ABSTRACT – Background: The choledocholithiasis has an incidence of 8-20% in patients with cholecystolithiasis. The preoperative diagnosis guides the interventional treatment on the biliary duct. 

Aim: To evaluate the sensitivity and specificity of the laboratory markers and imaging studies for choledocholithiasis preoperatively. 

Methods: The study comprised 254 patients divided into two groups: the control group (207 patients), patients without choledocholithiasis intraoperatively and cases group (47 patients), that enrolled the patients with choledocholithiasis intra-operatively. Were evaluated the laboratory markers, image exams and intra-operative diagnostic aspects. 

Results: The sample was homogeneous for age and gender. It was observed that 47% of the cases the patients did not show comorbidities. Hospitalization shows in cases group acute pancreatitis in 12.8%, jaundice in 30%, fever in 30% and pain in the right hypochondrium in 95%. By comparing them, was observed that fever and jaundice were the signs and symptoms with statistical significance. Patients with choledocholithiasis had transaminases, alkaline phosphatase, gamma-glutamyl transferase and higher bilirubin with statistical significance (p<0.001). In regard to imaging studies, ultrasound was fairly accurate for choledolithiasis and choledocholithiasis (p<0.001). 

Conclusion: Changes in canicular and transaminase enzymes are suggestive for preoperative choledocholithiasis; GGT showed better sensitivity and alkaline phosphatase greater specificity; ultrasonography and nuclear magnetic resonance cholangiopancreatography showed high specificity.

INTRODUCTION

The choledocholithiasis has an incidence of 8-20% in patients with cholelithiasis. The preoperative diagnosis determines the treatment consisting of intervention on the biliary duct in three stages: preoperative, intraoperative or postoperative. The intervention can occur via endoscopic or surgical approach. Thus, correct diagnosis is necessary for treatment option. Qualifying scores according to the risk for choledocholithiasis seems to decrease the unnecessary number of procedures.

The association between clinical, laboratory and ultrasound criteria has a sensitivity of 96-98% for diagnosis. The absence of these criteria takes less than 2% chance of choledocholithiasis.

The cholecystolithiasis have complications such as cholecystitis, cholestatic syndrome, hepatic abscesses, acute biliary pancreatitis and cholangitis. Chronic obstruction can trigger cirrhosis and portal hypertension. In 10 years of disease, 2-3% of patients will develop some of these complications. So, it is recommended that all patients who have no surgical contraindication be submitted to cholecystectomy.

For patients with symptomatic gallstones undergoing cholecystectomy with
possible symptoms correlated to choledocholithiasis, must be instituted intraoperative cholangiography for all patients. If calculi are detected should be performed endoscopic retrograde cholangiopancreatography in the same surgical moment, with common bile duct exploration or transcystic exploration.

This study aims to evaluate the sensitivity and specificity of the laboratory markers and choledocholithiasis imaging results, preoperatively.

METHODS

This study followed the ethical criteria recommended by Resolution 196/96 of the National Health Council (CNS) of the Ministry of Health, and was submitted for approval by the Ethics Committee in Research of the Hospital before its realization.

This is a retrospective study that included all patients of Regional Hospital of São José, SC, Brazil that looked for assistance at the surgical emergency from March 2013 to February 2014. The sample with suspected choledocholithiasis on admission consisted in 254 patients. They were divided into two groups: the control group (207 patients), without choledocholithiasis intraoperatively, and the case group (47 patients), with choledocholithiasis intraoperatively. Search was based on all records, taking in account the operation list performed in the hospital in that period of time. There was no contact with the patient.

The sample obeyed the following inclusion criteria: men and women over the age of 18 with diagnosis or suspicion of cholelithiasis, acute pancreatitis, cholangitis and choledocholithiasis, referenced to general surgery emergency service.

Exclusion criteria were patients undergoing cholecystectomy and those who did not undergo to surgery or had registration error by operation name.

