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RESEARCH ARTICLE

FATE OF DYSPEPTIC SYMPTOMS FOLLOWING LAP. CHOLECYSTECTOMY.

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Abstract

Background: Laparoscopic cholecystectomy is the standard treatment for symptomatic gallstone disease. Symptoms of abdominal pain, nausea, food intolerance, and others are common, and their relationship to biliary disease is often well known but other Gastro-Intestinal conditions may cause them also. Continuation of such symptoms post-operatively is the target of this study.

Aim of study: To assess the incidence, etiology, management and preventing measures of persistent dyspeptic symptoms following laparoscopic cholecystectomy.

Patients and methods: This is a Prospective study performed in Al-Fallujah teaching hospital on 136 patients undergoing laparoscopic cholecystectomy between September 2016 and September 2017. They were evaluated using a questionnaire for data collection; inquiring about: indication for laparoscopic cholecystectomy, characteristics of pain, and other associated dyspeptic and colonic symptoms. The patients were re-evaluated with the same questionnaires after surgery during a period from 2-12 weeks, and classified into two groups: first group includes patients get benefit of surgery (relieved symptoms) and those whom symptoms not eliminated by surgery (persistent symptoms). 21 patients were excluded from our analysis; five of them had conversion to open surgery & we lost contact with sixteen patients post-operatively.

Results: The median age of the remaining 115 patients was 34.4 year (range 17-55) years; 20 were men. All were diagnosed to have symptomatic gall stones disease and all were scheduled for laparoscopic cholecystectomy (L.C.). 16 patients (13.9%) had persistent symptoms post-operatively during the follow-up period. Our study concentrated on the correlation between the preoperative presentation and the continuation of post-operative symptoms. Statistical analysis showed that **food intolerance** and **nausea** were more common among those with a poor outcome after laparoscopic cholecystectomy.

Patients with persistent dyspeptic symptoms despite operation; their symptoms were indeed belongs to **GERD** and **P.U** disease in the majority of them.

Conclusion: Nonspecific dyspeptic symptoms like heartburn, food intolerance and nausea are not adequate reasons for taking the decision of laparoscopic cholecystectomy.

Patients with dyspeptic, or colonic symptoms should be thoroughly evaluated to avoid unnecessary cholecystectomy in those with other Gastro-Intestinal pathology that share the same symptoms of Gallstones.

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Introduction:-

Ten to fifteen percent of the western population had gallstones, and although most of them are asymptomatic, it was estimated that 1-2% will develop symptoms per year, for which cholecystectomy is to be performed and it will constitute one of the most common operation performed by general surgeons.^{1, 2, 3}

In Netherlands, about 32,000 patients diagnosed with this condition, and cholecystectomy is performed in 19,000 patients a year⁴,

While the prevalence in India is 6.12%.⁵

Most of patients are asymptomatic and about 20% of patients with gallstones develop clinical symptoms.^{6, 7}

Women are three times more likely to have cholelithiasis than men, and the first-degree relatives of patients having gallstones have two fold greater prevalence. Although two thirds of gallstones are asymptomatic, they may cause acute or chronic cholecystitis, biliary colic, pancreatitis, or obstructive jaundice. Acute cholecystitis is a severe form of symptomatic cholelithiasis, and 10%–30% of patients with acute disease develop life-threatening complications such as empyema, gangrene, or perforation.^{8, 9}

Acute cholecystitis is secondary to gallstones in 90 to 95% of cases. Obstruction of the cystic duct by a gallstone is usually the initiating event that leads to gallbladder distention, inflammation, and edema of the gallbladder wall. Why inflammation develops only occasionally with cystic duct obstruction is unknown. It is probably related to the duration of obstruction of the cystic duct.^{8, 10}

Symptomatic gallstone is typically diagnosed when episode of biliary pain had been occur, this biliary pain is defined as a severe steady pain, lasting more than 15-30 min, and usually located in the epigastric region and/or right upper quadrant (RUQ), sometimes radiating to the back,^{11, 12} Which is usually associated with dyspeptic symptoms.^{13, 14}

However, some patients experience mild dyspeptic symptoms without biliary colics.¹⁵

The most common presenting symptom of acute cholecystitis is upper abdominal pain accompanied occasionally by signs of peritoneal irritation. The pain may radiate to the right shoulder or scapula. The pain frequently begins in the epigastric region and then localizes to the right upper quadrant (RUQ), which may initially be colicky but almost always becomes constant. Nausea and vomiting are generally present, and fever may be noted, tachycardia, palpable gallbladder or fullness of the RUQ (30-40% of patients) and jaundice (~15% of patients).¹⁶

Patients with acalculous cholecystitis may present with fever and sepsis alone, without the history or physical examination findings consistent with acute cholecystitis.¹⁷

Cholecystitis may present differently in special populations - as in elderly and especially the diabetics - with vague symptoms and absence of many of the key historical and physical findings (e.g., pain and fever), with localized tenderness as the only presenting sign. It may progress to complicated cholecystitis rapidly and without warning. Again, in children, it may present without many of the classic findings. People at higher risk for cholecystitis include patients with sickle cell disease, serious illness, a requirement for prolonged total parenteral nutrition (TPN), hemolytic conditions, or congenital and biliary anomalies. The absence of physical findings does not rule out the diagnosis of cholecystitis.¹⁸

As clinical symptoms varies or are not consistently related to the presence of gallstones.¹⁹

Ultrasonography is recommended in correlation with other investigations²⁰,

Professional guidelines propose conservative treatment (wait and see) in asymptomatic cholelithiasis and cholecystectomy in symptomatic cholelithiasis.²¹

