MODERN MEDICINE AND PRACTICE
https://inovatus.es/index.php/ejmmp

EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 4 No. 8 (Aug - 2024) EJMMP ISSN: 2795-921X

DIAGNOSTIC AND THERAPEUTIC CHALLENGES OF MIRIZZI SYNDROME IN 28 PATIENTS IN GIT AND LIVER HOSPITAL IN MEDICAL CITY – BAGHDAD

Riyadh Jaleel, Wisam Asaad Hasan
Karbala center for Gastroenterology and Hepatology / Karbala Holy Health department, Karbala, Iraq

Sarmad Abdul Haleem Abed
Imam Al-Sadiq Teaching Hospital/Babylon Health Directorate, Babylon, Iraq

Abstract: Background: Mirizzi syndrome (MS) occurs when gallstone impaction in Hartmann's pouch results in extrinsic obstruction of the common bile duct, and fistulation may occur.

Methods: prospective study of patients who are surgically treated for MS from January 2021 to march 2023.Patient presentations, diagnostic methods, treatments and complications were recorded.

Results: twenty- eight patients were grouped according to a classification proposed by Beltran et al. 22 (78.5%), 5 (17.8%) and 1 (3.5 %) patients were classified as types I, II, and III respectively.

Magnetic-resonance- cholangiopancreaticography was the most sensitive imaging modality, suggesting MS in (90 %), followed by CT scan (39.2%) and ultrasonography (14.2%). Twelve underwent Endoscopic-retrograde- cholangiopancreaticography and 8(66.6%) suggested the presence of MS. MS was accurately diagnosed pre-operatively in 20 (71.4%) patients.

In type I, 21 (93.0%) patients underwent cholecystectomy and one patient underwent hepatico-enteric anastomosis.

In type II, 3 (66.7%) underwent cholecystectomy and 1 (27.8%) required hepatico- enteric anastomosis and 1 underwent choledochoplasty the patient with type III MS, required a stone extraction and keeping of the choledocoenteric fistula Laparoscopic cholecystectomy was attempted in 8 (28.5%) patients and 6 (75.0%) required conversion.

Conclusion: MS is a challenging condition and multimodal diagnostic approach has the greatest yield in achieving accurate pre-operative diagnosis.

If suspicion is high, a trial of laparoscopic dissection with low threshold for open conversion is recommended.

Keyword: Mirizzi syndrome (MS).

Introduction:

Mirizzi syndrome (MS) is a rare condition caused by the compression of the common hepatic duct due to stones located in the cystic duct or the neck of the gallbladder. The main symptoms noticed in patients with this condition are upper abdominal pain and jaundice (1)

It was first mentioned in 1905 by Kehr and later in 1908 by Ruge, who described it as a disease caused by the external obstruction of the bile duct associated with jaundice. Eventually, in 1948, the Argentinean surgeon Pablo Mirizzi published an article that established the eponym for this syndrome and defined it as the compression of a bile duct by a gallstone, associated with pressure ulceration generating local inflammation. The compression may lead to external obstruction, erosion, fibrosis or fistula with various levels of complexity (2-4).

The reported frequency of MS is approximately 0.05–4%. Based on data presented in articles, the overall frequency of MS was higher in females than in males. The proportion of females suffering from MS ranged between 55.6–77% (5-9).

However, the available data vary in different parts of the world. Thus, in well-developed countries and regions, such as Europe, MS is found in 0.5% of all cholecystectomies, but in Asia, Central and South America the statistics are generally higher and reach as much as 4.7–5.7% (2, 10, 11). In the population of patients undergoing endoscopic retrograde cholepancreatography (ERCP), the incidence of MS is estimated to be 1.07% (4).

1.1 Pathophysiology

The current knowledge on the pathophysiology of Mirizzi syndrome states that it is an external compression of the common hepatic duct (CHD) by a gallstone impacted in the gallbladder's Hartmann's pouch or the cystic duct

(12-14).

Previously, however, concepts for explaining the disease were different. Initially, Mirizzi thought that the syndrome he described was functional, rather than just mechanical. He believed that the inflammation

in the surrounding structures predisposes a "bile duct sphincter" to contract and cause biliary stenosis. Later, his theory was discarded due to the lack of any sphincter in that area [(12)]. There were reports of classifying Mirizzi syndrome as the compression of the bile duct by structures other than a gallstone, such as gallbladder cancer or a large, distended, inflammatory gallbladder, but some authors suggest avoiding such confusion and refer to MS as only a stone disease[(11)] . Isolated extrinsic compression of the CHD is considered to be the first stage of the syndrome. Prolonged, chronic compression caused by the stone on the gallbladder and CHD walls results in inflammation, ulceration and the formation of Cholecystobiliary fistulas of different stages of advancement. A cholecystoenteric fistula may also occur in the same way. These complications are recognized as the next stages of the Mirizzi syndrome [(4, 7, 12, 13, 15)] .

Beltrán et al. formed a list of nine characteristics of MS distorted anatomy based on previous reports [(12)].

The authors marked out:

1. Atrophic gallbladder with thick or thin walls;
2. Obliterated cystic duct;
3. Cystic duct—long, parallel to the common hepatic duct and with low insertion;
4. Cystic duct—short cystic duct with another anatomical variation;

5. Bile duct—partially obstructed due to the external compression or a gallstone eroding from the gallbladder;
6. Distal bile duct with normal thin walls and no distended lumen;
7. Proximal bile duct—dilated with inflamed walls;
8. Abnormal communication between the bile duct and the gallbladder;
9. Fistula between the gallbladder and stomach, duodenum, colon or other structures.

A long-lasting inflammatory process results in the formation of many dense, hard, fibrous adhesions between the gallbladder and the CBD, which are commonly found in patients with MS. Other signs that might suggest Mirizzi syndrome are a thick-walled gallbladder or a contracted gallbladder— especially when a fistula is present. However, when a fistula is absent, the gallbladder can be enlarged and inflamed due to a cystic duct blockage. Operating in the difficult anatomy and adhesions in MS is challenging and the dissection of Calot's triangle may lead to bile duct injury or bleeding[5, 16, 17].

