# Predicting the Diagnosis of Choledocholithiasis in Elderly Patients by Assessing Hepatic Functions

# Almohamad Almahmud Tamim\*, Alexey Klimov

Received: 26 April 2021 / Received in revised form: 23 July 2021, Accepted: 04 August 2021, Published online: 22 August 2021

© Biochemical Technology Society 2014-2021

© Sevas Educational Society 2008

#### **Abstract**

Choledocholithiasis occurs most ordinarily, the eventuality of common biliary duct stones increases significantly with the age of patients. Our study aimed to is to preoperatively investigate the levels of liver function indexes and results of diagnostic imaging, and their role in the early diagnosis of choledocholithiasis in elderly patients. This study included patients referred to the surgical department of the V. V. Vinogradov state medical center in Moscow, for the periods between 2018 - 2020. In this study, 127 patients were divided into two groups: the control group (104 patients), cases group (23 patients), and patients without choledocholithiasis intraoperatively, included the patients with choledocholithiasis intraoperatively. Laboratory markers were studied. The sample was congenerous for age and gender. Our results upon admission to hospital show in cases group biliary pancreatitis in 13%, obstructive jaundice in 30.4% and 91.3% abdominal pain in the right hypochondrium, obstructive jaundice was the clinical symptom with statistical significance (p < 0.05). Patients with choledocholithiasis had higher values of the gammaglutamyl transferase, alkaline phosphatase, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, and bilirubin (p < 0.01). The diagnostic imaging for the diagnosis of choledocholithiasis showed that ultrasound imaging had elevated specificity. By studying the changes that occur in the liver enzymes, parallel to results of imaging diagnosis, confirming the diagnosis preoperative choledocholithiasis can be predicted. Gamma-glutamyltransferase showed elevated sensitivity, while alkaline phosphatase showed elevated specificity, ultrasound imaging showed elevated specificity.

**Keywords:** Choledocholithiasis, Elderly, Diagnostic imaging, Canalicular and transaminases enzymes

#### Introduction

Choledocholithiasis occurs most ordinarily, the eventuality of common biliary duct stones (CBD) increases significantly in elderly patients (> 80 years old) and are observed in 33% of all patients with gallbladder calculi. In the Russian Federation,

#### Almohamad Almahmud Tamim\*, Alexev Klimov

Department of Surgery, Peoples' Friendship University of Russia (RUDN University), Moscow 117198, Russian Federation.

\*E-mail: almahmoudtamim@gmail.com

approximately 300,000 cholecystectomies are performed each year (McNicoll *et al.*, 2020; Tamim & Klimov, 2020).

The cholecystolithiasis has many complications includes liver abscesses, cholecystitis, cholangitis, acute pancreatitis, and others. About 2 to 3% of patients will suffer some of these complications within several years of the disease. Thus, Cholecystectomy is recommended for all patients without surgical contraindications (Jones *et al.*, 2021a; 2021b).

Many researchers recommend measuring the levels of alkaline phosphatase in patients with choledocholithiasis (Huh *et al.*, 2016; Khoury *et al.*, 2019), and some others referred that high alkaline phosphatase levels maybe help to determine patients with choledocholithiasis (Yurgaky-Sarmiento *et al.*, 2020). While (Mei *et al.*, 2019) proposed that an integration of the levels of bilirubin and alkaline phosphatase is more sensitive than only alkaline phosphatase levels in differentiation patients with choledocholithiasis from patients with other clinical disorders.

Thus, correct and timely diagnosis is essential for a treatment option. The correlation between laboratory, ultrasound, and clinical standards has a 96-98% sensitivity for diagnosis. Lacking these criteria takes less than a 2% chance of choledocholithiasis (Tozatti *et al.*, 2015; Kuzu *et al.*, 2017).

Our study aims to preoperatively investigate the levels of liver function indexes and results of diagnostic imaging in predicting the diagnosis of choledocholithiasis in elderly patients (Forouzesh *et al.*, 2019; Sargazi & Taghian, 2020).

### **Materials and Methods**

This research was a retrospective investigation of the patients referred to the surgical emergency of the Moscow City Clinical Hospital No.64 (CCH named after V.V. Vinogradov) in Moscow-Russia, for the period from 2018 to 2020.

The study followed the ethical criteria approved by the Ethics Committee in Research of the medical center and the Ministry of Health.

