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Cholecystitis (*Warm-e-Marara*) and its management: A Review

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Abstract
Cholecystitis is a common medical condition where inflammation occurs in gallbladder. This condition can be associated with or without the presence of gallstones. Bacterial infection accounts for 50% to 85% of the disease's onset. While there is a close relationship between the biliary system and the gut. According to doctrine of Unani Medicine disease occurs in the gall bladder is due to *Su-e-Mizaj, Su-e-Tarkeeb* or *Taffarruq-e-Itteshal*. They also mentioned that inflammation occurs in the marara is due to *Ghaleez wa Fasid Ghiza, Ehtebas Ghair Tabayi*. In Unani system of medicine Usool-e-Ilaj of cholecystis is based on usool-e-ilaj of *Amraz-e-Kabid*. There are various Unani drugs have been used for the management of *Amraz-e-Kabid* like Arque Kasni, Arque Mako, Majoon Dabidul Ward, Habbe Kabid Naushadri etc.

Keywords: cholecystitis, *warm-e-marara*, *amraz-e-kabid*, *su-e-mizaj*, *unani medicine*

Introduction
Cholecystitis is a medical condition where inflammation occurs in gallbladder [1]. This condition can be associated with or without the presence of gallstones [2]. It is classified in to two types i.e., acute cholecystitis and chronic cholecystitis [3]. It is found both in men and women but may have a propensity for certain populations [2]. Acute cholecystitis is defined as inflammation of the gallbladder and is usually caused by obstruction of the cystic duct [4] where as Chronic cholecystitis is a prolonged, sub-acute condition caused by the mechanical or functional dysfunction of the emptying of the gallbladder [3].
Acute cholecystitis (AC) is one of the most common surgical diseases. Bacterial infection accounts for 50% to 85% of the disease's onset. Since there is a close relationship between the biliary system and the gut [5].
Acute cholecystitis is most often caused by gall stones. Gall stones are one of the most common disorders of the gastrointestinal tract, affecting about 10% of people in Western society and more than 80% of people with gall stones are asymptomatic where as acute cholecystitis develops in 1-3% of patients with symptomatic gall stones [6].
Acute calculous cholecystitis (ACC) is the most frequent complication of cholelithiasis and represents one-third of all surgical emergency hospital admissions [7].
According to WHO, Gallstone disease is a major health problem in particularly, in developed world. It is also one of the leading causes of digestion-related hospital admissions with high healthcare costs in this countries [8].
Helminthic infection (ascariasis) is a major cause of biliary disease in developing countries in Asia, southern Africa, and Latin America. Obstruction of the cystic duct causes an inflammatory process to start. This results in acute cholecystitis. If the inflammation persists it may cause perforation or gangrene of the gall bladder [9].
Over 90% of cases of acute cholecystitis result from obstruction of the cystic duct by gall stones or by biliary sludge that has become impacted at the neck of the gall bladder [10].
Obstruction of the cystic duct causes the intraluminal pressure within the gall bladder to increase and, together with cholesterol supersaturated bile, triggers an acute inflammatory response. The trauma caused by the gall stones stimulates the synthesis of prostaglandins I_2 and E_2, which mediate the inflammatory response [11].
Secondary bacterial infection with enteric organisms (most commonly *Escherichia coli*, *Klebsiella*, and *Streptococcus faecalis*) occurs in about 20% of cases [12]. Biliary sludge is a mixture of particulate matter and bile, and it may stimulate microlithiasis. If the sludge persists-for example, because the patient has already had several pregnancies or is receiving total parenteral nutrition-gall stones can form [13].
Acute cholecystitis (AC) is a life-threatening emergency that commonly occurs as a complication of gallstones [14]. Severe right upper quadrant pain, abdominal guarding, fever, and a positive Murphy's sign with an elevated white blood cell count are the classical clinical manifestations of AC [15].
Although ultrasonography is typically the initial diagnostic examination in patients with suspected AC, computed tomography and magnetic resonance imaging are commonly performed to identify complications; cholescintigraphy is recommended in patients with equivocal findings on the other imaging modalities, as this technique has the highest diagnostic accuracy in the diagnosis of AC [16].
Imaging studies are also helpful in the timely detection of complications associated with AC. Although laparoscopic

cholecystectomy is considered the gold-standard treatment for AC [17] percutaneous gallbladder drainage with or without cholecystostomy tube placement is a safe, effective management technique for surgically high-risk patients with multiple medical conditions [18].

This treatment can be used as either a bridging therapy, with elective cholecystectomy performed at a later time after improvement of the patient's condition, or as definitive treatment in surgically unfit patients [19]. Radiologists play a pivotal role in the initial diagnosis and management of patients with AC [20]. Cholescintigraphy is the most sensitive imaging modality for cholecystitis [21].