1.2 Classification of Mirizzi Syndrome

Over time, different classifications have been proposed for this syndrome. The most widely accepted classification is from McSherry et al[18] published in 1982. It classifies Mirizzi syndrome into 2 types, based on endoscopic retrograde cholangiopancreatography (ERCP) findings:

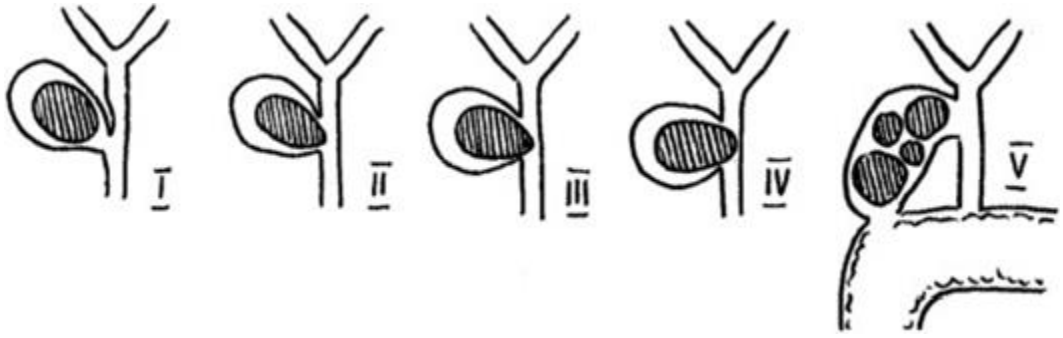
Type I involves extrinsic compression of the CBD, while in Type II, the Cholecystobiliary fistula is already established.

In 1989, Csendes et al. proposed a classification which expanded the one proposed by McSherry. The authors presented four types of the syndrome type I, which was equal to the McSherry type I; and types II–IV relating to the different stages of the fistula. Type II represents a cholecystobiliary fistula with up to one-third of bile duct wall erosion.

Type III consists of a fistula involving two-thirds of the bile duct wall. Finally, type IV refers to the complete destruction of the bile duct and its walls being fused with the gallbladder [19].

This classification remained unchanged for almost two decades, but in 2008 Csendes and Beltrán complemented the previous classification by adding types Va and Vb. Type Va includes an uncomplicated cholecystoenteric fistula, while type Vb represents a cholecystoenteric fistula followed by a gallstone ileus [20]. As seen in Fig 1.

Fig 1: Anatomical sketch of Mirizzi Syndrome according to Csendes and Beltrán (2008).



In 2009 Solis-Caxaj suggested a way to simplify Cesendes and Beltrán's classification into three types: types I and II were the same as McSherry's types regarding cholecystoenteric fistulas—IIIa (without gallstone ileus) and IIIb (with gallstone ileus) [21].

Based on this suggestion, Beltrán et al. validated the previous classification in 2012 by implementing Solis-Caxaj types IIIa and IIIb instead of types Va and Vb, but also resigned from the previous types II-IV and simplified them to types IIa (a fistula involving <50% of the bile duct diameter) and IIb (a fistula involving >50% of the bile duct diameter) [12].as seen in table 1 However, other classifications also exist. Starling and Matallana [22] divided Type I into 2 subtypes: Ia (long cystic duct) and Ib (short cystic duct).

Table 1: Three Mirizzi syndrome classifications

McSherry et al[18]	Csendes et al.-1989 and Complemented in 2008[19,23]	Beltrán 2012[12]
I Extrinsic compression CBD	I Extrinsic compression CBD	I Extrinsic compression CBD
II CBF	II CBF affects ＜33% of the CBD	IIa CBF affects ＜50% of the CBD
	III CBF affects 33-66% of the CBD	IIb CBF affects ＞50% of the CBD
	IV CBF affects ＞66% of the CBD	IIIa CBF with CEF and without gallstone ileus
	Va MS with CEF and without gallstone ileus	IIIb CBF with CEF and with gallstone ileus
	Vb MS with CEF and gallstone ileus	

1.2 Diagnosis:

Safe and effective surgical therapy is facilitated by accurate preoperative diagnosis. However, such diagnosis is often missed preoperatively, although more advanced cases of disease are easier to detect before surgery[4].

1.2.1 Symptoms, signs and Laboratory tests:

The clinical presentation of Mirizzi Syndrome ranges from asymptomatic to non-specific, to Several symptoms that were knowledged in patients suffering from MS. the most common symptoms were abdominal pain (incidence 65.7–100%) and jaundice (ranging between 45–87.5%). Other symptoms were nausea and vomiting (31–62%), cholangitis (up to 56%), fever (21–42%) and anorexia (11–29.2%) .[5, 6, 24, 25] Furthermore, Shirah et al. reported that there was a positive Murphy's sign in 50% of their patients during physical examination [5]. The mean duration of the various symptoms was determined to be between 3 to 24 months [14, 16] , but it is worth mentioning that Prasad et al. noticed that symptoms in patients suffering from uncomplicated gallstone disease lasted half as long as in those with MS[26].

The overall percentage of asymptomatic patients ranged between 3.7% and 17% [24, 27].The most common examinations are white blood cell count (WBC), alanine aminotransferase(ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin and gamma-glutamyl transpeptidase (GGT).

Leukocytosis was diagnosed in 73.4% of MS patients in the study by Shirah et al. [5]. Ahlawat reported elevated WBC only if acute cholecystitis, cholangitis or pancreatitis occurred along with MS[28]. Articles that present numerological data show that mean WBC levels are generally around the upper limit of normal levels or slightly beyond. A few papers specify the results for different types of MS. According to Payá-Llorente and Erben [14, 24], mean WBC levels were moderately lower when a cholecystobiliary fistula was present.

On the other hand, Lledó et al. presented contrary data with an inverted Trend [29]. ALT and AST levels are reported to be generally elevated in 39– 98% of tests for ALT and 37–89% for AST [5, 25, 27, 28, 30].

According to some of the articles, the mean levels of ALT and AST in MS patients are several times higher than normal and can reach 286 and 263 U/L, respectively. Data describing those parameters in relation to MS type are inconsistent. Erben et al. report a significant decline in AST and ALT levels from over 250 U/L to less than 100 U/L when there is a cholecystobilliary fistula, while Lledó et al. show a gradual growth in the levels of the parameters with the advancement of the fistula, but neither ALT or AST exceed 90 U/L in this study[7, 10, 24, 29].

