# Frequency of Opium Addiction among Inpatients and Outpatients with Common Bile Duct Stones

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# **ABSTRACT**

#### Background

Common bile duct (CBD) stone is the most common disorder in the biliary tract, which may lead to hospital admission. Opium addiction is one of the most challenging social and health issues in many societies. An important side effect of opium addiction is the Oddi's sphincter spasm; i.e., it is likely that the prolonged stasis of bile acid increases the risk of gallstone formation in the CBD.

#### Materials and methods:

This cross-sectional study was done from April 2019 to November 2019 in Ghaem Hospital in Mashhad, Iran. 400 patients aged 20-80 years were enrolled. All patients had a definite diagnosis of CBD stones and were candidates for endoscopic retrograde cholangiopancreatography (ERCP). Demographic information of patients, history of underlying diseases, liver laboratory disorders, the existence of concomitant gallbladder stones, and opium addiction information were collected.

#### Results

The average age of the patients with opium addiction was 65.12 years, and it was significantly higher than the mean age of the patients (61.41 years) without opium addiction (P=0.01). 74.3% were hospitalized, and 25.3% were outpatients. 35.5% of the patients were men, and 64.5% were women. Our study showed that 41.5% of the patients with CBD stones were opium-addicted. The average CBD stone size in patients with opium addiction (10.15±4.85 mm) was larger than in patients without opium addiction, but a t test showed that this difference was not significant (P = 0.9).

#### Conclusion

In this study of patients with CBD stones referred for ERCP, we observed a high prevalence of opium addiction in patients with CBD stones.

Keywords: Common bile duct, ERCP, Opium addiction

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#### INTRODUCTION

Gallbladder disorders affect millions of people worldwide every year. Common biliary tract diseases include gallstones, common bile duct (CBD) stones, and cholecyctitis (1). The CBD diameter differs from 6 mm to 12 mm based on different studies. It should be noted that the maximum size of the CBD diameter depends on the location, method of measurement, and age. Gallstones are also known as one of the factors that affect the size of the CBD (2, 3).

CBD stone is the most common disorder in the biliary tract, which may lead to hospital admission (4). It imposes a significant therapeutic-economic burden on the health system (5, 6). Evidence suggests that the incidence of gallstones has increased in recent decades (7). There are several methods for the diagnosis of CBD stones, including abdominal wall ultrasonography or endoscopic ultrasonography. Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure performed with special endoscopes, during which after an injection of contrast into the bile ducts, images are taken. It can also remove the bile duct stones and act as a therapeutic option (8).

According to the evidence, opium addiction is one of the most challenging problems in most societies, including Iran. Due to the proximity of Iran to Afghanistan, as the largest producer of opium in the world, opium addiction has a very high prevalence in Iran despite all campaigns against it (9).

Many patients mistakenly use opium as a pain reliever and as a treatment for hyperlipidemia, hypertension, diabetes, and other chronic diseases (10). One important side effect of opium addiction is Oddi's sphincter spasm. Therefore, over time due to bile stasis, the diameter of the duct increases (11, 12). According to studies on the dilation of the CBD, it is likely that the prolonged stasis of bile acid increases the risk of gallstone formation in the CBD. There seems to be a link between opium consumption and CBD stones.

In a study of 119 patients with Oddi sphincter disorder, Alizadeh and colleagues found that eight patients were opium addicted. Serum concentrations of liver aminotransferases and alkaline phosphatase were similar between the two groups. This study showed

opium addiction could increase the probability of papilla ulcerative and tumoral changes in patients with dysfunction of Oddi sphincter (13).

In the study of Dadpour and colleagues, the relationship between CBD diameter and opium addiction was investigated. The results of ERCP and abdominal ultrasonography of 40 patients with addiction were gathered. As opium used by patients with addiction has various degrees of impurity, the study demonstrated that higher opium purity induced more CBD dilatation (14).

The number of studies on the prevalence of addiction in patients with CBD stones is very limited, and only a few studies have examined the effect of addiction on the diameter of the CBD. Therefore, in the present study, we aimed to assess the frequency of opium addiction in patients with CBD stones to investigate the possible relationship between CBD stones and opium consumption.

## MATERIALS AND METHODS

## **Patient selection**

This cross-sectional study was done from April 2019 to November 2019 in Ghaem Hospital in Mashhad, Iran. A total of 400 patients (outpatients and inpatients) aged 20-80 years were enrolled. All patients had a definite diagnosis of CBD stones with ultrasonography and were candidates for ERCP.

## Measuring the data

A checklist was designed to collect the demographic and background information of patients, including sex, age, weight, history, underlying disease, CBD stone history in the first-degree relatives, liver disorders, history of concomitant gallbladder stones, and opium addiction information. No extra intervention was performed for patients except the usual treatment process.

The size of the stones was estimated through ultrasonography. When the stones were removed during ERCP, based on the size of the forceps biopsy opening, the dimension of the stones was estimated.

## Statistical analysis

We statistically analyzed the prevalence of opium

addiction and its association with the occurrence of CBD stones. To investigate the relationship between the qualitative variables, Chi-square test, and for the quantitative variables, *t* test was applied after confirming that data distribution was normal. P values<0.05 were considered statistically significant.

The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences with the registration number IR.MUMS.MEDICAL. REC.1398.501.

#### RESULTS

In this study, 400 patients with CBD stones referred for ERCP were evaluated. Out of the patients examined, 297 (74.3%) were hospital inpatients, and 101 (25.3%) were outpatients. Besides, 142 (35.5%) patients were men, and 258 (64.5%) were women. Table 1 summarizes the demographic data of the patients.

