Prevalence and Determinants of Persistent Dyspeptic Symptoms after Elective Laparoscopic Cholecystectomy

Adil Rahman Faraj Al-Budaerany* FICMS, **Muatez Mundhir Manhal*** FIBMS,
Jaber Qataa Jaber Al-Mohammedawi* FICMS

ABSTRACT

Background: Gallbladder diseases can give rise to dyspeptic or colonic symptoms. With the introduction of laparoscopic cholecystectomy, one could expect a decrease of the prevalence of post-cholecystectomy symptoms owing to advantages of minimally invasive techniques causing fewer adhesions and scar related problems

Objectives: To evaluate the fate of dyspeptic symptoms after laparoscopic cholecystectomy and to identify the factors associated with persistent dyspepsia.

Methods: A randomized prospective study that was conducted in the surgical unit, department of surgery, Al-Khidhir Hospital in Al-Muthanna province during a period of 18 months from Jan 2017 to July 2018. It included all patients visiting the outpatient clinic and emergency unit due to dyspeptic symptoms, then the assessment was done by different surgeons in the same surgical team in the hospital, and laparoscopic cholecystectomy scheduled for them. Patients who converted to open surgery or those who were unable to cooperate in answering the questionnaires post-operatively were excluded from the study. The total number of included patients was 100. Postoperative Reevaluation of the patients for the presence of dyspeptic symptoms was done in the outpatient clinic for three to four months.

Results: Preoperative symptoms were persisted postoperatively in 23% of study patients, most of these symptoms were dyspeptic symptoms (82.6%). Persistent symptoms were significantly associated with high body mass index level, smoking, and alcohol drinking (34.3%, P= 0.011 in obese; 52.2%, P= 0.001 in smokers; and 50%, P= 0.019 in alcohol drinkers).

Conclusion: Approximately three quarters of patients who underwent gallbladder surgery showed improvement in their abdominal symptoms irrespective of the cause. A modifiable associated factors for persistent symptoms were obesity, smoking, and alcohol drinking.

Keywords: Dyspepsia, cholecystectomy, laparoscopic, persistent, Iraq.

Iraqi Medical Journal Vol. 65, No. 2, July 2019; p.129-136.

Gall stone disease is a common disease affecting human beings[1]. In addition to abdominal pain, gallbladder stimulation by gallstones can give rise to gastrointestinal (GI) symptoms such as indigestion, nausea, vomiting and food intolerance[2]. Laparoscopic cholecystectomy (LC) has become the gold standard for treatment of symptomatic gallstones, due to lower morbidity, shorter hospital stays and earlier return work[3]. In almost all patients with gallstones, biliary pain disappears after cholecystectomy. However, the rates of relief from nonspecific GI symptoms tend to be low and heterogeneous in patients who undergo an elective cholecystectomy[4].

*Dept. of Surgery, Al-Khidhir Hospital in Al-Muthanna province, Iraq.
E-mail: dr_4mdl@yahoo.com

Research achieved in 1948 gave the first impression of dyspepsia, particularly flatulent dyspepsia, as considered as one of the manifestations of gallstone disease and advocated cholecystectomy for the same[5]. Dyspepsia defined as a collection of symptoms referable to the upper gastrointestinal tract, namely, epigastric discomfort or pain, postprandial heaviness; and early satiety. Associated complaints include: nausea, belching, bloating, and epigastric burn (heartburn)[6]. Post-cholecystectomy causes may be divided into four categories: first, common bile duct stones may have been overlooked. Second, other GI conditions such as gastroesophageal reflux, peptic ulcer

disease and functional dysmotility disorders may have coexisted and their symptoms erroneously attributed to gallstones. Third, loss of reservoir function of the gall bladder has been shown to result in a number of adverse changes: impairment of the antro-pyloric motor unit, increased duodenogastric reflux, increased gastroesophageal reflux[7] and a reduced bile salt pool which may result in subclinical fat malabsorption and diarrhea. Finally, the abdominal wound may result in pain from nerve damage or the development of an incisional hernia[8].

Persistent symptoms after cholecystectomy occur in up to 40% of patients. Although most of these complaints of mild and transient symptoms, severe pain persists as a long-term complaint in up to 10%. With the introduction of LC, one could expect a decrease of the prevalence of post-cholecystectomy symptoms owing to advantages of minimally invasive techniques causing fewer adhesions and scar related problems[9]. However, many studies have found that changes in abdominal symptoms after LC may differ according to the selection of patients and their preoperative conditions. Multiple factors were reported as predictors of poor outcomes in many different studies. The presence of GI diseases including irritable bowel syndrome or bloating, rather than the original gallbladder disease, was also related to the persistence of symptoms after cholecystectomy[10].