Complications of acute cholecystitis have a characteristic CT appearance and include necrosis, perforation, abscess formation, intraluminal hemorrhage, and wall emphysema [22].

There is various allopathic medicines available for the management of cholecystitis ike ursodeoxycholic acids, NSAID, Opium derivaties etc., have various side effects [23].

Unani Concept of Warm-e-Marara

According to doctrine of Unani Medicine disease occurs in the gall bladder is due to Su-e-Mizaj, Su-e-Tarkeeb or Taffarruq-e-Itteshal. Unani Scholars also described about Amraz-e-Marara, under the caption of Amraz-e-Kabid, they also mentioned that inflammation occurs in the mararaa is due to Ghaleez wa fasid ghiza, ehtebas ghair tabayi [24].

Most of the Great Unani scholars like Hippocrates, Galen, Zakaria Rhazi, Ali Ibn Abbas Majusi, Ibn-e-Sina, Ismail Jurjani, Ibn-e-Hubal Baghdadi etc., are described about the pathophysiology of this disease and also their treatment method by Mufarrad wa Murakkab Drugs like; Kasni, Mako, Karafs, Tukhm Soya, Khare Khasak, Hajrul Yahud, Afsanteen, Duqu, Habbul Qilt, Sirka, Arque Kasni, Arque Mako, Arque Ajwain, Majun Hajrul Yahood etc. [25] Currently most of them are scientifically proved for their lithotripsy, analgesic, hypolipidemic activities [26].

Management of Cholecystitis

Prevention of Cholecystitis

Some measures can reduce the risk of developing gallstones, and this can decrease the chance of developing cholecystitis [27].

- Avoiding saturated fats
- keeping to a regular breakfast, lunch and dinner times and not skipping meals
- exercising 5 days per week for at least 30 minutes each time
- losing weight, because obesity increases the risk of gallstones
- avoiding rapid weight loss as this increases the risk of developing gallstones
- A healthy weight loss is generally around 1 to 2 pounds, or 0.5 to 1 kilograms, of body weight per week [28].

The nearer a person is to their ideal body weight; the lower the risk will be of developing gallstones. Gallstones are more prevalent in people with obesity, compared with those who have an appropriate body weight for their age, height, and body frame [29].

Dietary management Cholecystitis

Cholesterol gallstones are among the most common gastrointestinal disorders in Western societies. Individuals with gallstones may experience various gastrointestinal symptoms and are also at risk of developing acute or chronic cholecystitis. Cholecystectomy is the most frequently recommended conventional treatment for symptomatic gallstones [28].

Bile acids (ursodeoxycholic acid or chenodeoxycholic acid) are also used in some cases to dissolve radiolucent stones, but these drugs can cause gastrointestinal side effects and there is a high rate of stone recurrence after treatment is discontinued. Lithotripsy is used in some cases in conjunction with ursodeoxycholic acid for patients who have a single symptomatic non-calcified gallstone [30].

There is evidence that dietary factors influence the risk of developing cholesterol gallstones. Dietary factors that may increase risk include cholesterol, saturated fat, trans fatty acids, refined sugar, and possibly legumes. Obesity is also a risk factor for gallstones. Dietary factors that may prevent the development of gallstones include polyunsaturated fat, monounsaturated fat, fiber, and caffeine [31].

Consuming a vegetarian diet is also associated with decreased risk. In addition, identification and avoidance of allergenic foods frequently relieves symptoms of gallbladder disease, although it does not dissolve gallstones. Nutritional supplements that might help prevent gallstones include vitamin C, soy lecithin, and iron. In addition, a mixture of plant terpenes (Rowachol) has been used with some success to dissolve radiolucent gallstones. The gallbladder flush is a folk remedy said to promote the passage of gallstones [32].

Usul-e-Ilaj of Warm-e-Marara

- Removed the real cause of disease
- Avoid from fatty, oily and Ghizae Kasif
- Use warm water for drinking purpose
- Be regular aerobic exercise
- At the time of pain used Arque Mako and arque Kasni 6 Tola each
- Dry Hammam is effective
- Correct the sue mizaj of Kabid
- Islahe Jigar
- Use of hepatoprotective Drugs [33].

Unani Pharmacotherapy for Warm-e-Marara

Basically two types of drugs are being used for the management of warme marara i.e. single and Compound drugs. Single Drugs like- Mako, Kasni, Khare Khasak, Jawakhar, Habbul Qilt, Hajrul Yahood, Chobchini, Kutki etc. where as compounds are- Arque Mako, Arque Kasni, Habbe Kabid Naushadri, Majoon Dabidul Ward, Sharbate Ward, Sharbate Jigar, Sharbate Deenar, Dawaul Kurkum etc are highly effective for the management of Amraz-e-Kabid wa Marara [25, 34, 35].