The results of ALP test are said to be elevated in even 93.8% of patients and its mean levels are reported to be approximately 324–402 U/L, but can be as high as 1236 U/L (10, 16, 25, 27, 30, 31).

Most authors concur that total bilirubin levels are elevated in MS patients— even in as many as 92.2% of them [6].Payá-Llorente as well as Lledó report increasing mean levels of bilirubin with the advancement of the cholecystobiliary fistula. Erben et al., however, present data showing a decline in bilirubin when there is a cholecystobiliary fistula. Interestingly, Payá-Llorente and colleagues report much lower bilirubin in Csendes type V, which may be due to a discharge of the bile straight to the intestines. Generally, the mean bilirubin levels are reported to be between 2–9.9 mg% (7, 10, 14, 16, 24, 29, 31).

The literature is consistent when it comes to GGT levels, which are commonly elevated according to multiple articles. The mean range could be depicted as 204–1018U/L [10]

1.2.2 imaging:

the following diagnostic modalities are currently widely in use, including: abdominal ultrasonography, CT, MRCP and ERCP

A: Abdominal US

US is used as a routine investigation for biliary disease. This technique can reveal gallstones and cholecystitis and reveal evidence of Mirizzi Syndrome such as an atrophic gallbladder and ectatic common hepatic duct with a normal distal CBD, or edematous gallbladder caused by acute cholecystitis.

[7] Existing Literatures confirms a diagnostic accuracy of 29%, with a sensitivity between 8.3% and 27%. [6, 7, 32, 33].

In one study involving 198 patients, the sensitivity of ultrasound for Mirizzi Syndrome was as high as 77.8%.

B: CT

Although no specific radiological features of Mirizzi Syndrome can be recognized on CT imaging, this technique can be very effective in detecting the cause and location of biliary obstruction. [20, 27, 34]

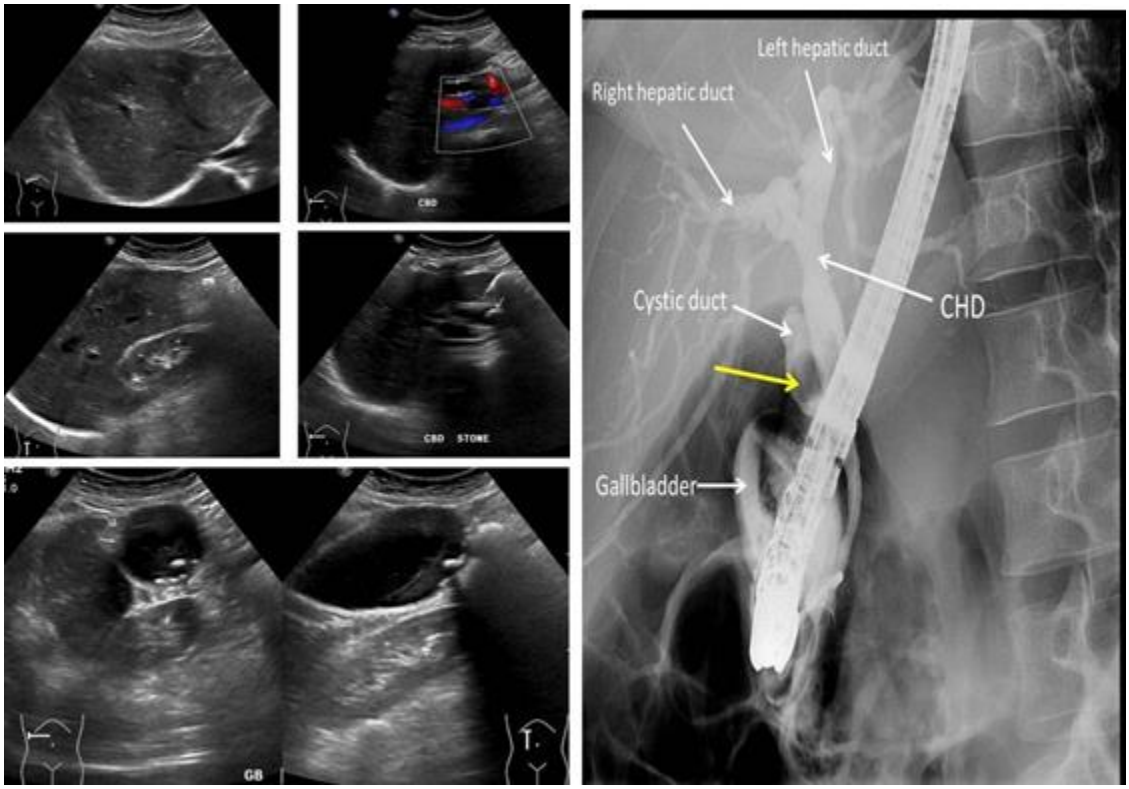
CT is also useful for differentiating hepatic portal or hepatic infiltration of tumors. [35]

In patients with Cholecystobiliary fistula, CT scanning is valuable in distinguishing Mirizzi Syndrome from neoplasia. For example, Fabien et al [36] reported 5 cases in whom CT scan adequately diagnosed Mirizzi Syndrome, and concluded that adequate diagnosis can be reached on the basis of clinical symptoms and images on a CT scan.

C: MRCP

At present, MRCP is the preferred diagnostic tool, and is a noninvasive imaging technique with a 50% diagnostic accuracy rate.[37]

MRCP can delineate the typical characteristics of Mirizzi Syndrome, such as a stone in the common hepatic duct (CHD), extrinsic compression of the CHD, and dilatation of the CHD with normal-sized CBD. MRCP confirmation is required when ultrasound examination detects a dilated bile duct with evidence of obstructive jaundice or stone impaction in the bile duct. Biliary and pancreatic ducts can also be assessed by MRCP, which can create superior images of inflammation around the gallbladder. Such inflammation is characteristic of Mirizzi Syndrome, and can therefore be used to distinguish biliary conditions including cancer. [38] However, MRCP is not efficient at localizing a cholecystocholedochol fistula.



