



## Case report

## Pearl-white gallstones: A report of a case and a chemical analysis by FTIR and XRD

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## ARTICLE INFO

## Keywords:

Pearl-white gallstones

FTIR

XRD

Cholesterol

## ABSTRACT

**Introduction:** Gallstones' color is usually yellow, brown, black or more commonly a mixture of two or more of these colors in different proportions, depending on their composition, with yellow being the most commonly encountered color. Pearl-white gallstones are a very rare entity that has not been studied and reported sufficiently.

**Case presentation:** Our patient is a 44-year-old lady who was suffering from recurrent attacks of epigastric and right hypochondrial abdominal pain that was aggravated by consumption of fatty meals. Ultrasound Imaging revealed multiple gallbladder stones. After an elective cholecystectomy unusual pearl-white gallstones were found inside a distended gallbladder filled with transparent thick fluid.

**Chemical analysis:** To evaluate the chemical composition of these stones Fourier-transform infrared (FTIR) spectroscopy and X-Ray Diffraction (XRD) tests were performed and revealed that these stones are composed of cholesterol (99.6%) and calcium carbonate (0.4%).

**Discussion:** Gallstones are bile depositions of a solid consistency formed inside the gallbladder. Cholesterol, bilirubin, and other substances are involved in the composition of different kinds of gallstones. The presence of gallstones alone inside the gallbladder is usually presented as colicky abdominal pain. Cholecystectomy is a simple surgical removal of the gallbladder from its bed and is the definitive treatment of gallstone disease.

**Conclusion:** Pearl-white gallstones are rarely encountered and lack information about their pathogenesis, thus prompting further evaluation and studying.

### 1. Introduction

Gallstones are solid stone-like objects formed as deposits of bile in the gallbladder or bile ducts that vary in size, shape, and color [1]. They are mainly composed of cholesterol, bilirubin, or substances like calcium salt precipitates [2]. There are a number of classifications for gallstones based on their components, the most common of which are pure cholesterol stones which are mainly composed of cholesterol, pigment stones which are mainly composed of bilirubin, and mixed composition stones which are composed of mixtures of bilirubin, cholesterol and calcium salts in different proportions [3–5]. The most common color of gallstones is yellow. However, based on the proportion of substances forming the gallstones, their colors may vary and range between yellow, brown, and black [6,7]. Interestingly, we report the first case of pearl

white gallstones in Jordan and the Arab population that were discovered after a laparoscopic cholecystectomy in a 44-year-old female. This case report has been reported in line with the SCARE Criteria [8].

### 2. Case presentation

A 44-year-old female, with a free past medical and surgical history, presented to the Outpatient Department (OPD) with recurrent episodes of epigastric and right hypochondrial pain radiating to the right shoulder for two weeks duration. The pain was associated with nausea and vomiting and was exacerbated by eating fatty food. An ultrasound was done and revealed multiple hyperechoic gallstones with posterior acoustic shadowing (Fig. 1). Ten days after the diagnosis, the patient underwent an elective laparoscopic cholecystectomy. The surgery was

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<https://doi.org/10.1016/j.ijscr.2021.106449>

Received 5 September 2021; Received in revised form 21 September 2021; Accepted 21 September 2021

Available online 24 September 2021

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**Fig. 1.** Ultrasonographic imaging showing multiple hyperechoic gallstones with posterior acoustic shadowing.

performed under general anesthesia. An infra-umbilical incision (open method) was used to introduce the first trocar (optic port) and then insufflations followed to create pneumoperitoneum. Epigastric trocar and 2 other 5-mm subcostal trocars at midclavicular and anterior axillary lines were inserted. A distended gallbladder was noticed. Aspiration revealed a large amount of transparent sticky fluid (mucocele). Sharp and blunt dissection in Calot triangle was done to reveal the cystic duct and artery, which were clipped proximally and distally and cut in-between. The gallbladder was dissected from its bed and retrieved outside. Upon opening the gallbladder, pearl-white gallstones were noticed (Fig. 2). The obtained gallstones were not saved or placed in any kind of reagents.