Patients had medication for psychiatric conditions, psychological disease, personality disorders and neuroticism showed poor outcomes[11]. Patients with poor outcomes after cholecystectomy also showed decreased compliance, which complicates the effectiveness of treatment[12]. Initial laboratory studies in the workup for post-cholecystectomy symptoms usually include, U/S of the abdomen to evaluate the liver, biliary tract, pancreas and surrounding areas[13]. Some individuals may benefit from diet modification, such as a reduced fat diet, following cholecystectomy. In the absence of gallbladder, bile enters the intestine constantly, but in small quantities. Thus, it may be insufficient for digestion of fatty foods. The patient is recommended dietary restriction table with fatty foods, enzyme preparations, antispasmodics, sometimes cholagogue[14]. The aim of this study was to evaluate the fate of dyspeptic symptoms after laparoscopic cholecystectomy and to identify the factors associated with persistent dyspepsia.

Methods

This is a randomized prospective study that was conducted in the surgical unit, department of surgery, Al-Khidhir Hospital in Al-Muthanna province during a period of 18 months from January 2017 to July 2018 (The first 14 months for collection of sample and the last four months for postoperative evaluation of patients).

The study population included all patients visiting the outpatient clinic and emergency unit due to dyspeptic symptoms, then the assessment was done by different surgeons in the same surgical team in the hospital, and LC scheduled for them. All patients were placed on an elective operation after assessment by the surgical team, and the diagnosis of cholelithiasis was confirmed by ultrasonography in all cases. Patients who converted to open surgery or those who were unable to cooperate in answering the questionnaires post-operatively were excluded from the study. Twelve patients were excluded (three patients due to conversion to open surgery and nine were unable to cooperate) patients excluded, the total number of included patients was 100. Preoperative information was collected by a questionnaire including patient demographics (Age and gender of the patient, Body Mass Index, and social habits as smoking and alcohol drinking), characteristics of pain (site, duration, frequency, quality, periodicity, precipitating and relieving factors), other dyspeptic symptoms (nausea, vomiting, heartburn, food intolerance, and early satiety), and colonic symptoms (bloating, constipation,

diarrhea). Investigation was done preoperatively as CBC, LFT, S. Amylase and U/S. Patients with a history of cholestatic jaundice secondary to gall stones disease, abnormal liver function tests, or dilated CBD, were scheduled preoperatively for endoscopic retrograde cholangiopancreatography (ERCP) and sphincterotomy before planning for L.C.

A standard technique for LC was practiced; nasogastric tube was not used routinely but occasionally. Following general anesthesia and positioning of the patient and draping, insufflation was achieved through a Veress needle. CO_2 was used as the insufflation gas. A 30 degrees' camera used through 10 mm port. Standard procedure was done through four ports technique with sharp and blunt dissection with/without electrocautery. Perioperative cholangiography was not available. Postoperative Reevaluation of the patients for the presence of dyspeptic symptoms was done in the outpatient clinic for three to four months and by certain investigations (Urea breath test, MRCP & ERCP, and OGD) were added to clarify the reason behind continuation of dyspeptic symptoms.

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Pearson's Chi–square test was used to assess statistical association between persistent post-operative dyspeptic symptoms and different variables. A level of P – value less than 0.05 was considered significant.

Results

The study involved 100 patients who had symptomatic gallstone disease and scheduled or and treated with L.C. The mean age of the patients was 41.7 ± 6.9 years; 73% were females and 43% were overweighed. More than three quarters (77%) were nonsmokers and 92% were not drinkers, (Table 1).

Figure 1 shows the distribution of study patients by diagnosis. The majority of study patients were diagnosed as chronic cholecystitis.

Characteristics of preoperative pain of study patients is shown in table 2. We noticed that the most common site of pain was right upper quadrant (72%) and 62% of patients complained from radiated pain in the right shoulder. Heavy fatty meal was the most common precipitating factor of pain (44%) and the pain was relieved in more than half of patients (62%) by fasting.