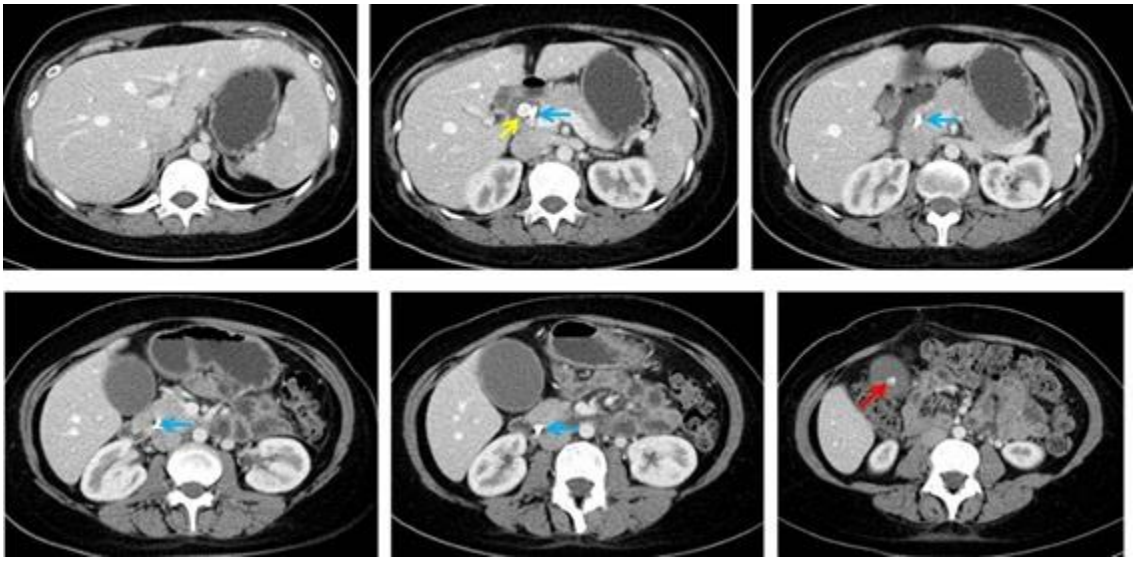


Fig 2: **30 years old female with Mirizzi syndrome type I**
(radiology cases **Case contribution: Dr Radhiana Hassan)**

D: ERCP

Despite its invasiveness, ERCP is considered a gold standard diagnostic tool for Mirizzi Syndrome with a mean sensitivity rate of 76.2%.[40, 41] Indeed, Xie-qun et al [27] reported a 100% sensitivity rate for ERCP. This technique yields superior visualization of the extra-hepatic bile ducts, and can clearly show extrinsic compression by impacted gallstones in the CBD with resulting proximal biliary dilatation. Furthermore, ERCP can accurately determine the presence and location of fistula and biliary obstruction. Therapeutic decompression by papillotomy and stent or nasal bile drainage (NBD) can be achieved during ERCP. [27, 42] Moreover, an endoscopic NBD tube placed during ERCP allows the outcome of surgery to be assessed through endoscopic NBD cholangiography, thus facilitating minimally invasive laparoscopic surgery for Mirizzi Syndrome. [42] However, ERCP can also be associated with devastating complications such as cholangitis or pancreatitis. and its application in patients suffering Mirizzi Syndrome should be considered with significant caution. [12]

E: Other modalities of diagnosis

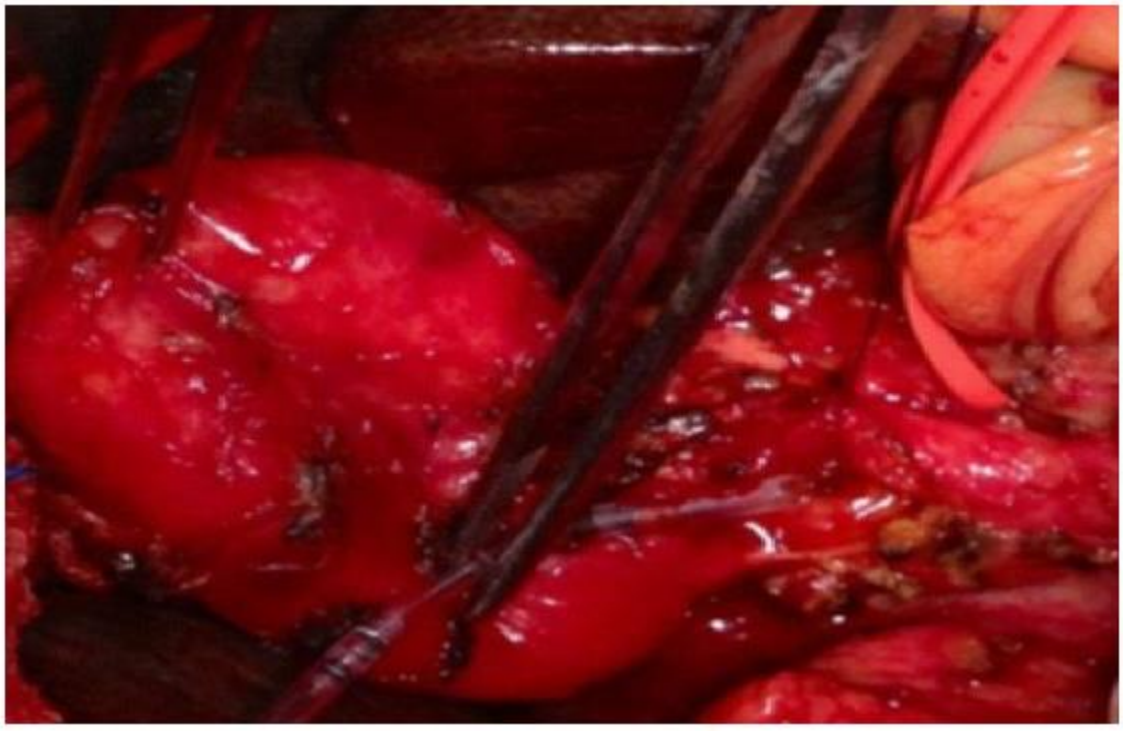
The combination of ≥2 diagnostic modalities has become commonplace in the management of Mirizzi Syndrome. However, this practice is not supported by strong evidence and there is currently no consensus among experts in terms of the added benefit of this practice. [44]