Management of Cholecystitis

Medical management of Cholecystitis

Most patients with acute cholecystitis respond to conservative, first line management: the gall stone disimpacts and falls back into the gall bladder, which allows the cystic duct to empty. If the gall stone does not disimpact, complications-such as advanced cholecystitis (gangrenous cholecystitis or emphysema of the gall bladder) or perforation-may result [36].

Immediate measures should be taken to rest the gall bladder;

this will subdue the inflammatory process in most patients. Patients should be fasted, rehydrated with intravenous fluids, and given oxygen therapy and adequate analgesia [37]. Indometacin (25 mg three times daily for a week) can reverse the inflammation of the gall bladder and the contractile dysfunction seen in the early stages (first 24 hours) of cholecystitis [38]. The prokinetic action of indometacin will also improve postprandial emptying of the gall bladder in patients with gallbladder disease [39].

A single intramuscular dose of diclofenac (75 mg) may substantially decrease the rate of progression to acute cholecystitis in patients with symptomatic gall stones [40]. Because of the risk of superimposed infection, intravenous antibiotics should be started empirically if the patient has systemic signs or if no improvement is seen after 12-24 hours. A second generation or newer cephalosporin should be used (for example, cefuroxime 1.5 g every 6-8 hours) with metronidazole (500 mg every 8 hours). Non-operative management-solvent dissolution therapy or extracorporeal shockwave lithotripsy-has been used with variable results to treat chronic cholecystitis in patients unfit for surgery, but it has no place in the management of acute cholecystitis [41].

Surgical management

About 20% of patients with acute cholecystitis need emergency surgery. Such surgery is indicated if the patient's condition deteriorates or when generalized peritonitis or emphysematous cholecystitis is present. These features suggest gangrene or perforation of the gall bladder [42].

Cholecystectomy

The timing of surgery for the 80% of patients without evidence of gangrene or perforation is under debate. Open cholecystectomy traditionally has been performed 6-12 weeks after the acute episode to allow the inflammatory process to resolve before the procedure (interval surgery) [43].

Patients with acute cholecystitis who undergo early laparoscopic cholecystectomy have lower complication rates and lower conversion rates than open cholecystectomy and shorter hospital stays than that undergoing interval surgery. Early surgery for acute cholecystitis also has a lower conversion rate than delayed surgery (which is performed during the index admission after conservative management and after symptoms has lasted 3-5 days) [44].

Early laparoscopic surgery is safe and feasible in patients with acute cholecystitis. If early intervention-less than 72 hours after symptoms started-can be achieved, “edema planes” present during this period allow the gall bladder to be dissected laparoscopically. Although it is desirable to operate within this time period, it is often difficult to do so in clinical practice. By the time inflammation has been present for more than 72 hours; features of chronic inflammation (such as fibrosis) predominate and make it more difficult to dissect the gall bladder. The optimal treatment for patients presenting with acute cholecystitis should be resuscitation followed by laparoscopic cholecystectomy on the next available surgical list [45].

Percutaneous cholecystostomy

Percutaneous cholecystostomy is a minimally invasive procedure that can benefit patients with serious co-morbidity who are at high risk from major surgery. Percutaneous cholecystostomy can be performed at the bedside under local anaesthetic and is suitable for patients in intensive care units and those with burns. It is the definitive treatment in patients with acalculous cholecystitis (see below), or it may be used as a temporising measure-to drain infected bile and delay the need for definitive treatment [46].

Percutaneous cholecystostomy gives clinical improvement in about three quarters of patients. Mortality after this procedure is related to comorbidity (for example, pneumonia or myocardial infarction) or pre-existing sepsis.

An incomplete or poor response to cholecystostomy within the first 48 hours may indicate causes of sepsis other than cholecystitis, inadequate antibiotic coverage, possible complications (such as dislodgement of the drainage tube), or necrosis of the wall of the gall bladder [47].

Patients can undergo cholecystectomy after percutaneous cholecystostomy. In patients unfit to be given a general anesthetic, the drain can be left in place for more than six weeks to allow radiological extraction of calculi at a later date [48].

Conclusion

Cholecystitis, defined as a type of acute or chronic inflammation occurring in the gallbladder caused by infection, bile stimulus, reflux of pancreatic juice to the biliary passage, as well as bilirubin and lipoid metabolic disorder. Lifestyle modification is a best approach to prevention of cholecystitis. For symptomatic cholecystitis, antibiotics and antispasmodic treatment are conventional therapy while cholecystectomy or laparoscopic cholecystectomy is also appropriate modalities of treatment. Unani treatment is based on multidirectional approach.

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