127 patients were divided into two groups: the control group (104 patients), cases group (23 patients), and patients without choledocholithiasis intraoperatively, included the patients with choledocholithiasis intraoperatively. The average age of the



patients was over 75 years, with suspicion or diagnosis of choledocholithiasis, biliary pancreatitis, cholelithiasis, and cholangitis. Age, gender, and clinical symptoms (pain in the upper right part of the abdomen, jaundice, cholangitis, and pancreatitis) were recorded. The following tests have been carried out - total bilirubin, alkaline phosphatase (ALP), glutamic oxaloacetic transaminase (GOT), gamma-glutamyl transferase (GGT), and glutamic pyruvic transaminase (SGPT).

Detecting the choledocholithiasis presence, gallstones, and dilatation of the biliary tract were conducted using diagnostic imaging included: ultrasound imaging and computed tomography (CT). Data were analyzed using (Microsoft Excel 2016) and the statistical program StatPlus v.5 and MedCalc v.19.

#### **Results and Discussion**

The sample was congenerous for gender and age as shown in **Table 1**.

Table 1. Patient distribution according to gender and age

Characteristic		Case group (n= 23)	Control group (n=104)
Gender	Male	14 (60.87%)	68 (65.39%)
	Female	9 (39.13%)	36 (34.61%)
Age average		75±19.54	85±22.64

According to the clinical symptoms upon admission to the hospital, it was observed in the case of group 30.4% with obstructive jaundice, 91.3% with abdominal pain, and 13% with biliary pancreatitis. After comparison of the two groups, it was found that obstructive jaundice was the clinical symptom, which has statistical significance (p < 0.05) (**Table 2**).

**Table 2.** Patient distribution according to the clinical symptoms upon admission to the hospital

Clinical sym	ptoms	Case group (n= 23)	Control group (n=104)
Cholangitis	Yes	5 (27.7%)	2 (1.92%)
	No	18 (78.3%)	102 (98.08%)
Obstructive jaundice		7 (30.4%)	4 (3.8%)
Abdominal pain		21 (91.3%)	101 (97.1%)
Biliary pancreatitis		3 (13%)	90 (86.5%)

Through the results presented in (**Table 3**), it is shown that the levels of glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (SGPT), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), and total bilirubin in patients of the case group are significantly higher than theses in the control group. There were no significant differences in total bilirubin and direct bilirubin levels between the two groups (p < 0.05).

**Table 3.** The results of the enzymatic tests for both the control group and the case group (mean, SD).

Lab test	Case group (n= 23)	Control group (n=104)
GOT (UL)	64.4±73.3	34.8±65.5
SGPT (UL)	86.3±96.8	36.14±61.8
GGT (IU/L).	422±512.5	101±169.4
ALP (UL)	294±224.4	94.6±53.7
Direct bilirubin(µmol/L)	5.25±0.77	4.89±0.64
Total bilirubin (μmol/L)	10.58±2.87	9.89±1.9

Our research results, represented in (**Table 4**) displayed that glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (SGPT), and alkaline phosphatase (ALP) have similar sensitivity, with elevated specificity for alkaline phosphatase. On the other hand, gamma-glutamyl transferase (GGT) presented elevated sensitivity (92.8%) nonetheless low specificity (62.1%) (p < 0.05).

**Table 4.** Results of Receiver Operating Characteristic curve (ROC) of the enzymatic tests, confidence interval (CI) 95%.

Lab test	Sensitivity %	Specificity %
GOT	72.5	69.6
SGPT	76.4	58.7
GGT	92.8	62.1
ALP	79.3	98.7

The results of the diagnostic imaging for the diagnosis of choledocholithiasis, presented in the table (**Table 5**) showed that ultrasound imaging had elevated specificity.

**Table 5.** Results of Receiver Operating Characteristic curve (ROC) of the diagnostic imaging, confidence interval (CI) 95%.

Diagnostic imaging	Sensitivity %	Specificity %
Ultrasound imaging	32	96
Computed tomography (CT)	56	85

In our study, the sample was congenerous for gender and age, it is consistent with what was previously published by (Tozatti *et al.*, 2015; Wang *et al.*, 2019), while results of (Parreira *et al.*, 2004) were different from ours concerning gender. As (Worku *et al.*, 2020) showed that choledocholithiasis cases were accompanied by other causes, such as cholangitis or acute pancreatitis, which is consistent with what was mentioned in this study.