In biliary pain without stones, cholecystectomy is occasionally indicated¹⁵ following additional surgical consultation.²²

Elective cholecystectomy is commonly performed in about 70% of the symptomatic patients.²³

Laparoscopic cholecystectomy was introduced in 1987 by Mouret & had rapidly gained popularity & was subsequently considered the standard treatment for symptomatic Gallstones disease, with advantages over open cholecystectomy through reducing postoperative hospitalization; pain; morbidity with better cosmeses & considerable financial saving.²⁴

Treatment of symptomatic gallbladder stones with cholecystectomy is followed by cure or improvement of symptoms in about 90% of patients^{25, 26}. However, in 20%-30% of patients pain and dyspeptic symptoms still persist^{27, 28}. That's why recognition of patients with a high risk of negative outcomes is crucial. In literature, the presence of pre-operative dyspeptic symptoms, psychotropic medication, and a long history of biliary pain attacks are recognized as a potential predictors of poor outcome and persisting pain at 6 months post-cholecystectomy^{29, 30}. Despite clinical experience showed that most patients experience a great reduction of symptoms at 6 weeks post-cholecystectomy³¹

No studies have explored predictors of symptomatic outcome at this time point. The present prospective follow-up study aims at the identification and the valuation of predictors of negative symptomatic outcomes at 6 weeks after cholecystectomy.³²

Few patients will continue to have dyspeptic symptoms after laparoscopic cholecystectomy.

Research done in 1948 gave the first impression of dyspepsia, especially flatulent dyspepsia, as being one of the manifestations of gallstone disease and advocated cholecystectomy for the same.³³

Dyspepsia refers to a constellation 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).³⁴

An agreed international definition of dyspepsia is "episodic or persistent abdominal symptoms, looks often related to the intake of food, which patients or physicians believe to be due to disorder of the proximal portion of the digestive tract, the symptoms included in this generic definition of dyspepsia agreed at the Maastricht consensus conference 1997 are: pain or discomfort in the upper abdomen, nausea & vomiting, early satiety, epigastric fullness & regurgitation".³⁵

The term "post cholecystectomy symptoms" is more accurate to describe all the symptoms related to biliary or non-biliary causes, the reported incidence of persistent symptoms after cholecystectomy varies widely. Although most patients with irritable bowel syndrome localize their worst pain to the lower abdomen, they can have pain anywhere in the abdomen & often have dyspepsia. Increasingly experienced doctors recognize typical biliary pain as severe epigastric &/or right upper quadrant in location, often accompanied by vomiting, at intervals of weeks to months.^{17, 18, 36}

Patients and Methods:

Prospective study had been done in Al-Fallujah teaching hospital on 136 patients visiting the outpatient clinic and emergency unit and assessed by different surgeons in the same surgical team in our hospital, and laparoscopic cholecystectomy scheduled for them, Five patients were converted to open surgery and were excluded from analysis & sixteen patients were unable to cooperate in answering the questionnaires postoperatively also excluded the remaining 115 patients were included in our study, 95 of them were females and 20 of them were males admitted for laparoscopic cholecystectomy between (Sep. 2016 - Sep. 2017) was recruited into the study. All patients were placed on an elective operation after assessment by surgical team, and the diagnosis of cholelithiasis was confirmed by ultrasonography in all cases.

Questionnaire sheet (data sheet)

The symptom profile of the patients was evaluated by a questionnaire preoperatively, which was include: the **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). Also it involved some investigations (CBC, LFT, S. Amylase, US). Laparoscopic cholecystectomy was carried out as a four ports technique with sharp and blunt dissection \pm electro cautery. Perioperative cholangiography was not available. Patients with a history of cholestatic jaundice secondary to gallstones disease whether presented clinically, abnormal liver function tests, or dilated common bile duct, were scheduled preoperative for endoscopic retrograde cholangiopancreatography (ERCP) and sphincterotomy before planning L.C.

Re-evaluation of the patients post-operatively was conducted in the outpatient clinic or by telephone(for those with no post-operative symptoms), for 2 to 12 weeks after surgery; and classified into two groups: first group includes patients get benefit of surgery (relieved symptoms); 99 patients, and those whom symptoms not eliminated by surgery (persistent symptoms); 16 patients, and certain investigations as (Urea breath test, MRCP&ERCP, and OGD) were added to clarify the reason behind continuation of symptoms.

Statistical Analysis

Simple comparisons of preoperative symptoms of patients involved in our study with persistent symptoms after laparoscopic cholecystectomy and those with successful outcome were performed ($p < 0.05$ was accepted as significant). Analysis of the associated symptoms was subdivided into dyspeptic and colonic symptoms.

Aim of study:

To assess the incidence, etiology, management and preventing measures of persistent dyspeptic symptoms following laparoscopic cholecystectomy.

Results:**3.1. Age and Gender distribution**

In this study 115 patients were diagnosed to have symptomatic gallstone disease.

They were scheduled and treated with laparoscopic cholecystectomy. They were 95 females (82.6%) and 20 male (17.4%) as shown in (figure 3.1).