The whole procedure was thoroughly explained to the patient. The post-operative course went smoothly without any complications. The patient was seen in the clinic two weeks later and was doing well.

### 3. Chemical analysis

#### 3.1. Materials and methods

For this study, we used Fourier-transform infrared (FTIR) spectroscopy and X-Ray Diffraction (XRD) analysis to identify the main composition material of the gallstones. The gallstones were first cleaned



**Fig. 2.** Pearl-White gallstones.

by distilled water to remove any residual or foreign materials. Then they were crushed into fine powder.

#### 3.1.1. Fourier-transform infrared (FTIR) spectroscopy

Fourier-transform infrared (FTIR) technique is used to obtain the infrared spectrum of transmission or absorption of a sample to identify the organic compounds in the sample by identifying the different functional groups. The technique has been widely used in medicine since the 1960s [9,10].

In our study, the samples were homogenized with KBr and prepared in a pellet shape. FTIR analysis were performed using FTIR spectrometer of Bruker Tensor 27 FT in the spectral region  $400$  to  $4000\text{ cm}^{-1}$  with a spatial resolution of  $4\text{ cm}^{-1}$ . About  $5\text{ mg}$  of the fine powder was mixed with KBr and pressed into disk shape for measurements. The FTIR spectra were compared with IR spectra database and with other data reported in other sources.

#### 3.1.2. X-Ray diffraction (XRD)

X-ray powder diffraction (XRD) technique was used to identify the crystalline phase of the stones. Powder material of the stones were compressed in the holder and measured using continuous scanning mode on PANalytical diffractometer system (X'Pert PRO) using Cu tube and using diffraction intensities from  $2\text{Å}$  to  $60\text{Å}$ .

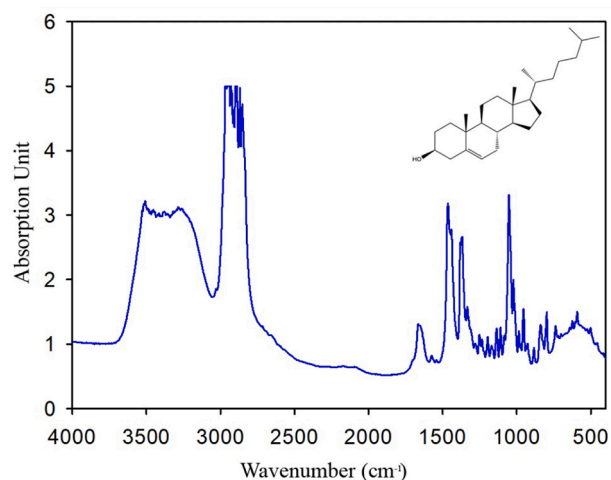
### 3.2. Results

#### 3.2.1. Fourier-transform infrared (FTIR) spectroscopy

The analysis of the spectrum is based on comparison with standard Control spectra from the Literature spectra of pure cholesterol, bilirubin, and calcium carbonate standard [9,11–13].

The FTIR spectrum in (Fig. 3) shows that the composition of the stones is dominated by cholesterol crystal. The presence of Cholesterol is characterized by broad and intense band attributed to O–H stretching around  $3420\text{ cm}^{-1}$  and a strong peak around  $2892$  due to  $\text{CH}_2$  symmetric stretching vibration. Other peaks attributed to cholesterol molecule is the double band ( $\text{C}=\text{C}$ ) in the second ring of cholesterol molecule is detected at  $1664\text{ cm}^{-1}$ . Finally, the cholesterol molecule is identified through the peak at  $1465\text{ cm}^{-1}$  which is related to asymmetric stretching vibration of  $\text{CH}_2$  and  $\text{CH}_3$  groups and the peak at  $1381\text{ cm}^{-1}$  which is attributed to the  $\text{CH}_2$  and  $\text{CH}_3$  bending vibration of cholesterol molecule.

