74.2% of the patients had elevated ALT and AST enzymes, respectively, from 2 to 10 times the normal range. The duration of the symptoms, in 69.7% of the patients was less than 3 days, and 22.5% of the patients underwent surgical procedure change (from laparoscopic to open). About 10.1% of the patients experienced intraoperative bleeding, and time of hospitalization for 6.7% of the patients was longer than 3 days. Also, 43.8% of the surgical difficulty was reported by the surgeon (the severity of the operation has been assessed based on adhesion, hemorrhage during surgery and duration of surgery). Concerning postoperative enzymatic changes, only 25 patients were referred for evaluation of enzymatic changes, among whom, 16 cases had decreased liver enzymes, 4 had elevated liver enzymes, and 5 patients were in the normal range (Table 1).

In this study, Chi-square test was used in order to examine the relationship between ALT elevation and other variables such as incidence of hemorrhage during surgery, surgical procedure change (laparoscopic to open), report of surgical difficulty by the surgeon, post-surgical enzyme changes, and duration of hospitalization. But no significant correlation was observed between any of the studied variables and ALT elevation

( $P > 0.05$ ). Table 2 shows the details of this statistical test in terms of the aforementioned variables.

Also, Chi-square test was used to examine the relationship between AST elevation and other variables such as incidence of hemorrhage during surgery, surgical procedure change (laparoscopic to open), report of surgical difficulty by the surgeon, post-surgical enzyme changes, and duration of hospitalization. But there was no significant correlation between any of the studied variables and AST elevation ( $P > 0.05$ ). Table 3 shows the details of this statistical test in terms of the aforementioned variables.

**Table 1. Demographic and descriptive characteristics of the studied patients**

Variable	Number	%
Sex:		
Man	36	40.4
Female	53	59.6
ALT enzyme:		
Up to 2 times normal	28	31.5
2-10 times the normal limit	61	68.5
AST enzyme:		
Up to 2 times normal	23	25.8
2-10 times the normal limit	66	74.2
Duration of symptoms:		
Less than 3 days	62	69.7
More than 3 days	27	30.3
Changing surgical method (Laparoscopic to open):		
Yes	20	22.5
No	69	77.5
Bleeding during surgery:		
Yes	9	10.1
No	80	89.1
Duration of hospitalization:		
Less than 3 days	83	93.3
More than 3 days	6	6.7
Surgical difficulty report:		
Yes	39	43.8
No	50	56.2
Enzymatic changes after surgery:		
Decreased	16	18
normal	5	5.6
Increased	3	3.4
Unchecked	65	73

**Table 2: Relationship between ALT elevation and the studied variables (Chi-squared test)**

liver enzyme ALT	2-10 times normal N(%)	2 times normal N(%)	P- value (significance level)
Incidence of bleeding during surgery:			
Yes	6 (9.8)	3 (10.7)	0.584
No	55(90.2)	25 (89.3)	
Changing surgical method (Laparoscopic to open):			
Yes	12 (19.7)	8 (28.6)	0.251
No	49 (80.3)	20 (71.4)	
Surgical difficulty report by the surgeon:			
Yes	30 (49.9)	31 (50.8)	0.101
No	9 (32.1)	19 (69.9)	
Enzymatic changes after surgery:			
Decreased	14 (23)	2 (7.1)	0.098
normal	2 (3.3)	3 (10.7)	
Increased	1 (1.6)	2 (7.1)	
Unchecked	44 (72.1)	21 (75)	
Duration of hospitalization:			
Less than 3 days	56 (91.8)	27 (96.4)	0.382
More than 3 days	5 (8.2)	1 (3.6)	

**Table 2: Relationship between AST elevation and the studied variables (Chi-squared test)**

liver enzyme AST	2-10 times normal N(%)	2 times normal N(%)	P- value (significance level)
Incidence of bleeding during surgery:			
Yes	7 (10.6)	2 (8.70)	0.576
No	59 (89.4)	21 (51.9)	
Changing surgical method (Laparoscopic to open):			
Yes	14 (21.2)	6 (26.1)	0.414
No	52 (78.8)	17 (73.9)	
Surgical difficulty report by the surgeon:			
Yes	31 (47)	8 (34.8)	0.221
No	35 (53)	15 (65.2)	
Enzymatic changes after surgery:			
Decreased	14 (21.2)	2 (8.7)	0.066
normal	2 (3)	3 (13)	
Increased	1 (1.5)	2 (8.7)	
Unchecked	49 (74.2)	16 (69.6)	
Duration of hospitalization:			
Less than 3 days	60 (90.9)	22 (95.6)	0.156
More than 3 days	6 (9.1)	1 (4.4)	