The identified variables were: age, gender, comorbidities, and reason for admission (presence of pain in the right upper quadrant, fever, jaundice, acute pancreatitis). The entry of lab test results were analyzed - total bilirubin and fractions, glutamino pyruvic transaminase (SGPT), gamma-glutamyl transferase (GGT) and alkaline phosphatase (AP). Imaging studies were: total abdominal ultrasound as the presence of gallstones, biliary tract dilatation and choledocholithiasis; CT scan showing dilatation of the bile ducts and the presence of choledocholithiasis; magnetic nuclear resonance cholangiopancreatography with the presence of choledocholithiasis.

Was considered diagnostic of acute pancreatitis when two or more of these criteria were present: 1) acute or persistent abdominal/epigastric pain, often radiating to the back; 2) serum amylase or lipase three times the reference value; and 3) characteristic of acute pancreatitis in computed tomography with contrast, ultrasound or nuclear magnetic resonance.

For the diagnosis of cholangitis was taken into consideration the triad of Charcot (pain in the right upper quadrant, fever and jaundice). Jaundice was defined as serum total bilirubin greater than 5 mg/dl. It was considered main bile duct/common bile duct dilated when it was in caliber greater than 6 mm.

Regarding complications were considered the ones occurred in the in- and out-patient follow-up till surgical release.

The diagnosis of choledocholithiasis was performed intraoperatively and verified through the surgical descriptions. As hospitalization time, was considered the day of the surgery until hospital discharge; so, the preoperative hospital stay was not considered, and also not the time as outpatient.

Were enrolled only patients who met the inclusion criteria.

Multivariate analysis was performed using SPSS version 17.0® from database typed in Microsoft Excel® 2007. The significance level was 95% (p < 0.05), with values between 5% and 10% considered borderline.

RESULTS

The sample was homogeneous for age and gender. It was observed that in case group, 47% of patients showed no comorbidity conditions (Table 1).

| TABLE 1 - General characteristics of the study population (n=254) |
|---------------------------------------------------------------|
| **General characteristics** | **With choledocholithiasis** | **Without choledocholithiasis** | **p** |
| | n=47 | n=207 | |
| **Gender** | | | 0.649 |
| Female | 29 (62) | 137 (66) | |
| Male | 18 (38) | 72 (34) | |
| **Age** | | | 0.072 |
| >5 | 49 ± 15.7 | 56 ± 18.17 | |
| ≤5 | 55 ± 17.3 | 61 ± 18.75 | |
| **Comorbidities** | | | 0.013 |
| HAS | 4 (8) | 19 (9) | |
| HAS + DM | 4 (8) | 23 (11) | |
| Others | 17 (37) | 29 (15) | |
| **Without comorbidities** | | | |
| 22 (47) | 136 (65) | |

1 HAS = systemic arterial hypertension; DM = diabetes mellitus; *Values expressed as mean and standard deviation.

Regarding the reason for hospitalization, was observed in case group 12.8% with acute pancreatitis, 30% jaundice, fever 30% and 95% pain in the right hypochondrium. Comparing the two groups it was found that jaundice, and fever were the clinical signs and symptoms with statistical significance (Table 2).

| TABLE 2 - Reasons for hospitalization (n = 254) |
|-----------------------------------------------|
| **Hospitalization reasons** | **With choledocholithiasis** | **Without choledocholithiasis** | **p** |
| | n (%) | n (%) | |
| CHOLANGITIS | | | <0.001 |
| Yes | 9 (19) | 1 (1) | |
| No | 38 (81) | 206 (99) | |
| PAIN ON RIGHT HYPOCHONDRIUM | | | 0.344 |
| Yes | 45 (95) | 203 (98) | |
| No | 14 (30) | 26 (12) | |
| Jaundice | 14 (30) | 6 (3) | 0.003 |
| BILIARY ACUTE PANCREATITIS | | | 0.896 |
| Yes | 6 (12.8) | 182 (87) | |
| No | 248 (49.7) | 222 (100) | |

Patients with choledocolithiasis had transaminases, alkaline phosphatase, higher gamma-glutamyl transferase and bilirubin than the group without choledocolithiasis with statistical significance (Table 3). It is observed that AST, ALT and alkaline phosphatase showed similar sensitivity, but only alkaline phosphatase showed high specificity. GGT showed high sensitivity (93%) but low specificity (63%) (Table 4).