Several studies reported an increase in bilirubin and gamma-glutamyl transferase levels in cases of choledocholithiasis (Tetangco *et al.*, 2016; Khoury *et al.*, 2019; Mei *et al.*, 2019). In the study of (Pereira-Limâ *et al.*, 2000) they found that the alkaline phosphatase was elevated in 74.7% of the patients with choledocholithiasis, which is inconsistent with our research results. Also (Campos *et al.*, 2004) reported similar results, with transaminases varying significantly. In the diagnosis of

choledocholithiasis, ultrasonography showed a sensitivity, specificity of 34% and 95% respectively (Tozatti *et al.*, 2015). This is consistent with the findings of the current study. On the contrary, (Torres *et al.*, 1997) revealed that ultrasound had a sensitivity, specificity of 73.3%% and 95% respectively, for choledocholithiasis, this conflict may be due to dependence on the study operator, and this technical complexity can change depending on the patient's physique (Tozatti *et al.*, 2015).

According to (Orman *et al.*, 2018), the specificity of computed tomography in identifying the presence of choledocholithiasis was 76.9%. These authors present the ultrasonography and magnetic resonance cholangiopancreatography (MRCP) for choledocholithiasis diagnosis with a specificity of 40.8%, 86.4%, respectively. This confirms the heterogeneousness of studies on computed tomography as a diagnostic imaging method for preoperative choledocholithiasis (Costi *et al.*, 2014).

#### Conclusion

In conclusion, we conclude that abnormally levels of glutamic oxaloacetic transaminase, alkaline phosphatase, gamma-glutamyl transferase, glutamic pyruvic transaminase, and bilirubin, can be used as prognostic indicators for preoperative choledocholithiasis in elderly patients. Diagnosis can be confirmed with the help of imaging studies, where ultrasound imaging showed elevated specificity.

**Acknowledgments:** This paper was financially supported by the Ministry of Education and Science of the Russian Federation on the program to improve the competitiveness of Peoples' Friendship University of Russia (RUDN University) among the world's leading research and education centers in 2016-2020.

#### Conflict of interest: None

## Financial support: None

**Ethics statement:** This research followed the ethical criteria recommended by the order of the Ministry of Health of the Russian Federation No. (647n) of 31 August 2016, which was submitted for approval by the Ethics Committee in Research of Moscow City Clinical Hospital.

#### References

- Campos, T. D., Parreira, J. G., Moricz, A. D., Rego, R. E. C., Silva, R. A., & Pacheco Junior, A. M. (2004). Fatores preditivos de coledocolitíase em doentes com litíase vesicular. *Revista da Associação Médica Brasileira*, *50*(2), 188-194. doi:10.1590/S0104-42302004000200037
- Costi, R., Gnocchi, A., Di Mario, F., & Sarli, L. (2014). Diagnosis and management of choledocholithiasis in the golden age of imaging, endoscopy and laparoscopy. *World Journal of Gastroenterology: WJG*, 20(37), 13382-13401. doi:10.3748/wjg.v20.i37.13382