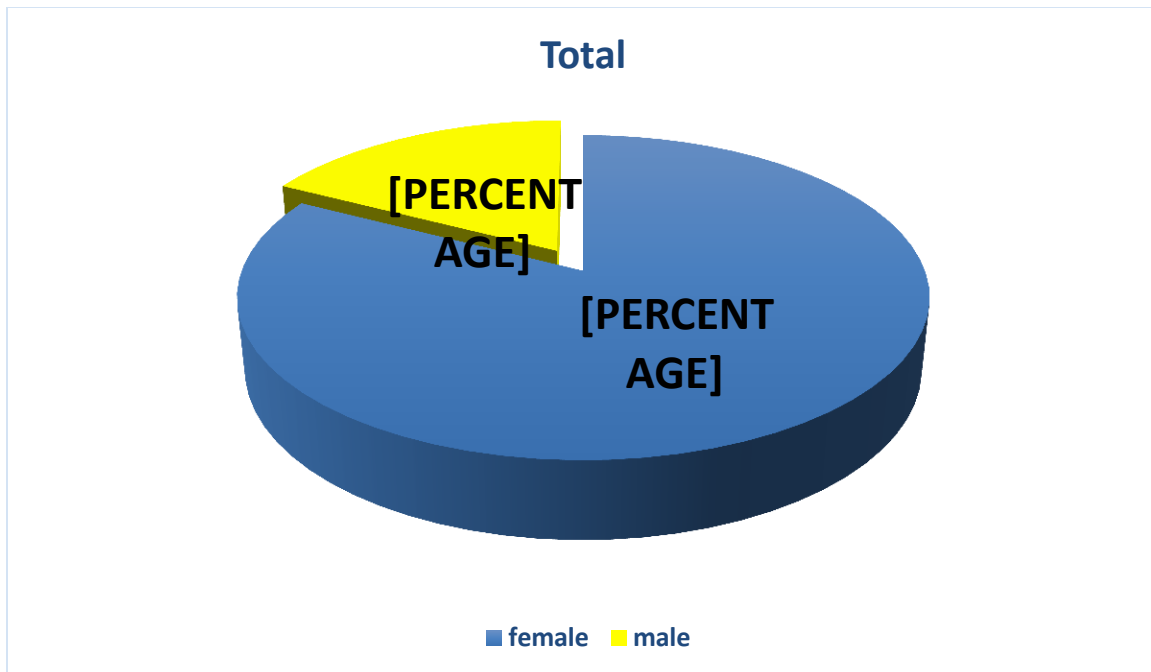


Figure 3.1: gender distribution.

Patient's age ranged from 17 to 55 years with a mean of 34.4 years, and standard deviation (SD) of ± 9.568 years. The highest proportion of patients was found in the age group [31 – 40] y (33%).

The proportion of females was much more than male. (Table 3.1).

Table 3.1: Distribution of patients according to age & Gender.

Gender	Age groups					Total	%
	≤ 20 y	21 – 30 y	31 – 40 y	41 – 50 y	> 50 y		
Female	2	24	32	21	16	95	82.6
Male	–	3	6	7	4	20	17.4
Total	2	27	38	28	20	115	–
%	1.7	23.5	33	24.4	17.4	–	100

3.2. Pre-operative presenting symptoms: All our patients had pain as their presenting symptoms, a high proportion of patients [68 (59%)] presented with food intolerance followed by nausea [57 (49.6%)] patients, while diarrhea was the least presenting symptom [4 (3.5%)] patients (figure 3.2).

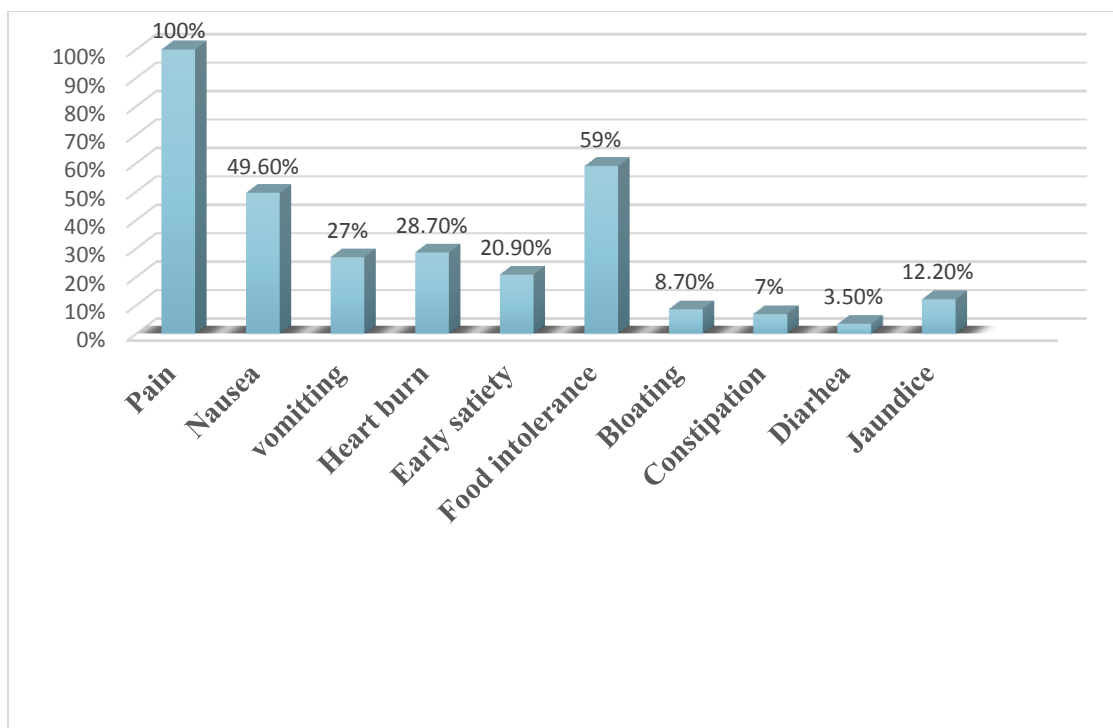


Figure 3.2: Pre-operative presenting symptoms.

*Patient might have more than one symptom.

3.3. Pre-operative pain analysis:

The most common site of pain at presentation was in the Rt. upper quadrant 65 (56.5%); and the majority of patients experienced radiation to the Rt. shoulder 69 (60%).