With regard to imaging tests, it was observed that ultrasound had good accuracy for cholelithiasis and choledocolithiasis (p < 0.001), but with low positive predictive value (Table 5).
TABLE 3 - Results of laboratory tests of the analyzed population (n=254)

| Exams                      | With choledocholithiasis | Without choledocholithiasis | p    |
|----------------------------|--------------------------|----------------------------|------|
|                            | n=47                     |                            | n=207|
| TGO¹                        | 68 ± 68.7                | 38 ± 69.7                  | 0.003|
| TGP²                        | 92 ± 70.8                | 42 ± 67.9                  | 0.001|
| GGT³                        | 452 ± 561.4              | 105 ± 184.3                | 0.013|
| Alkaline phosphatase*       | 202 ± 238.1              | 92 ± 67.9                  | 0.002|
| Total bilirubin*            | 2.33 ± 5.03              | 0.81 ± 2.1                 | 0.004|
| Direct                     | 1.66 ± 3.5               | 0.08 ± 1.17                | 0.001|
| Indirect                   | 0.81 ± 2.4               | 0.51 ± 2.81                | 0.006|

¹TGO=transaminase glutamino-oxalacetic; ²TGP=transaminase glutamino-piruvic; ³GGT=gama-glutamil transferase *Values expressed as mean and standard deviation

TABLE 4 - Presence or absence of laboratory abnormalities and their sensitivity and specificity for the diagnosis of choledocholithiasis (n = 254)

| Exams                      | Sensibility % | Specificity % | p    | VPPE | VPN* |
|----------------------------|---------------|---------------|------|-----|------|
|                            | n=47          | n=207         |      |     |      |
| TGO¹                       | 70            | 68            | 0.043| 0.33| 0.90 |
| TGP²                       | 74            | 59            | 0.050| 0.29| 0.91 |
| Alkaline phosphatase       | 78            | 99            | 0.039| 0.90| 0.84 |
| GGT³                       | 93            | 63            | 0.042| 0.25| 0.96 |
| Total bilirubin            | 29            | 97            | 0.050| 0.70| 0.86 |

¹TGO=transaminase glutamino-oxalacetic; ²TGP=transaminase glutamino-piruvic; ³GGT=gama-glutamil transferase *Values given by the ROC curve (Receiver Operating Characteristic); +positive predictive value; *negative predictive value

TABLE 5 - Imaging tests performed (n = 254)

| Exams                      | With choledocholithiasis | Without choledocholithiasis | p    | VPPE | VPN* |
|----------------------------|--------------------------|----------------------------|------|-----|------|
|                            | n=47                     |                            | n=207|     |      |
| USG¹                       | 29 (61)                  |                            | 192 (62) | 0.001| -    | -    |
| Cholelithiasis             | 17 (36)                  |                            | 16 (47) | 0.046| 0.51 | 0.86 |
| Biliary dilatation         | 16 (34)                  |                            | 9 (25)  | 0.064| 0.64 | 0.86 |
| Choledocholithiasis        | 33 (63)                  |                            | 0 (0)   |      |     |      |
| TC²                       | 16 (34)                  |                            | 13 (6)  | 0.001| 0.55 | 0.96 |
| CholangioRNM³               | 14 (29)                  |                            | 2 (1)   | 0.001| 0.87 | 0.96 |

¹USG=ultrasonography; ²TC= abdominal tomography; +positive predictive value; **negative predictive value

ColangioRNM=nuclear cholangioresonance; ¹USG=ultrasonography; ²TC= abdominal tomography; +positive predictive value; **negative predictive value

Ultrasoundography had a sensitivity of 34% and specificity of 95% for the diagnosis of choledocholithiasis (with 95% CI, p=0.46). Regarding the tomography, the results of sensitivity and specificity were 55% and 86% respectively. Cholangioresonance had 73% sensitivity and 91% specificity.