Table 3 shows the distribution of study patients by presence of pre and postoperative symptoms. We noticed that the most common presenting symptoms preoperatively were nausea (86%) then food intolerance (79%). Preoperative symptoms were relieved postoperatively in 77% of study patients, and most of the persisting symptoms were dyspeptic symptoms (82.6%) and the main cause was GERD (63.2%).

Postoperative pain was persisted in 13% of patients, more than half of them was in the epigastric region (53.8%), (Table 4).

We noticed that the prevalence of persistent dyspeptic symptoms was significantly increasing (P=0.011) as the BMI level increased and the highest prevalence was seen in obese patients (34.3%). Regarding smoking, 52.2% of smokers were complaining from postoperative persistent dyspeptic symptoms with a significant association between smoking and persistent dyspeptic symptoms (P=0.001). Prevalence of persistent dyspeptic symptoms was significantly higher in alcohol drinkers than that in non-drinkers (50% versus 16.3%, P=0.019). No significant association (P≥ 0.05) between persistent dyspeptic symptoms and both of age and gender. (Table 5).

No significant association (P= 0.272) between persistent dyspeptic symptoms and preoperative diagnosis. (Table 6).

Table 1: Distribution of study patients by demographic data.

Demographic Data	No. (n=100)	Percentage (%)
Age (Years)		
< 30	21	21.0
30 - 49	68	68.0
≥ 50	11	11.0
Gender		
Male	27	27.0
Female	73	73.0
BMI level		
Normal	22	22.0
Overweight	43	43.0
Obese	35	35.0
Smoking		
Yes	23	23.0
No	77	77.0
Alcohol Drinking		
Yes	8	8.0
No	92	92.0

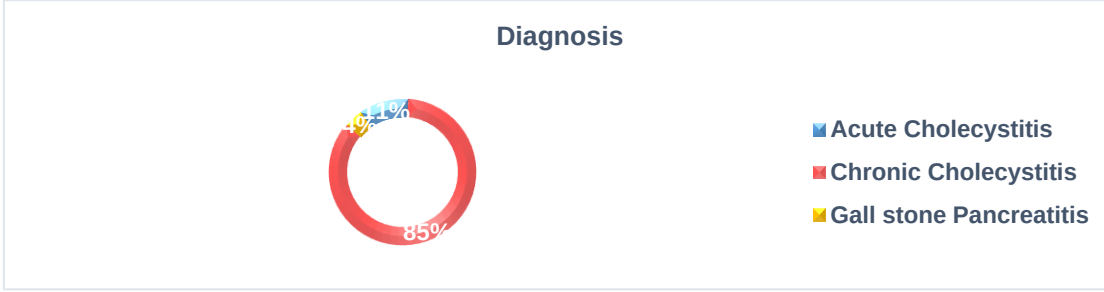

Figure 1: Distribution of study patients by diagnosis

Table 2: Distribution of study patients by characteristics of preoperative pain.

Characteristics of preoperative pain	No. (n=100)	Percentage (%)
Site		
Right upper quadrant	72	72.0
Epigastric	17	17.0
Lower abdomen	11	11.0
Radiation		
No Radiation	7	7.0
Right Shoulder	62	62.0
Back	13	13.0
Mixed	18	18.0
Precipitating Factor		
Stress	21	21.0
Heavy Fatty meal	44	44.0
Hunger	16	16.0
Medications	19	19.0
Relieving Factors *		
Analgesia	31	21.0
Fasting	62	53.0
Acid lowering agents	36	26.0

* Some of patients were relieved their pain by more than one way

Table 3: Distribution of study patients by presence of pre and postoperative symptoms.

Variable	No. (n= 100)	Percentage (%)
Preoperative Symptoms		
Nausea	86	86.0
Food intolerance	79	79.0
Vomiting	54	54.0
Early satiety	31	31.0
Heart burn	27	27.0
Bloating	11	11.0
Constipation	7	7.0
Diarrhea	3	3.0
Jaundice	8	8.0
Persistence postoperative symptom		
Not present (Asymptomatic)	77	77.0
Dyspeptic symptoms	19	19.0
Colonic symptoms	3	3.0
Jaundice	1	1.0
Causes of persistent postoperative dyspeptic symptoms	**n= 19**	
GERD	12	63.2
IBS	4	21.1
Duodenal Ulcer	2	10.5
CBD stone	1	5.3

Table 4: Distribution of study patients by site of persistence postoperative pain.