Fatty meals were the predominant precipitating factor in 66 patient (57.4%); and 65 (56.5%) of all patients their pain respond to analgesics (figure 3.3).

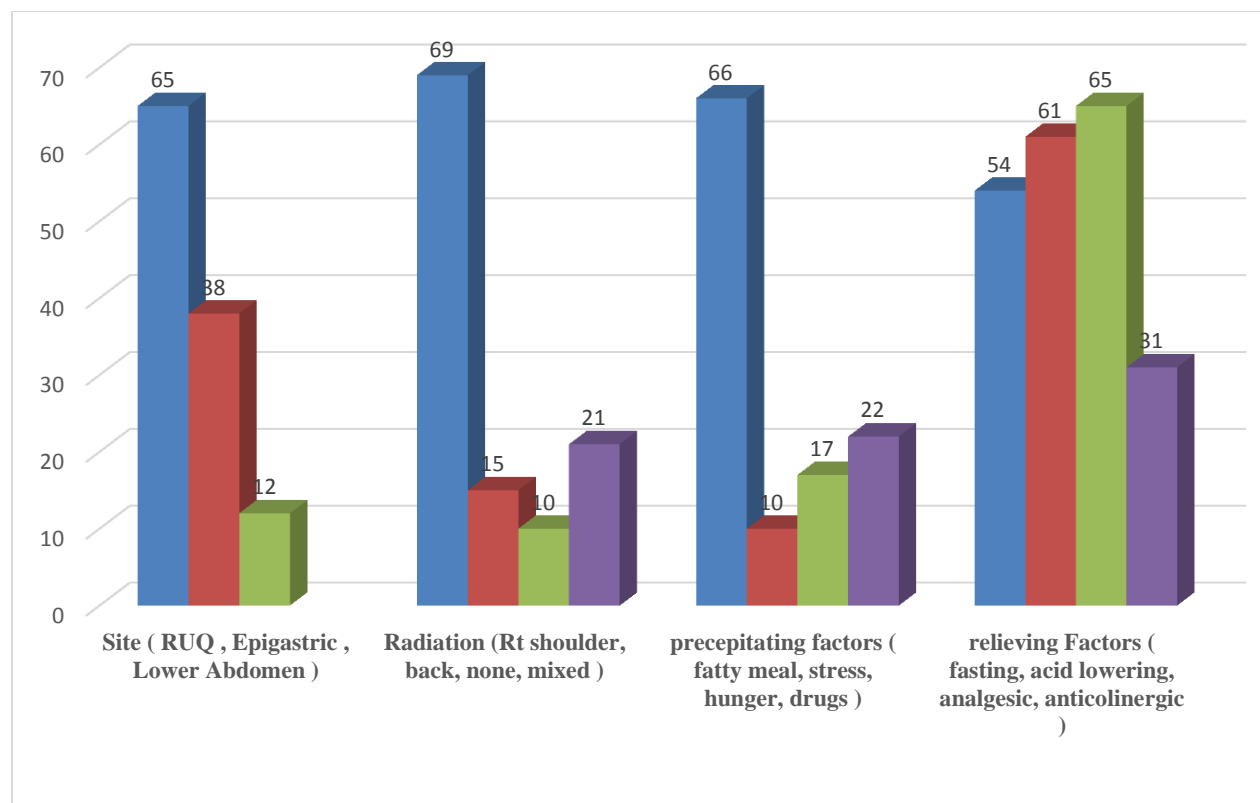


Figure 3.3: pre-operative pain analysis.

* Multiple factors might relief pain in the same patient

3.4. Ultrasound finding:

All patients were evaluated preoperatively with abdominal ultrasound and the majority had normal size gall bladder (71.3%), with normal wall thickness (65.2%). (Table 3.2.)

Table (3.2) Ultrasound finding.

Total No. Of patients	Gallbladder status			Wall thickness	
	Normal	Distended	Contracted	Normal	Thick
115	82	13	20	75	40
	71.3%	11.3%	17.4%	65.2%	34.8%

3.5. Pre-operative diagnosis:

Depending on clinical presentation and investigations our patients were categorized as chronic cholecystitis (72%) and acute cholecystitis (23%). (Figure 3.4)