- Forouzesh, M., Valipour, R., Shekari, A., Barzegar, A., & Setareh, M. (2019). Comparison of Methadone Level Measurement by Enzyme Immunoassay with Gas Chromatography–Mass Spectrometry. *Journal of Advanced Pharmacy Education & Research*, 9(4), 105-108.
- Huh, C. W., Jang, S. I., Lim, B. J., Kim, H. W., Kim, J. K., Park, J. S., Kim, J. K., Lee, S. J., & Lee, D. K. (2016). Clinicopathological features of choledocholithiasis patients with high aminotransferase levels without cholangitis: Prospective comparative study. *Medicine*, 95(42). doi:10.1097/MD.0000000000005176
- Jones, M. W., Genova, R., & O'Rourke, M. C. (2021a). Acute Cholecystitis. Endotherapy in Biliopancreatic Diseases: ERCP Meets EUS: Two Techniques for One Vision, 509-516. https://www.ncbi.nlm.nih.gov/books/NBK459171/
- Jones, M. W., Guay, E., & Deppen, J. G. (2021b). Open Cholecystectomy. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK448176/
- Khoury, T., Adileh, M., Imam, A., Azraq, Y., Bilitzky-Kopit, A., Massarwa, M., Benson, A., Bahouth, Z., Abu-Gazaleh, S., Sbeit, W., et al. (2019). Parameters suggesting spontaneous passage of stones from common bile duct: a retrospective study. Canadian Journal of Gastroenterology and Hepatology, 2019. doi:10.1155/2019/5382708
- Kuzu, U. B., Ödemiş, B., Dişibeyaz, S., Parlak, E., Öztaş, E., Saygılı, F., Yıldız, H., Kaplan, M., Coskun, O., Aksoy, A. et al. (2017). Management of suspected common bile duct stone: diagnostic yield of current guidelines. *Hpb*, 19(2), 126-132. doi:10.1016/J.HPB.2016.11.003
- McNicoll, C. F., Pastorino, A., Farooq, U., & St Hill, C. R. (2020). Choledocholithiasis. *StatPearls [Internet]*.
- Mei, Y., Chen, L., Zeng, P. F., Peng, C. J., Wang, J., Li, W. P., Du, C., Xiong, K., Leng, K., Feng, C. L. et al. (2019). Combination of serum gamma-glutamyltransferase and alkaline phosphatase in predicting the diagnosis of asymptomatic choledocholithiasis secondary to cholecystolithiasis. World Journal of Clinical Cases, 7(2), 137. doi:10.12998/WJCC.V7.I2.137
- Orman, S., Senates, E., Ulasoglu, C., & Tuncer, I. (2018). Accuracy of Imaging Modalities in Choledocholithiasis: A Real-Life Data. *International Surgery*, *103*(3-4), 177-183. doi:10.9738/INTSURG-D-16-00005.1
- Parreira, J. G., Rego, R. E. C., Campos, T. D., Moreno, C. H., Pacheco Jr, A. M., & Rasslan, S. (2004). Fatores preditivos de coledocolitíase em doentes com pancreatite aguda biliar. Revista da Associação Médica Brasileira, 50, 391-395.
- Pereira-Lima, J. C., Jakobs, R., Busnello, J. V., Benz, C., Blaya, C., & Riemann, J. F. (2000). The role of serum liver enzymes in the diagnosis of choledocholithiasis. *Hepato-Gastroenterology*, 47(36), 1522-1525. https://europepmc.org/article/med/11148992
- Sargazi, M., & Taghian, F. (2020). The Effect of Royal Jelly and Exercise on Liver Enzymes in Addicts. *Archives of Pharmacy Practice*, 11(2), 96-101.
- Tamim, A. A., & Klimov, A. (2020). Study of the Features of Choledocholithiasis in Elderly Patients. *Journal of Biochemical Technology*, 11(4), 65-68.

- https://jbiochemtech.com/article/study-of-the-features-of-choledocholithiasis-in-elderly-patients
- Tetangco, E. P., Shah, N., Arshad, H. M. S., & Raddawi, H. (2016). Markedly elevated liver enzymes in choledocholithiasis in the absence of hepatocellular disease: case series and literature review. *Journal of investigative Medicine High Impact Case Reports*, 4(2), 2324709616651092. doi:10.1177/2324709616651092
- Torres, O. J. M., Cintra, J. C. A., Cantanhede, E. B., Melo, T. C. M., Macedo, E. L., & Dietz, U. A. (1997). Ultrasonography value and of alkaline phosphatase in choledocholithiasisdiagnosis. *JBM*, 73(4), 42-46.
- Tozatti, J., Mello, A. L. P., & Frazon, O. (2015). Predictor factors for choledocholithiasis. *ABCD. Arquivos Brasileiros de Cirurgia Digestiva (São Paulo)*, 28(2), 109-112. doi:10.1590/S0102-67202015000200006
- Wang, C. C., Tsai, M. C., Wang, Y. T., Yang, T. W., Chen, H. Y.,

- Sung, W. W., Huang, S. M., Tseng, M. H., & Lin, C. C. (2019). Role of cholecystectomy in choledocholithiasis patients underwent endoscopic retrograde cholangiopancreatography. *Scientific Reports*, *9*(1), 1-7. doi:10.1038/S41598-018-38428-Z
- Worku, M. G., Enyew, E. F., Desita, Z. T., & Moges, A. M. (2020). Sonographic measurement of normal common bile duct diameter and associated factors at the University of Gondar comprehensive specialized hospital and selected private imaging center in Gondar town, North West Ethiopia. *PloS* one, 15(1), e0227135. doi:10.1371/journal.pone.0227135
- Yurgaky-Sarmiento, J., Otero-Regino, W., & Gómez-Zuleta, M. (2020). Elevated transaminases: a new tool for the diagnosis of choledocholithiasis. A case control study. *Revista Colombiana de Gastroenterologia*, 35(3), 319-328. doi:10.22516/25007440.446