Other, less traditional modalities of diagnosis are also reported in the literatures. For instance, percutaneous trans hepatic cholangiography offers a reasonable option for diagnosis and the relief of obstructive symptoms preoperatively, especially when endoscopic treatment fails. [45, 46] Furthermore, intraductal ultrasonography can expose defects in the ductal mucosa, suggesting the presence of a cholecystocholedochol fistula.[31, 38, 46] During the intraductal ultrasonography (IDUS) procedure, the probe is inserted up until it reaches biliary bifurcation and after imagining it is withdrawn in a stepwise manner. The criterion for diagnosing Mirizzi syndrome by IDUS is a “caplike” reflex, with or without an acoustic shadow seen in a ductal structure next to the CBD at the level of obstruction. According to Wehrmann et al., the most meticulous disclosure of stones located in the bile duct was achieved with IDUS (sensitivity 95%, specificity 92%), while MRCP achieved a level of sensitivity of 80% and a specificity of 83%.

Endoscopic ultrasound (EUS) can also be performed prior to ERCP to further evaluate the bile ducts and pancreas and to determine the cause of biliary strictures. For example, Rayapudi et al[45] reported one case of Mirizzi Syndrome Type 1 by EUS examination. By comparing endoscopic ultrasonography (EUS)—linear or radial—and intraductal ultrasonography, IDUS is superior to EUS in particular with regard to accuracy, sensitivity and specificity. Additionally, EUS lacks the clear anatomical guide (the CBD) that IDUS has by definition. The information provided by IDUS was used to specify an appropriate surgical approach and enabled the surgeons to create direct patient management. It led to a higher rate of minimally invasive surgery being carried out on patients [31].

1.2.3 Intraoperative diagnosis

Intraoperative diagnosis A large number of patients are only diagnosed with Mirizzi Syndrome during surgery.[15] Surgery can reveal a range of signs associated with Mirizzi Syndrome, such as an edematous or atrophic gallbladder with distortion of Calot triangle, an impacted gallstone in the infundibulum or the neck of the cystic duct, thick fibrosis around Calot triangle, and adhesions under the liver space. Cholecystobiliary fistula is strongly suspected if the extraction of an impacted stone is followed by the leakage of bile from the bile duct.[27, 35, 47] Furtherintraoperative cholangiography can then be used to ascertain the position and dimension of the fistula, detect stones in the duct, and verify the integrity of the bile duct wall, as well as retrieve residual stones in the postoperative setting. However, there is some concern that this technique is challenging to perform and carries a significant risk for secondary injury to the bile duct due to the distorted anatomy commonly encountered at Calot triangle.[20]



1.3 Treatment of Mirizzi Syndrome

Surgical management is the mainstay treatment for Mirizzi Syndrome, although this is challenging for several reasons.

First, there is a low index of suspicion for this condition among surgeons, largely owing to its rarity, as gallbladder surgery is often performed in patients with relatively shorter histories of illness, long before the onset of Mirizzi Syndrome. [41]

Secondly, preoperative diagnosis is often missed, thus impacting upon the ability to treat this condition during surgery.

Thirdly, distortion of the anatomy by dense adhesions due to longstanding inflammation and the advancement of Cholecystobiliary or cholecysto- enteric fistula, increases the risk of bile duct injury or massive hemorrhage during dissection of Calot triangle.[44]

1.3.1 Open surgical approach

Traditionally, laparotomy has been considered as the technique of choice for the management of Mirizzi Syndrome. This is largely due to its relative safety when compared with the laparoscopic technique which is associated with high conversion rates (11.1–80%) and an increased incidence of bile duct injury.

However, laparotomy has the advantage of better visualization, haptic feedback, and gallbladder calculus removal before cholecystectomy despite its more invasive nature, high complication rate, and longer postoperative hospital stay.

Total cholecystectomy is feasible in cases of Mirizzi Syndrome Type I which are not associated with Cholecystobiliary fistula.

When severe inflammation impedes the safe dissection of Calot triangle, retrograde fundus-first cholecystectomy or partial (subtotal) cholecystectomy (PC or SC) can be applied. [27, 29] Occasionally, it is necessary to visualize the CBD to manage other causes of obstructive jaundice. One earlier case reported intraoperative bile duct injury which was managed by Roux-en-Y hepaticojejunostomy (RYHJ).[33]

PC or SC leaves a cuff of gallbladder or cystic duct remaining that can be used to repair the fistula of CBD (choledochoplasty), a technique applicable in Mirizzi Syndrome type II and selected type III cases.[7, 27, 36, 44, 48] However, choledocho-enteric anastomosis is a preferred alternative to this method.

Some authors consider that it is safer to curve the fundus of the gallbladder and extract its contents before applying PC or SC. This procedure has also been used in laparoscopic cholecystectomy.

1.3.2 Preoperative biliary decompression.

In order to avoid postoperative complications, Le Roux et al[36] applied preoperative drainage with endoscopic stent, or a nasobiliary drain placement by ERCP to avoid the insertion of T-tubes or abdominal drains. Preoperative biliary drainage facilitates the intraoperative identification of the main bile duct. For Type IV, there is consensus that the best surgical technique is cholecystectomy and RYHJ. However, some authors support the view that the presence of a fistula with a diameter wider than two-thirds of the CBD (Type III and Type IV) should warrant RYHJ. [6, 27, 29, 32]

The safest approach to manage Mirizzi Syndrome Type V is always laparotomy.

Patients and Methods

From January 2021 to march 2023, 28 consecutive patients prospectively diagnosed and underwent surgery for MS at the Department of Gastroenterology and Hepatology teaching hospital at medical city Baghdad. Each patient’s demographics, clinical presentation, diagnostic method, treatment procedure, complications and follow-up were all recorded and tabulated.

The pre-operative workup indicated by the patient symptoms, signs and findings of initial investigations imaging of ultrasound or CT scans Subsequently, magnetic resonance cholangiopancreatography (MRCP) was performed where additional information is required for delineation of the biliary tracts. the Endoscopic retrograde cholangiopancreatography (ERCP) was usually performed as a therapeutic procedure when the patient had concomitant cholangitis with an obstructed biliary system secondary to suspected MS.