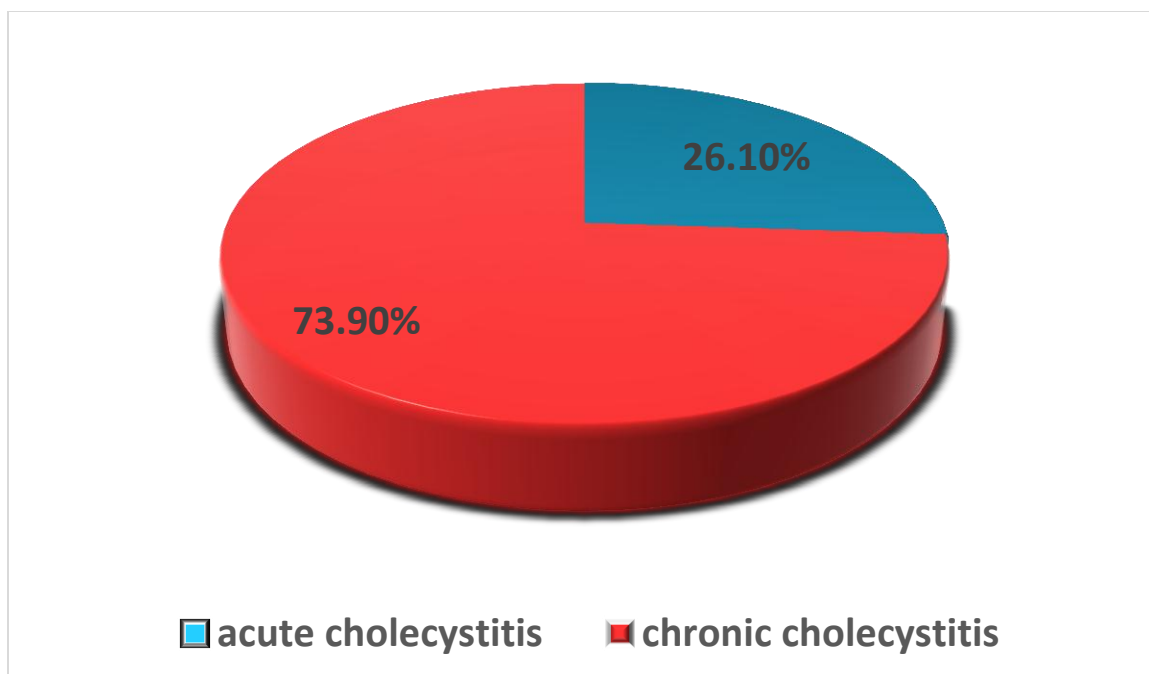


Figure 3.4 pre-operative diagnosis.

3.6.post-operative sample classification:

Post-operatively Sixteen patients (13.9%) reported symptoms similar to those present before surgery and were defined as the group with **persistent symptoms**. Patients who became symptoms free were 85 patients (86.1%) and were defined as the group with **relieved symptoms**. (fig3.5)

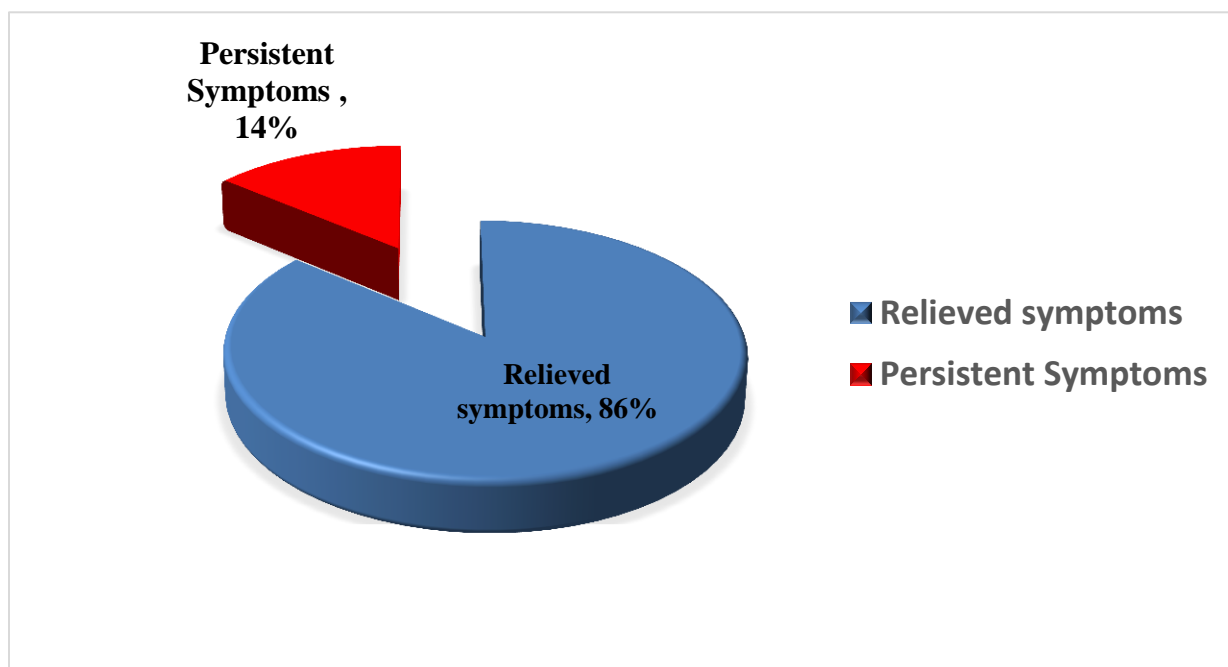


Figure 3.5 post-operative sample classification.

3.7. Association between Pre-operative diagnosis and post-operative symptoms persistence:

Table (3.3) shows the association between Pre-operative diagnosis (acute or chronic cholecystitis) and postoperative symptoms. The highest prevalence of postoperative persistent symptoms was seen among patients who were diagnosed as acute cholecystitis (16.7%) but the association between prevalence of postoperative persistent symptoms and pre-operative diagnosis was statistically not significant ($P=0.612$).

[There is no statistical significance; $P > 0.05$ between pre-operative diagnoses (acute or chronic cholecystitis) with post-operative persistence of symptoms].

Table 3.3: Distribution of patients according to pre-operative diagnosis and correlation with symptoms persistence post-operative.