The most used surgical procedure was cholecystectomy, due to 207 patients showed no calculi evidence. Only one cholecystectomy was performed with choledocholithiasis evidence in imaging exams, being held endoscopic retrograde cholangiopancreatography postoperatively.

For patients with choledocholithiasis in imaging, the most widely used laparoscopic procedure was cholecystectomy associated to choledochotomy.

Postoperative complications were higher in the group with choledocholithiasis, with statistical significance (Table 6).

Patients with choledocholithiasis had discharged an average of 9.21 days (variance 7.02) and no choledocholithiasis with an average of 3.71 days (variance 6.94) (p=0.18).

TABLE 6 - Postoperative complications of the operations performed for patients with cholelithiasis and choledocholithiasis (n=254)

| Postoperative complications | With choledocholithiasis | Without choledocholithiasis | p    |
|-----------------------------|--------------------------|-----------------------------|------|
|                            | n=47                     | n=207                       |      |
| Residual calculi            | 3 (6)                    | 0 (0)                       | 0.001|
| Biliary fistula             | 3 (6)                    | 4 (2)                       |      |
| Infection in surgical site  | 4 (8)                    | 11 (5)                      |      |
| Pulmonary complications     | 1 (2)                    | 2 (1)                       |      |
| Urinary complications       | 0 (0)                    | 2 (1)                       |      |
| Death                       | 3 (6)                    | 3 (1)                       |      |
| Others                      | 0 (0)                    | 7 (3)                       |      |
| No complications            | 33 (34)                  | 181 (87)                    |      |

This paper presented homogeneous sample; by gender, it was different from the literature; for age, showed no differences to the already was published. Among the comorbidities, Citra et al refer as associated factors diabetes mellitus, obesity and dyslipidemia with statistical significance, which disagrees with the present study that, although the sample had statistical significance, showed no specific comorbidity related to choledocholithiasis²₄.

Fields et al. (2004) presented a study with 23 cases of choledocholithiasis without cholangitis or acute pancreatitis, which differs from the population studied in this paper²₄.

It was observed that patients with choledocholithiasis showed elevation of bilirubin; but what stood out most was increased GGT. Citra et al found that alkaline phosphatase was altered in 98% of cases, which differs from the present study². Fields et al. (2004) showed similar results, with transaminases changing significantly²₄.

Citra et al showed that ultrasonography had a sensitivity of 73.3% and specificity of 95% for choledocholithiasis. These results conflict with the present study. This discrepancy can be attributed by being the exam operator dependent and that technical difficulty may vary according to the patient body type, which is not addressed in this study²₂.

According to William et al (2009), nuclear magnetic colangiopancreatorensonance has a sensitivity of 85% and specificity of 93%, which corroborates with these findings. These authors present the CT with a specificity of 65-93% which emphasizes the heterogeneity of the studies over computed tomography as diagnostic method for pre-operative choledocholithiasis²₂,²₄.

Choledocholithiasis treatment differs in main bile duct calculi guidelines. William et al (2009) show that patients with it should undergo endoscopic retrograde cholangiopancreatography preferably at the same time of cholecystectomy. In service where this study was prepared this type of therapy is not available; one patient was referred to another hospital for resolution of symptoms after cholecystectomy²₂.

CONCLUSION

Changes in canalicular and transaminase enzymes are suggestive for preoperative choledocholithiasis; GGT showed better sensitivity and alkaline phosphatase greater specificity; ultrasonography and nuclear magnetic resonance cholangiopancreatography showed high specificity.

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