Persistence postoperative pain site	No. (n=13)	Percentage (%)
Epigastric	7	53.8
Right upper quadrant	4	30.8
Lower abdomen	2	15.4

Table 5: Association between persistence dyspeptic symptoms and general characteristics

Variable	Postoperative Dyspeptic Symptoms		Total (%) n= 100	P - value
	Persist (%) n= 19	Relieved (%) n= 81		
Age (Years)				
< 30	3 (14.3)	18 (85.7)	21 (21.0)	**0.81**
30 - 49	14 (20.6)	54 (79.4)	68 (68.0)	
≥ 50	2 (18.2)	9 (81.8)	11 (11.0)	
Gender				
Male	6 (22.2)	21 (77.8)	27 (27.0)	**0.617**
Female	13 (17.8)	60 (82.2)	73 (73.0)	
BMI Level				
Normal	1 (4.5)	21 (95.5)	22 (22.0)	**0.011**
Overweight	6 (14.0)	37 (86.0)	43 (43.0)	
Obese	12 (34.3)	23 (65.7)	35 (35.0)	
Smoking				
Smokers	12 (52.2)	11 (47.8)	23 (23.0)	**0.001**
Non-smokers	7 (9.1)	70 (90.9)	77 (77.0)	
Alcohol Drinking				
Yes	4 (50.0)	4 (50.0)	8 (8.0)	**0.019**
No	15 (16.3)	77 (83.7)	92 (92.0)	

Table 6: Association between persistence dyspeptic symptoms and pre-operative diagnosis

Pre-operative Diagnosis	Postoperative Symptoms		Total (%) n=100	P- value
	Persist (%) n= 19	Relieved (%) n= 81		
Chronic Cholecystitis	14 (16.5)	71 (83.5)	85 (85.0)	**0.272**
Acute Cholecystitis	4 (36.4)	7 (63.6)	11 (11.0)	
Gall stone Pancreatitis	1 (25.0)	3 (75.0)	4 (4.0)	

——————————Discussion

Dyspepsia is pain or discomfort centered in the upper abdomen. It is prevalent in 40 - 60% of the general population [15]. Studies suggest that patients with gallstones who had dyspeptic symptoms without biliary colic are less likely to improve following cholecystectomy. Nearly, 70% of these patients will still benefit from surgery. This suggests that some of the dyspeptic symptoms may be caused by gallstones [16]. Other studies have shown that biliary pain is relieved in greater than 95% of patients after LC in one year of follow-up [17]. In the current study, 100 patients with symptomatic gallstone treated with L.C were involved, 19 (19%) of them showed persistent dyspeptic symptoms postoperatively which was lower than that shown by a study in USA (2004), as noticed that pain and dyspeptic symptoms were persisting in (25% and 43%) of patients respectively [18], also lower than a study in USA (2011) when reported that 41% of patients complained from the persistent dyspeptic symptoms [19]. The reason may be that majority of our patients (85%) had chronic cholecystitis and severe pathologic changes are usually related with a high rate of symptom relief.

The mean age was 41.7 ± 6.9 years; female's predominance observed (73%), and 43% of them were overweighed. Seventy-seven percent were nonsmokers and 92% were not drinkers, similar to an Egyptian study (2018), in which the mean age was 41.85 ± 5.22 years with female predominance observed (75.9%) [20]. Another similar results found in studies conducted in India (2012) [21] and (2013) [22] when showed that the mean age of presentation was 40.6 years. The current study was similar to many other studies, in which the disease showed higher prevalence among females as compared to males, as observed in two studies conducted in USA (2013) [23] and the other in (2011) [19] and its attributed to the role of female sex hormones. The relation between estrogen receptors and cholesterol synthesis has been studied in many studies [24]. In the present study, chronic cholecystitis was the most obvious diagnosis (85%). Differently, Indian researchers (2016) found that acute cholecystitis was the main diagnosis than chronic cholecystitis (22.2% and 7.41%) respectively [22].