Pre-operative Diagnosis	Postoperative Symptoms		Total (%) n=115	P- value
	Persist (%) n= 16	Relieved (%) n= 99		
Acute Cholecystitis	5 (16.7)	25 (83.3)	30 (26.1)	0.612
Chronic Cholecystitis	11 (12.9)	74 (87.1)	85 (73.9)	

3.8. Post-operative symptoms:

The highest proportion of patients with persistent symptoms post-operatively; presented with pain in the epigastric region; 9 (56.25%); while the least, presented with pain in the lower abdomen 3 (18.75%) (Figure 3.6)

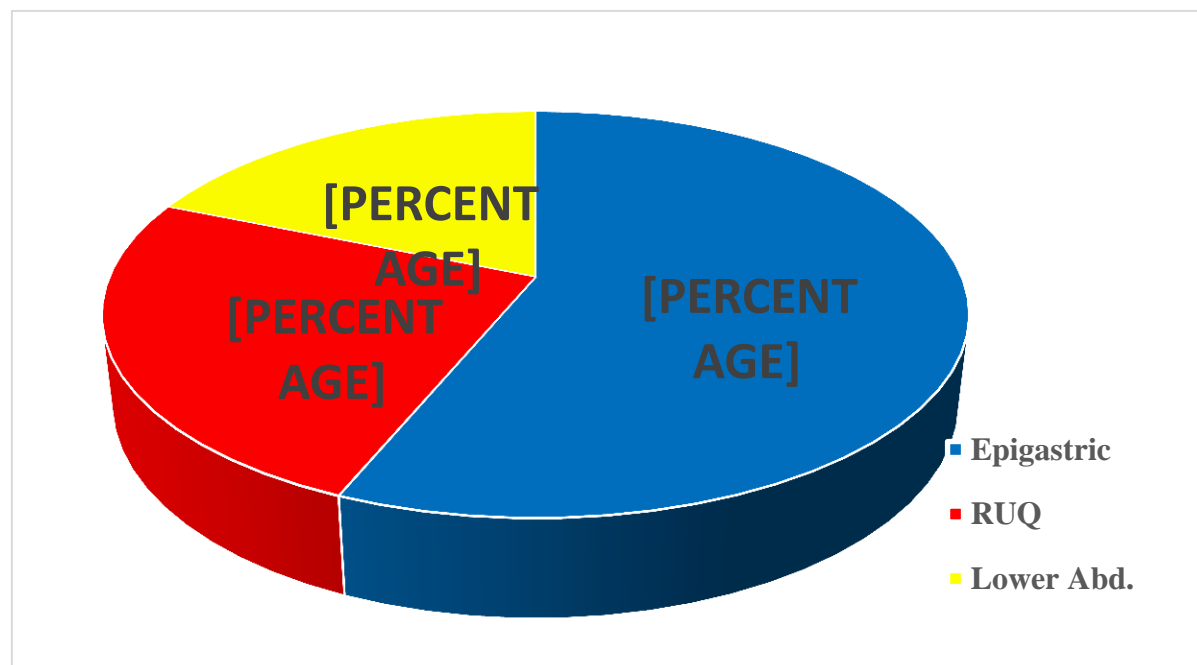
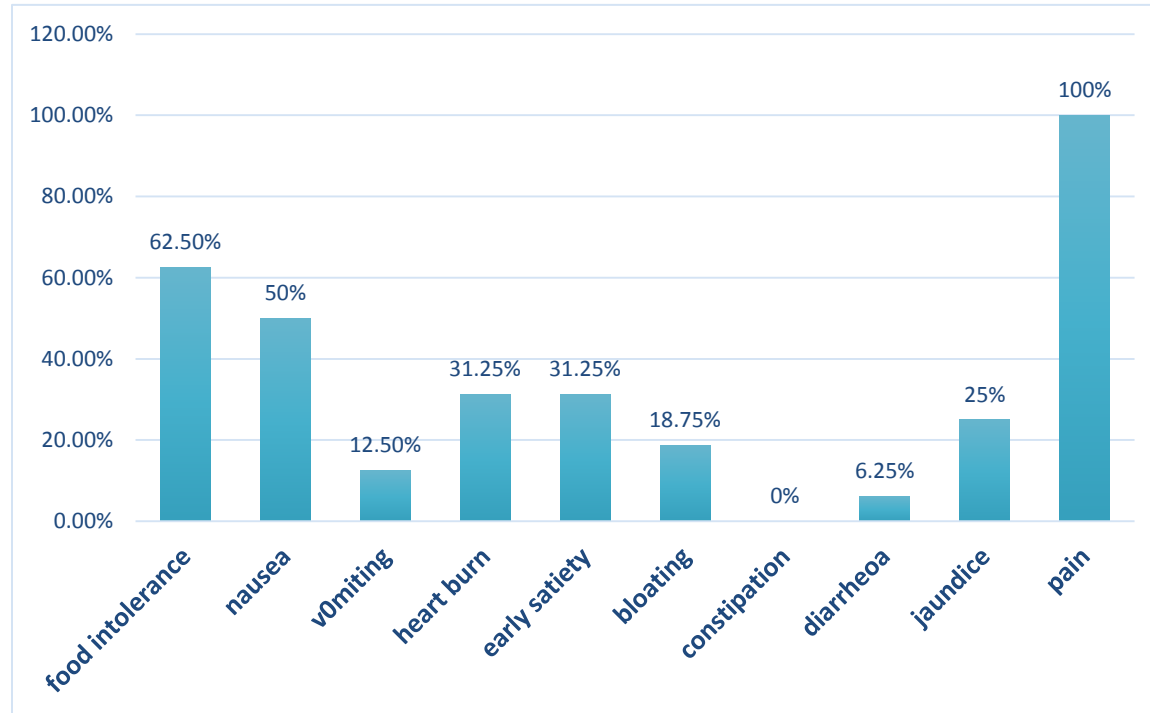


Figure 3.6: distribution of pain in cases of persistent symptoms.**3.9. Post-operative symptoms:**

In addition to pain; other dyspeptic symptoms (food intolerance, nausea, heartburnetc.) And they were 10 (62.5%) patient; And among dyspeptic symptoms food intolerance were the most common one (62.5%) (figure3.7)

Figure 3.7 Detailed distribution of symptomatic patients according to their symptoms.**3.10. post-operative investigations for persistent symptoms group:**

Patients with symptoms of pain and dyspepsia undergo several investigations as shown in (table 3.4) it shows, that the majority of patients; 6 (37.5%) had GERD findings on OGD; CBD stone and DU share the same percentage (2 patients 12.5%); and the least percentage was found in GU; Gastritis; and dyskinesia (1 patient 6.25%) for each one.