Our analysis showed that there were 166 (41.5%) patients with opium addiction. The type of addiction among patients is specified in <u>Table 2</u>.

Of the patients, 235 (58.8%) had gallbladder stones, 75 (18.8%) had a history of a previous cholecystectomy, and 273 (68.3%) patients had liver test disorders. The frequency of associated underlying diseases is shown in Table 3. Hypertension was the most common among our patients.

Table 1: Demographic data of the patients

Patient	Category	Frequency	Frequency percent
Sex	Male	142	35.3%
	Female	258	64.5%
Hospitalization	Inpatient	297	74.3%
	Outpatient	101	25.3%
Average weight (kg)	With addiction	61.8	-
	Without addiction	63.7	-

Table 2: The frequency of opium abuse, smoking, nas, and alcohol consumption in the patients

Addiction	Frequency%
Opium	41.5%
Cigarette smoking	13%
Nas	4.5%
Alcohol	1%

The average age of the patients with opium addiction was 65.12 years, and it was significantly higher than the mean age of patients (61.41 years) without opium addiction (P = 0.01). Besides, the average CBD stone size in patients with opium addiction ( $10.15\pm4.85$  mm) was larger than in patients without opium addiction, but a t test showed that this difference was not significant (P = 0.9).

Comparing the sex distribution, the Chi-square test results showed a statistically significant difference between men and women (P = 0.001), as opium addiction was more common among men. However, we found no significant association between the occurrence of gallbladder stones and addiction in patients with opium addiction (P = 0.7), and no statistically significant association between patients with co-morbidities and opium addiction (P = 0.7) either.

## DISCUSSION

In this study, the frequency of opium addiction in 400 patients with CBD stones referred for ERCP was evaluated. We found that 166 (41.5%) patients had opium addiction, which indicates a high prevalence of opium addiction in patients with CBD stones. Comparing it with the prevalence of opium addiction in the general population of Iran, reported in other studies (3% and 16.4%) it indicates a significant difference in the prevalence of addiction between these patients and the general population (15, 16).

Considering the mechanism of Oddi's sphincter spasm caused by opium and biliary stasis after a long time, this research raised the question that there could be a link between opium use and the formation of CBD stones. As the long-term use of opium and its derivatives can increase the diameter of the ducts by retaining the bile, identifying this group of patients and giving them awareness can be rewarding.

The prevalence of gallbladder stones was 41.9% in patients with opium addiction and 58.1% among patients without opium addiction, but the difference was not

Table 3: Frequency of associated underlying diseases

Disease	Frequency	Frequency%
Diabete	21	12.1%
Hypertension	60	34.7%
Coronary vascular disease	19	11%

statistically significant (P=0.7). This may indicate the role of stasis, due to opium addiction, in the formation of CBD stones more than gallbladder stones. The reason that only 68.3% of the patients in our study had abnormal liver enzymes could be the partial obstruction of CBD. The present findings are in line with previous reports on the dilating effects of opiates on CBD. In fact, the use of opium for a long period of time results in CBD dilatation by inducing sphincter spasms (14). Dadpour and colleagues in their study examined the relationship between CBD diameter and opium addiction, while all their patients had opium addiction. However, in our study, only the prevalence of opium addiction in patients with CBD stones was investigated.

The mean age of the patients with and without opium addiction was 65.12 and 61.41 years. Even though the age difference seems small, a statistical analysis of the mean age between the two groups showed a significant difference (P=0.01), as also reported in other studies (9). This observation indicates an increase in the prevalence of CBD stones by aging as well as by opium addiction. These findings can be justified, given that aging is known to be one of the risk factors for gallstones (17). Therefore, in investigating the effect of opium addiction on the formation of CBD stones, there are several factors to consider, including age and the duration of opium use.

CBD dilation in patients with opium addiction can mislead physicians when facing liver diseases and bile ducts disorders. Dilated CBD is attributable to lesions such as stones, stenosis, and tumors. Several paraclinical options exist for the diagnosis of the etiology, which are mostly aggressive, time-consuming, and costly. They may also result in misdiagnosis and unnecessary interventions. Thus, if the physician is aware that opium addiction itself can cause dilation of the bile ducts, the diagnosis could be simpler, faster, and cheaper. Although Alizadeh's study showed that opium use could increase the probability of papilla ulcerative and tumoral changes (13), in our study, none of the 400 patients with CBD stones evaluated with ERCP showed evidence of bile duct malignancy. This indicates a very low ultrasonography error in differentiating gallstones from malignancy, and indicates the suitability of this tool for initial examination.

In this study, 59.2% of men and 31.8% of women

had an addiction, and this difference was statistically significant (P=0.001). In various studies, the prevalence of CBD stones in women was higher than in men (1-3). The higher prevalence of CBD stones in women may be due to factors such as pregnancy, sex steroids, and the use of exogenous steroids (20,21). We found a significant association between sex and opium addiction.

The results of the present study could lead to further studies on the relative prevalence of opium addiction in patients with CBD stones to reveal the side effects of opium and to understand the relationship between opium abuse and damage to various organs of the body. Our findings could also help to inform society, prevent drug abuse, and to improve treatment results to eventually increase the quality of life.

#### Limitations

This study was conducted in a single center, so the results cannot accurately be generalized. Further multicenter studies with a larger population are therefore recommended.

#### CONCLUSION

It was found that opium addiction among patients with CBD stones is significantly higher than the addiction rate in the general population. This could indicate a possible relationship between opium abuse and the formation of biliary stones. To prove this association, more extensive studies are required.

### CONFLICT OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

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