## Discussion

The present study is a cross-sectional study that was performed during 2015-16 on all patients with a diagnosis of acute cholecystitis who were admitted to the surgical ward of Firoozgar Hospital in Tehran. It was designed and performed in order to evaluate the effect of preoperative transaminase enzymes disorder on laparoscopic cholecystectomy

outcomes. The results of this study showed that during this period, 89 patients with acute cholecystitis were hospitalized, of whom 59.6% (54 cases) were female and the rest were male. The mean and standard deviation of the age of the patients was  $48.6 \pm 18.71$  and the minimum and maximum ages were 20 and 87, respectively. The analytical results of the study showed that there was no statistically significant relationship

between the increase in liver enzymes (SAT and ALT) and the variables such as incidence of hemorrhage during surgery, surgical procedure change (laparoscopic to open), surgical difficulty report by the surgeon, changes in enzymes after surgery, and duration of hospitalization ( $P>0.05$ ).

The research that has been performed specifically in line with our objectives are not adequate, but in general, the results of our study are consistent with some similar studies in this field. The results of a study by Ahmad NZ et al (2011) -which aimed at the necessity of checking the LFT enzymes routinely before and after laparoscopic cholecystectomy because of surgeons concerns and fears of increased ALT and AST enzymes and their possible effect on liver failure due to pneumoperitoneum- indicated that there was no need to provide these tests because AST changes had no effect on the patient's outcomes of laparoscopic cholecystectomy (14). In another study by Robinson et al which was performed with the aim of examining the importance of preoperative laboratory tests on 387 patients, the findings showed that the necessary pre-operative inspections including history, examination, and ultrasonography were important but routine laboratory tests including liver enzymes were not that significant (15). A study by Halevy et al have also concluded that accurate evaluation of liver enzymes is not necessary for laparoscopic surgery, and changes in liver tests up to 70% do not even have adverse effects. Also, this study showed that in the majority of patients, there happened a significant increase in the levels of ALT and AST liver enzymes after laparoscopic cholecystectomy surgery, compared to the time before the surgery, but it returned to the normal limit after 72 hours (16).

However, our results were not consistent with some other studies; for example, in a study by Lim Kr et al which aimed at determining the factors affecting the conversion of laparoscopic surgery to open surgery in patients with acute coloxystrectomy, patient's age, total number of white blood cells, Billy Rubin Total and Akalen Phosphatase were identified as the most important independent variables affecting the conversion of laparoscopic surgery to open one (17). The study by Oymaci et al., which was conducted on 414 patients with laparoscopic cholecystectomy, showed that a total of 8% of the surgeries (33 cases) underwent conversion to open surgery. Also, in this study, increased age, associated illness, elevated liver enzymes and elevated alkaline phosphatase were mentioned as common factors

affecting the conversion of the surgery to open surgery, so that 23 out of 33 patients whose surgery had been converted to open surgery had elevated ALT and AST liver enzymes (18). The study by Vijay Kassa et al., aimed at evaluating the risk factors of surgical difficulty of laparoscopic cholecystectomy on 60 patients with cholecystectomy symptoms, showed that the rate of conversion of laparoscopic surgery to open was 3/3%, and variables such as age, male gender, fever during attack, thickness of the gallbladder wall, number of leukocytes, and increased liver enzymes were identified as the most important factors influencing the change of laparoscopic surgery to open (19).

As can be seen, some studies have emphasized the necessity of checking liver enzymes especially ALT and AST before determining the type of surgery, whether it is laparoscopic or open; some other studies, by contrast, has concluded that the precise evaluation of them is not necessary. Due to this issue and considering the fact that the present study is a cross-sectional analysis and its sample size is not large enough, the researchers, therefore, propose conducting randomized clinical trials with sufficient sample size so as to further clarify the issue. Another important limitation that should be mentioned is the lack of complete referral of patients for postoperative liver enzyme testing, which could affect the outcome of the study.

## Conclusions

The results of the study indicated that even in the case of simultaneous incidence of acute cholecystitis with elevated liver enzymes, it is possible to perform most cases of cholecystectomy by laparoscopic methods and that it is highly dependent on the experience of the surgeon and anatomy of biliary ducts. Therefore, this study suggests that performing cholecystectomy by a laparoscopic method in the condition of acute cholecystitis is feasible-if the surgeon agrees by providing the patient with sufficient information about the surgical procedure change- even with the presence of increased liver enzymes.

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**Conflict of interests:** None

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