Table 3.4: investigations analysis of symptomatic patients.

	L.F.T.	C.B.C	amylase	U/S	MRCP/ ERCP	Urea breath test	O.G.D.	Colonoscopy
Epigastric (9)	N	N	N	N	—	4 +ve (2 respond to eradication therapy)	7 (6 GERD , 1 gastritis)	—
R U Q (4)	3 elevated TSB	N	N	N	2 CBD Stone 1 dyskinesia	—	1 DU	—
Lower Abd. (3)	N	N	N	2 gaseous abdomen 1 normal	—	—	N	N

*N = normal results.

3.8. Post-operative diagnosis for persistent symptoms:

Collectively speaking, post-operative diagnosis was: GERD 6 (37.5%); while GU; Gastritis; & Dyskinesia share the same percentage 1 (6.25%) for each one (figure 3.8).

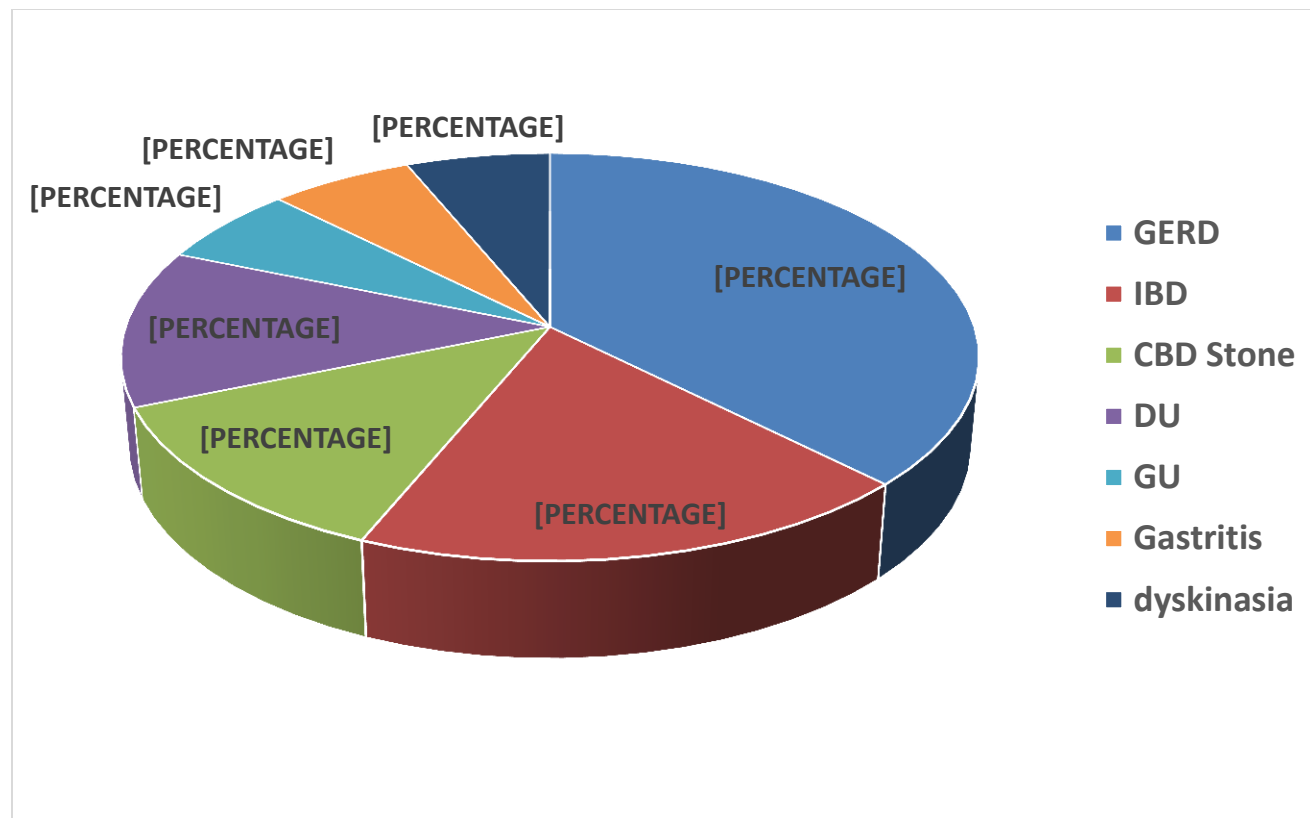


Figure 3.8: causes of dyspepsia post-operatively.

Discussion:-

Most people with gallbladder stones never become patients as they remain asymptomatic. Elective cholecystectomy is performed in 70% of patients with symptomatic cholelithiasis.³⁶ Aiming at a release from pain and symptoms and preventing complications. Postoperatively, a significant group of patients report persisting symptoms.^{37, 38}

Furthermore, cholecystectomy entails the risk of common bile duct injury and mortality in 0.5% and 0.2% of the patients, respectively.^{39, 40} Therefore, performance of elective cholecystectomy should be considered critically and recognition of patients with a higher risk negative outcomes is crucial.⁴¹

Dyspepsia has been defined as a set of symptoms, related or unrelated to food ingestion, localized to the upper half of the abdomen. Dyspepsia has been divided into: **1. Organic dyspepsia**, in which improvement of the underlying condition would result in elimination of dyspepsia, e.g. peptic ulcer, biliopancreatic etiologies;