All postoperative complications were graded according to the Clavien-Dindo classification recorded up to 30 days or within the same hospital stay. Late complications were defined as complications that occurred more than 30 days after the initial surgery, most of our patients had been followed during the period of study by frequent out -patient visits.

Data was reported as means ± SD or percentages for continuous variables and frequencies and percentages for categorical variables. Comparisons were performed using chi-square or Fisher exact tests for nominal variables, and independent 2-tailed t test for continuous variables. The database was processed with the statistical software SPSS 21 (IBM, Armonk, NY, USA).

Results

During the study period, 28 (3.2%) patients were diagnosed with MS among 850 patients who underwent cholecystectomy.

The mean age at presentation (45 years old) and the range (24-66 years) and higher frequency in women (64.2% of cases).

Patients were classified based on the classification proposed by Beltran et al. The most sensitive investigation in prediction of MS was MRCP, which was suggestive in 18 (90 %) out of 20 performed, followed by CT scan which was suggestive in 11 (39.2 %) out of 28 performed and US suggestive in 4 (14.2 %) out of 28 performed (Table 1).

Of the 20 patients who underwent MRCP, 6 had intra-operative confirmation of fistulae, of which 1 (16.6 %) had MRCP images that could have suggested the presence of fistula pre-operatively; which is Beltran type 2 fistula. The presence of fistulae could not be identified on other imaging modalities.

ERCP was performed in 12 patients, of which 8 (66.6%) were suggestive of MS.

MS was accurately diagnosed pre-operatively in 20 (71.4%) of patients regardless of diagnostic modality.

Laparoscopic cholecystectomy was attempted in 8 (28.5%), of which 2 (25.0%) were successful.

In patients with MS type I, 21 (95.4%) of the 22 underwent either a subtotal or total cholecystectomy, with 1 requiring Roux-loop cholangioenterostomy due to intra-operative injury to the biliary tree.

For patients with type II MS, 3 (60.0%) of the 5 underwent either subtotal or total cholecystectomy with primary closure of the fistula, the other 2 requiring a hepatico-enteric anastomosis and choledochoplasty.

In 1 patient with type III MS, required a stone extraction and keeping of the choledocoenteric fistula (Table 2).

Post-operativecomplications were graded according to the Clavien-Dindo classification and occurred in 5 (17.8%) patients, 1 (1.5%) grade 1 complication, 2(12.5%) grade II, 1 (3%) grade III and 1 (1.5%) grade IV, and late complications were seen in 4 (14.2%) patients, most notably that of cholangitis (Table 3).

There was no significant difference between intraoperative, postoperative, late and total complications in patients who had an accurate preoperative diagnosis versus those who did not.

Table. 2 Overview of clinical presentation

Clinical findings	total
Patient characteristics Age, years, (mean) (range) Gender, M: F	45 24-66 10:18
Clinical manifestations, n (%) Abdominal pain Obstructive jaundice Nausea/vomiting Fever Anorexia	20 (71.4%) 14 (50%) 12 (42.8%) 8 (28.5%) 8 (28.5%)
Physical examination, n (%) Abdominal tenderness	10 (35.7%)
Liver function tests Elevated AST, *n* (%) AST, U/L, mean (range) Elevated ALT, *n* (%) ALT, U/L, mean (range) Elevated ALP, *n* (%) ALP, U/L, mean (range) Elevated bilirubin, *n* (%) Bilirubin, U/L, mean (range)	24 (85.7%) 230 (20–1,102) 27 (96.4%) 268 (36–1,065) 26 (92.8%) 288 (54–1,023) 27 (96.4%) 104 (7–330)
Radiological investigations Ultrasonography,n (%) suggestive of MS CT scan, n (%) suggestive of MS MRCP n (%) suggestive of MS ERCP n (%) suggestive of MS	28(100%) 4 (14.2%) 28(100%) 11 (39.2%) 20 (71.4%) 18 (90%) 12 (42.8%) 8(66.6%)
Pre-operative diagnosis of Mirizzi syndrome, n (%)	20 (71.4%)

Table 3 Operative findings and procedures based on Beltran classification

herapeutic interventions	All (*n* = 28)	Beltran I (*n* = 22) (78.5%)	Beltran II (*n* = 5) (17.8%)	Beltran III (*n* = 1) (3.5%)
Surgical approach, n (%) Open approach Laparoscopic, Successful Converted to open	20 (71.4%) 8(28.5%) 2(25%) 6(75%)	14(63.6%) 8 (36.36%) 2(25%) 6(75%)	5(100%)	1(100%)
Surgical procedure, n (%) Total cholecystectomy Subtotal cholecystectomy Choledochoplasty Hepaticoenterostomy	18(64.2%) 9(32.1%) 1(3.57%) 2(7.14%)	14(63.63%) 8(36.36%) 0 1(4.5%)	4(40%) 1(20%) 1(20%) 1(20%)	0 0 0 0

stone extraction and keeping the CEF	1(3.57%)			1(100%)
Management of fistula Primary closure Choledocho-enteric anastomosis Choledochoplasty	3(10.7%) 1(3.57%) 1(3.57%)	0 0 0	3(60%) 1(20%) 1(20%)	0 0 0

Discussion

MS is a rare sequelae of gallstone disease, but it grants several challenges to the surgeon. The main challenge in management of MS is in achieving an accurate pre-operative diagnosis.

In this study, MS was diagnosed preoperatively in 71.4% of the cases, it is acceptable percentage related to the accurate diagnosis in our tertiary center. This is compatible with Many literatures have studied the rates of pre- operative diagnosis of MS built on the classification proposed by Beltrán et al[20].[23] with highly variable rates of accurate pre-operative imaging diagnosis ranging from 8 to 82%[1, 7, 20].

The mean age at presentation (45 years old) and the range (24-66 years) and higher frequency in women (64.2% of cases).

At initial presentation and diagnosis, the most common symptom in our patients was abdominal pain, followed by jaundice and fever compatible with other papers, where the most common symptoms were abdominal pain (incidence 65.7–100%) and jaundice (ranging between 45–87.5%). Other symptoms were nausea and vomiting (31–62%), cholangitis (up to 56%), fever (21–42%) and anorexia (11–29.2%) [5, 6, 24, 29].