This study showed that postoperative pain was persisted in 13% of patients, 53.8% of them was in the epigastric region, differed from that done in 2009 in Netherlands as show right upper quadrant pain was the major site (66.5%) and most of them had dyspeptic symptoms and about (37.8%) respond to analgesia [25]. Furthermore, dyspeptic symptoms in this study were the commonest presentation (82.6%), GERD had the highest postoperative percentage (63.2%). In line to that in India (2009), in which noticed that persistence of symptoms ranged from not at all for belching to a maximum of 16.7% for epigastric pain [22], this was in consistent to a Korean study in 2014, when 18.5% of patients showed exacerbated symptoms at six months after surgery [11], but slightly higher than that in China (2017), in which 10% of the patients complained upper abdominal pain after cholecystectomy [26]. In comparison to study in Netherlands (2009), different results observed as they

found persistence of dyspeptic symptoms was in 10-40% of patients, which could be due to the shorter follow-up period [25]. The divergent results could also be due to the lack of an objective assessment by the use of dyspepsia scores, to the sample size in each study, functional post-cholecystectomy syndrome which might develop, duration of preoperative symptoms and administration of choleric medication.

In the current study, persistent dyspeptic symptoms were significantly increasing as the BMI level increase (P= 0.011). More than half of the smokers (52.2%) had postoperative persistent dyspeptic symptoms which were significantly related to persistent dyspeptic symptoms (P= 0.001). Persistent dyspeptic symptoms were significantly higher in alcohol drinkers (50%, P=0.019). In contrary, a study done in Korea 2017 by comparing symptomatic and asymptomatic patients post-operatively, there were no significant differences in BMI, smoking and drinking alcohol (P > 0.05) [27].

No significant association (P ≥ 0.05) between persistent dyspeptic symptoms and age, gender and preoperative diagnosis (P > 0.05) in accordance to a study conducted in Korea (2014), where no correlation observed between symptoms and gender, age and previous diagnosis [11] and also agreed to an Italian one conducted in 2003, in which improved and unimproved patients in regard to the dyspeptic symptoms did not significantly differ in terms of sex and age [28]. Although controversy remains whether cholecystectomy should be performed in gallstone patients with dyspeptic or colonic symptoms, many reports show that atypical symptoms are improved after cholecystectomy in gallstone patients, suggesting the need to offer cholecystectomy to these patients [16]. Considering that these studies found chronic cholecystitis in 95% of cases after cholecystectomy, atypical abdominal symptoms are likely to occur as a result of chronic inflammation. In conclusion, approximately three quarters of patients who underwent gallbladder surgery showed improvement in their abdominal symptoms irrespective of the cause. A modifiable associated factors for persistent symptoms were obesity, smoking, and alcohol drinking.

References

1. Bittner R. Laparoscopic Surgery: 15 Years after Clinical Introduction. World J Surg. 2006; 30:1190-1203.
2. Finan KR, Leeth RR, Whitley BM, Klapow JC, Hawn MT. Improvement in gastrointestinal symptoms and quality of life after cholecystectomy. Am J Surg. 2006; 192:196–202.
3. Keus F, De Jong JA, Gooszen HG, Van Laarhoven CJ. Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis. Cochrane Database Syst Rev 2006; 4: CD006231.
4. Bitzer EM, Lorenz C, Nickel S, Dörning H, Trojan A. Assessing patient-reported outcomes of cholecystectomy in short-stay surgery. Surg Endosc. 2008; 22:2712–2719.
5. Comfort MW, Gray HK, Wilson JM. The Silent Gallstone: A Ten to Twenty Year Follow-up Study of 112 Cases. Ann Surg. 1948;128(5):931-7.
6. Mearin F, Calleja JL. Defining functional dyspepsia. Rev EspEnferm Dig. 2011;103(12):640-7.
7. Jazrawi S, Walsh TN, Byrne PJ, Hill AD, Li H, Lawlor P, et al. Cholecystectomy and oesophageal reflux: a prospective evaluation. British journal of surgery. 1993 Jan;80(1):50-3.
8. Bansal S, Jain S, Daga RN, Vyas KC. Prevalence of Post-Cholecystectomy Symptoms: Long Term Outcome after Open versus Laparoscopic Cholecystectomy. World Journal of Surgical Research. 2014 Mar 17;3(2).
9. Post-cholecystectomy syndrome. WebMD. Archived from the original on 2007-07-02. Retrieved 2009-03-07. http://www.webmd.com/hw-popup/Postcholecystectomy-syndrome
10. Svebak S, Søndenaa K, Hausken T, Søreide O, Hammar A, Berstad A. The significance of personality in pain from gallbladder stones. Scand J Gastroenterol. 2000; 35:759–764.
11. Kim GH, Lee HD, Kim M, Kim K, Jeong Y, Hong YJ, et al. Fate of dyspeptic or colonic symptoms after laparoscopic cholecystectomy. Journal of neurogastroenterology and motility. 2014 Apr;20(2):253.
12. Kirk G, Kennedy R, McKie L, Diamond T, Clements B. Preoperative symptoms of irritable bowel syndrome predict poor outcome after laparoscopic cholecystectomy. Surg Endosc. 2011; 25:3379–3384.