2. Functional dyspepsia, also known as nonorganic, idiopathic or essential dyspepsia, where no identifiable explanation for the symptoms could be said; and

3. Non-investigated dyspepsia, which needs further investigations to deduce the cause.⁴²

GERD and Peptic ulcer disease remains one of the most common causes of dyspepsia. There is level I evidence supporting the treatment of H. pylori infections in patients with duodenal or gastric ulcers. However, conflicting results are available regarding the benefits in non-ulcer dyspepsia.^{43, 44}

Gallstone disease is a common surgical problem worldwide; quite a number of patients of cholelithiasis present with only dyspeptic symptoms. According to Niranjana et al, laparoscopic cholecystectomy was responsible for relief of dyspeptic symptoms. Out of these, biliary pain, nausea and vomiting had better outcome than belching, flatulence and heartburn.⁴⁵

There has been conflicting evidence about the role of laparoscopic cholecystectomy in curing dyspepsia.⁴⁶

115 patient included in our study with the majority of cases were female (82.6%) and female: male ratio (4.75:1) as females predominantly developed gall stones disease compared to male, and symptoms persist in 13.9% of patients; 11% of them among females as they are the majority of our sample.

Manas et al also showed female predominance as (96%) and symptoms persist in (18.5%) and the majority of them were females. The same was seen in Konsten et al; while velpen et al study revealed a different percentage for those with symptoms persistence as it was only 5%.^{47- 49}

According to pre-operative assessment our study shows that the highest percentage of patient had pain sited at the Rt. upper quadrant of the abdomen (56.5%) and the majority described radiation to Rt. shoulder (60%) and their pain responded well to analgesia (56.5%). The **dyspeptic symptoms** was far more than **colonic symptoms**. MC Metens et al show RUQ was the major site of pain (66.5%) and most of them had dyspeptic symptoms rather than colonic symptoms, and about (37.8%) responded to analgesia.⁴¹

In our study the highest prevalence of postoperative persistent symptoms was seen among patient who were diagnosed as acute cholecystitis (16.7%) but despite that, this difference was statistically not significant ($P=0.612$), while Manas et al describe acute cholecystitis as the main diagnosis followed by chronic cholecystitis with a percent's (22.22% and 7.41%) respectively with symptoms persistence (7.4% and 0%) respectively as miss diagnosis may occur more in acute cases.⁴⁶

The follow up of our cases in the study revealed post-operative persistent symptoms in about 16 patients (13.9%). More than half of them (56.25%) had epigastric pain, while only (18.75%) had lower abdominal pain. This can be explained by the later discovery that the major cause in persistent symptoms was due to causes related to an upper abdominal pathology (GERD, PU....etc.)^{43,44}

Manas et al showed (18.5%) symptoms persistence with majority of epigastric pain (11.1%).⁴⁷

The majority of patients with persistent symptoms in our study have dyspeptic symptoms (62%), which is the same result of both MC Metens et al and Manas et al (57.3%) this may be due to dyspepsia, being the most common presenting clinical symptom in most of the upper G.I. problems. Mark meta-analysis showed persistent colonic symptoms were the predominant symptoms and diarrhea the commonest one (30-140%).^{41, 50}

In our study 13 patients with persistent symptoms, had symptoms that can be included under the heading of "dyspepsia". In 7 of them, the detailed investigations, diagnosed them with a variety of upper G.I. diseases (PU, gastritis, CBD stones, and dyskinesia) while the majority showed evidence of GERD (6.37%) out of those with symptoms persistence (13.9%), this is comparable with Howden CW et al.⁵¹

In our study, we didn't have any evidence supporting the old theory of long cystic duct stump, and the role of cystic duct stump in post cholecystectomy syndrome was evaluated by Rogy et al, They concluded that cystic duct stump is hardly ever a cause of recurrent symptoms in itself and total excision of cystic duct does not eliminate the existence of post cholecystectomy symptoms.⁵²

On reviewing the literature, some papers had shown that, removal of gall bladder in chronically ill patients may increase the risk of perpetuating; the symptoms secondary to decrease in lower esophageal sphincter pressure, increasing duodeno-gastric reflux, or inducing sphincter of Oddi dysfunction^{53, 54}. This would explain persistence of symptoms as a direct outcome of cholecystectomy, rather than the presence of a second preoperative pathology, other than gallstones.

Conclusion:-

- 1) Patients with pre-operative dyspeptic symptoms, have an increased risk of negative post-cholecystectomy outcomes.
- 2) Performance of elective cholecystectomy should be considered critically and recognition of patients with a higher risk negative outcomes is crucial.
- 3) Food intolerance or non-specific dyspepsia are not adequate reasons for laparoscopic cholecystectomy.
- 4) In general there is agreement that symptomatic Gallstones should be treated, but the decision whether abdominal symptoms are really related to Gallbladder stones remain a diagnostic challenge for clinicians and whether cholecystectomy is the proper therapeutic option to relieve those symptoms.

Recommendation:-

1. Patient with dyspeptic symptoms and gallstone need to be evaluated with OGD before establishing operation
2. Patient with gallstones and lower abdominal symptoms should be thoroughly evaluated to avoid unnecessary cholecystectomy for patients with IBS.
3. We recommend to do further study with larger sample and for more than 12 weeks follow up.
4. Surgeons should be aware that the subgroup of patients whose preoperative symptoms include, heart burn, food intolerance, abdominal bloating and altered bowel habit may in fact have 'silent gall stones'. Such patients are unlikely to benefit from laparoscopic cholecystectomy.
5. A symptom-specific approach should lead to optimization of the indication of cholecystectomy.

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