US in MS has a reported sensitivity of as low as 14.2%, due to the close proximity of the cystic and CBD[37]. On the other hand, CT scans, when compared with ultrasonography, fails to provide any further information, due to its lower sensitivity of detecting biliary stones, with only 79% of stones visible on ultrasonography being visualized on CT[58].

The main value of CT scans is to rule out malignancies that are known to occur in up to 25% of the cases of MS [58].this is not the case in our study, we had no malignancy.

MRCP in MS has a high specificity in the detection of gallstone and bile duct stenosis, and in showing the extent of inflammation around the GB [38] In our study, the sensitivity of MRCP was 90%, and was performed in 71.4 % of our cohort. It is compatible with literatures that are showing a mean sensitivity rate of 76.2%.[40, 41]

The sensitivity of ERCP, on the other hand, was lower at 66.6%. However, it remains a valuable adjunct because it allows delineation of the level and extent of biliary obstruction, as well as closer evaluation of ductal abnormalities, including fistulae [7]. Furthermore, ERCP allows the application of sphincterotomies or biliary stent insertion. This decompresses the biliary system and allows temporization of emergent surgical procedures but we tried to avoid it in patients when possible because of the risk of cholangitis.

Apart from MRCP in only one patient, none of the pre-operative investigations allowed to confidently report the presence of fistulation in MS. Thus, a multimodality approach with MRCP for imaging and subsequent ERCP for clarification and possible therapeutic intervention are recommended.

Achieving pre-operative staging of the types of MS still remains a challenge. In a series by Tan et al.[59] bile duct injuries were seen in 4 (16.7%) out of 24 patients, all of which occurred in patients in whom pre-operative diagnosis of Mirizzi syndrome was not known in study we have one biliary injury. making a

preoperative diagnosis is still difficult. Many authors underline the importance of a preoperative diagnosis of MS to avoid exposing surgeons to difficult operating conditions and therefore to limit complications by choosing the right approach[60-63]. Along with a precise diagnosis, proper treatment must follow.

Based on the Beltran's classification, type I in our study accounts for 78.5 % of cases, and types II and III for (17.8%) and (3.5 %) respectively. the incidence of type I is higher. It is compatible with other literatures which are showed that Mirizzi type I (54.5–83%) and Mirizzi type II (11.1%27.3 %) are the most commonly reported classifications. Other type of Mirizzi Syndrome is relatively low in incidence[44, 48].

At present, Mirizzi Syndrome is managed without well-developed, internationally-recognized clinical guidelines.

Furthermore, advancement in diagnostic techniques has not made it easier for a confirmed diagnosis to be made before surgery, even though diagnostic rates have improved markedly.

Open cholecystectomy is in general accepted as the procedure of choice, yet some studies recommend a laparoscopic approach, which is said to be safe, especially when there is no Cholecystobiliary fistula [16, 60]. This reflects the technical challenge in the dissection of the Calot's triangle in the setting of MS with chronic fibrosis of the area.

However, it is crucial that MS is diagnosed preoperatively when planning laparoscopic treatment. Research shows a high conversion rate when the diagnosis is not made prior to the surgery and this increases with the advancement of the disease [60, 64].that what had been done in our study.

In patients with MS type I, 21 (95.4%) of the 22 underwent either a subtotal or total cholecystectomy, with 1 requiring a hepaticojejunostomy in addition to the cholecystectomy, due to intra-operative injury to the biliary tree.

For patients with type II MS, 3 (60.0%) of the 5 underwent either subtotal or total cholecystectomy, three of them underwent primary closure of the fistulae with 2 requiring a hepatico-enteric anastomosis and choledochoplasty.

In patients with type III MS, 1 required stone extraction and keeping of the CEF.

Several diagnostic and therapeutic algorithms have been proposed for MS [5, 33, 48]. But There is as yet no conventional agreement as to which kind of approach should be administered to treat a specific type of the disease.

We rarely use T-tube insertion into the bile duct if necessary, to decompress the bile duct or to shape the duct in order to minimize the risk of bile leakage, especially when the quality of tissue repair is doubtful. This technique can also be used to dispose of retained stones during intervention radiology.

Conclusion

MS is a challenging condition and the multimodal diagnostic approach is recommended to achieve accurate pre-operative diagnosis. In cases where the clinical suspicion is high despite equivocal imaging studies, a trial of laparoscopic dissection with a low threshold for open conversion is recommended.

References

1. Al-Akeely, M. H.; Alam, M. K.; Bismar, H. A.; Khalid, K.; Al-Teimi, I.; Al-Dossary, N. F., Mirizzi syndrome: ten years experience from a teaching hospital in Riyadh. *World journal of surgery* **2005,** *29*, 1687-1692.