13. Filip M, Saftoiu A, Popescu C, Gheonea DI, Iordache S, Sandulescu L, et al. Post-cholecystectomy syndrome-an algorithmic approach. J Gastrointestin Liver Dis. 2009 Mar 1;18(1):67-71.
14. Danley T, St Anna. "Clinical inquiry. Postcholecystectomy diarrhea: what relieves it?". The Journal of Family Practice L (2011). 60 (10): 632c–d.
15. Teams RM, Drossman DA, Corazziari E, Talley NJ, Thompson WG, Whitehead WE. The Functional Gastrointestinal Disorders, The Rome Criteria II. Appendix A: diagnostic criteria for functional gastrointestinal disorders [monografía en Internet]. Rome: Degnon Associates, Inc; 2005 [citado: 26 de diciembre de 2005].
16. Mentes BB, Akin M, Irkörücü O, Tatliciolu E, Ferahköe Z, Yildinm A, et al. Gastrointestinal quality of life in patients with symptomatic or asymptomatic cholelithiasis before and after laparoscopic cholecystectomy. Surgical endoscopy. 2001 Nov 1;15(11):1267-72.
17. Niranjan B, Chumber S, Kriplani AK. Symptomatic outcome after laparoscopic cholecystectomy. Trop Gastroenterol. 2000 Jul-Sep;21(3):144-8.
18. Lublin M, Crawford DL, Hiatt JR, Phillips EH. Symptoms before and after laparoscopic cholecystectomy for gallstones. The American Surgeon. 2004 Oct 1;70(10):863.
19. Thistle JL, Longstreth GF, Romero Y, Arora AS, Simonson JA, Diehl NN, et al. Factors that predict relief from upper abdominal pain after cholecystectomy. Clinical Gastroenterology and Hepatology. 2011 Oct 1;9(10):891-6.
20. Soliman WM, Hablus MA, Zaghloul KM, Elahawal LM, Alattar AA. Features of Upper Abdominal Pain that Predict Symptoms Relief after Cholecystectomy in Patients with Uncomplicated Gallstones Disease. Journal of Surgery [Jurnalul de chirurgie]. 2018;14(1):105-7.
21. Nagaraj SK, Paul P, Kumar MK, Muninarayanapp S, Anantharamaiah H. Risk factors and the biochemical evaluation of biliary calculi in rural kolar, karnataka, India: a rural perspective of an urban disease (2012). JCDR 6: 364-368.
22. Gaharwar A. Factors favouring cholelithiasis in north Indian population. IOSR Journal of Pharmacy. 2013 Jun;3(5):01-3.
23. Dua A, Desai SS, Kuy S, Sharma R, Jechow SE, McMaster J, et al. Gender based differences in management and outcomes of cholecystitis. The American Journal of Surgery. 2013 Nov 1;206(5):641-6.
24. Cirillo DJ, Wallace RB, Rodabough RJ, Greenland P, LaCroix AZ, Limacher MC et al. Effect of estrogen therapy on gallbladder disease. Jama. 2005 Jan 19;293(3):330-9.
25. Mertens MC, De Vries J, Scholtes VP, Jansen P, Roukema JA. Prospective 6 weeks' follow-up post-cholecystectomy: The predictive value of pre-operative symptoms. Journal of Gastrointestinal Surgery. 2009 Feb 1;13(2):304-11.
26. Zhang J, Lu Q, Ren YF, Dong J, Mu YP, Lv Y, et al. Factors relevant to persistent upper abdominal pain after cholecystectomy. HPB. 2017 Jul 1;19(7):629-37.
27. Shin Y, Choi D, Lee KG, Choi HS, Park Y. Association between dietary intake and postlaparoscopic cholecystectomic symptoms in patients with gallbladder disease. The Korean journal of internal medicine. 2018 Jul;33(4):829.
28. Lorusso D, Porcelli P, Pezzolla F, Lantone G, Zivoli G, Guerra V et al. Persistent dyspepsia after laparoscopic cholecystectomy. The influence of psychological factors. Scandinavian journal of gastroenterology. 2003 Jun;38(6):653-8.

IMJ 2019; 65(2): 129-136.