2. Senra, F.; Navaratne, L.; Acosta, A.; Martínez-Isla, A., Laparoscopic management of type II Mirizzi syndrome. *Surgical Endoscopy* **2020,** *34*, 2303-2312.
3. Mithani, R.; Schwesinger, W. H.; Bingener, J.; Sirinek, K. R.; Gross, G. W., The Mirizzi syndrome: multidisciplinary management promotes optimal outcomes. *Journal of Gastrointestinal Surgery* **2008,** *12*, 1022-1028.
4. Chen, H.; Siwo, E. A.; Khu, M.; Tian, Y., Current trends in the management of Mirizzi Syndrome: A review of literature. *Medicine* **2018,** *97* (4).
5. Shirah, B. H.; Shirah, H. A.; Albeladi, K. B., Mirizzi syndrome: necessity for safe approach in dealing with diagnostic and treatment challenges. *Annals of Hepato-biliary-pancreatic Surgery* **2017,** *21* (3), 122-130.
6. Kumar, A.; Senthil, G.; Prakash, A.; Behari, A.; Singh, R. K.; Kapoor, V. K.; Saxena, R., Mirizzi's syndrome: lessons learnt from 169 patients at a single center. *Annals of Hepato-Biliary- Pancreatic Surgery* **2016,** *20* (1), 17-22.
7. Cui, Y.; Liu, Y.; Li, Z.; Zhao, E.; Zhang, H.; Cui, N., Appraisal of diagnosis and surgical approach for M irizzi syndrome. *ANZ journal of surgery* **2012,** *82* (10), 708-713.
8. Wani, N. A.; Khan, N. A.; Shah, A. I.; Khan, A. Q., Post-cholecystectomy Mirizzi's syndrome: magnetic resonance cholangiopancreatography demonstration. *Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association* **2010,** *16* (4), 295.
9. Nassar, A. H.; Nassar, M. K.; Gil, I. C.; Ng, H. J.; Yehia, A. M., One-session laparoscopic management of Mirizzi syndrome: feasible and safe in specialist units. *Surgical Endoscopy* **2021,** *35*, 3286-3295.
10. Gonzalez-Urquijo, M.; Gil-Galindo, G.; Rodarte-Shade, M., Mirizzi syndrome from type I to Vb: a single center experience. *Turkish Journal of Surgery* **2020,** *36* (4), 399.
11. Ibrarullah, M.; Mishra, T.; Das, A., Mirizzi syndrome. *Indian Journal of Surgery* **2008,** *70*, 281-287.
12. Beltrán, M. A., Mirizzi syndrome: history, current knowledge and proposal of a simplified classification. *World journal of gastroenterology: WJG* **2012,** *18* (34), 4639.
13. Ji, Y.; Gao, Y.; Xie, M., The use of different pathology classification systems in preoperative imaging of Mirizzi syndrome. *Archives of Medical Science* **2019,** *15* (5), 1288-1293.
14. Payá-Llorente, C.; Vázquez-Tarragón, A.; Alberola-Soler, A.; Martínez-Pérez, A.; Martínez-López, E.; Santarrufina-Martínez, S.; Ortiz-Tarín, I.; Armañanzas-Villena, E., Mirizzi syndrome: a new insight provided by a novel classification. *Annals of Hepato-biliary-pancreatic Surgery* **2017,** *21* (2), 67-75.
15. Rohatgi, A.; Singh, K., Mirizzi syndrome: laparoscopic management by subtotal cholecystectomy. *Surgical Endoscopy And Other Interventional Techniques* **2006,** *20*, 1477-1481.
16. Kamalesh, N. P.; Prakash, K.; Pramil, K.; George, T. D.; Sylesh, A.; Shaji, P., Laparoscopic approach is safe and effective in the management of Mirizzi syndrome. *Journal of Minimal Access Surgery* **2015,** *11* (4), 246.
17. Davlatov, S.; Rakhmanov, K.; Abduraxmanov, D.; Qurbonov, N.; Vafayeva, I., Current State of The Problem Treatment of Mirizzi Syndrome (Literature Review). *International Journal of Pharmaceutical Research* **2020,** *12* (Suppl. ry 2), 1931-1939.
18. McSherry, C., The Mirizzi syndrom: suggested classification and surgical therapy. Surg Gastroenterol 1982, 1, 219-225.

19. Csendes, A.; Diaz, J. C.; Burdiles, P.; Maluenda, F.; Nava, O., Mirizzi syndrome and cholecystobiliary fistula: a unifying classification. Journal of British Surgery 1989, 76 (11), 1139- 1143.
20. Beltran, M. A.; Csendes, A.; Cruces, K. S., The relationship of Mirizzi syndrome and cholecystoenteric fistula: validation of a modified classification. World journal of surgery 2008, 32, 2237-2243.
21. Solis-Caxaj, C. A., Mirizzi syndrome: diagnosis, treatment and a plea for a simplified classification. World journal of surgery 2009, 33 (8), 1783-1784.
22. Starling, J. R.; Matallana, R. H., Benign mechanical obstruction of the common hepatic duct (Mirizzi syndrome). Surgery 1980, 88 (5), 737-740.
23. Csendes, A.; Muñoz, C.; Albán, M., Síndrome de Mirizzi-Fístula colecistobiliar, una nueva clasificación. Rev Chil Cir 2007, 59 (Suppl), 63-64.
24. Erben, Y.; Benavente-Chenhalls, L. A.; Donohue, J. M.; Que, F. G.; Kendrick, M. L.; Reid-Lombardo, K. M.; Farnell, M. B.; Nagorney, D. M., Diagnosis and treatment of Mirizzi syndrome: 23-year Mayo Clinic experience. Journal of the American College of Surgeons 2011, 213 (1), 114-119.
25. Seah, W. M.; Koh, Y. X.; Cheow, P. C.; Chow, P. K.; Chan, C. Y.; Lee, S. Y.; Ooi, L. L.; Chung, A. Y.; Goh, B. K., A retrospective review of the diagnostic and management challenges of Mirizzi syndrome at the Singapore General Hospital. Digestive Surgery 2018, 35 (6), 491-497.
26. Prasad, T. L.; Kumar, A.; Sikora, S. S.; Saxena, R.; Kapoor, V. K., Mirizzi syndrome and gallbladder cancer. Journal of Hepato-Biliary-Pancreatic Surgery 2006, 13 (4), 323-326.
27. Xu, X.-q.; Hong, T.; Li, B.-l.; Liu, W.; He, X.-d.; Zheng, C.-j., Mirizzi syndrome: our experience with 27 cases in PUMC Hospital. Chinese Medical Sciences Journal 2013, 28 (3), 172- 177.
28. Ahlawat, S. K.; Singhania, R.; Al-Kawas, F. H., Mirizzi syndrome. Current treatment options in gastroenterology 2007, 10 (2), 102-110.
29. Lledó, J. B.; Barber, S. M.; Ibañez, J. C.; Torregrosa, A. G.; Lopez-Andujar, R., Update on the diagnosis and treatment of mirizzi syndrome in laparoscopic era: our experience in 7 years. Surgical Laparoscopy Endoscopy & Percutaneous Techniques 2014, 24 (6), 495-501.
30. Waisberg, J.; Corona, A.; Abreu, I. W. d.; Farah, J. F. d. M.; Lupinacci, R. A.; Goffi, F. S., Benign obstruction of the common hepatic duct (Mirizzi syndrome): diagnosis and operative management. Arquivos de gastroenterologia 2005, 42, 13-18.
31. Wehrmann, T.; Riphaus, A.; Martchenko, K.; Kokabpick, S.; Pauka, H.; Stergiou, N.; Frenz, M., Intraductal ultrasonography in the diagnosis of Mirizzi syndrome. Endoscopy 2006, 38 (07), 717-722.