The Calcium bilirubinate was hard to be identified in the stones. Usually, it is characterized by doublet absorption peaks at  $3398\text{ cm}^{-1}$



**Fig. 3.** Fourier-transform infrared (FT-IR) spectrum of the gallstone with the main fingerprint in the region  $4000$ – $400\text{ cm}^{-1}$ . Inset is the chemical structure of cholesterol.

(sharp peak) and  $3264\text{ cm}^{-1}$  (broad peak), both peaks are attributed to N—H stretching vibration of the pyrrole groups. Another characteristic band for Calcium bilirubinate is at  $1254\text{ cm}^{-1}$  which is also attributed to (C—O) stretching or C—N stretching. A triplet peaks at 1663, 1624, and  $1566\text{ cm}^{-1}$  that identifies Calcium bilirubinate also is missing in the FTIR spectrum.

### 3.2.2. X-Ray diffraction (XRD)

X-Ray Diffraction (XRD) data was analysed using Match software with COD Inorganic 2011.06.14 database to identify the main crystalline phases in the stones. (Fig. 4) shows the XRD patterns for the stones. The intense reflection peaks indicated to the existence of crystallised cholesterol in its two phases: anhydrous and monohydrate. Dominant peak of anhydrous cholesterol at  $2\theta$  around 5.1 and 7.66, and 14.76. The monohydrate is indicated by  $2\theta$  at 15.62, 16.18, 17.48, 18.16, 19.10, 20.58 and  $23.12^\circ$ . Calcium carbonates are detected by the main peak at  $2\theta = 43.8$ .

In conclusion, the gallstones were composed of Cholesterol molecules based on the results of FTIR and XRD analysis. The XRD showed that the cholesterol is dominant with 99.6% and only 0.4% of calcium carbonates.

## 4. Discussion

Gallstones were described firstly by Antonio Benivenius in 1507 and are defined as solid bile deposits in the form of abnormal masses in the gallbladder or biliary tract that vary in size, shape, color, and composition depending on the solubility and saturation of composing substance [14,15]. Gallstones are composed mainly of cholesterol, bilirubin, phospholipids, mucopolysaccharides, glycoproteins, and calcium phosphate, bilirubinate, carbonate, and palmitate [16–19].

Gallstones are generally found in 10–15% of adult population [20]. In the United States, gallstone disease affects 14.2 million females (16.6%) and 6.3 million males (7.9%) ranging between 20 and 70 years of age, with an incidence rate of 0.63/100 persons each year and a mortality rate of 0.6% [20–22].

A variety of mechanisms stand behind the pathophysiology of gallstones such as bile super-saturation, alteration of bile composition, gallbladder mucus overproduction, biliary stasis, and decreased gallbladder motility [23,24].

Several factors are responsible for the increased incidence of gallstone disease. Elevated estrogen levels related to pregnancy, combined oral contraceptives use, and hormonal therapy have been reported to increase the levels of cholesterol in bile and decrease the motility of the gallbladder [25,26]. Increased age over the age of 40 [27,28], dietary

choices represented by increased fat intake, refined sugars, and low fiber diets have demonstrated an association with the prevalence of gallstone disease [29,30]. Moreover, rapid weight loss, physical inactivity, obesity, insulin resistance, and type II Diabetes Miletus (DM) play major roles in assessing the formation of gallstones [31–34].

Gallstone disease may present as an abdominal, shoulder, or back-pain, fever, nausea, and vomiting [35–38]. Jaundice and dark urine may occur because of Common Bile Duct (CBD) obstruction leading to the entry of bilirubin into the bloodstream [39,40]. Moreover, scanty bile secretions in small bowels caused by CBD obstruction may lead to pale stool [41].

Such disease may complicate into acute cholecystitis [42], acute cholangitis [43], pancreatitis as a result of pancreatic duct obstruction [44], cholecystoenteric fistula between an inflamed gallbladder and adjoining part of the gastrointestinal tract [45], Bouveret's syndrome which is known as bowel obstruction by large gallstones in the duodenal bulb [46], gallbladder empyema (suppurative cholecystitis) [47], and gallbladder cancer [48].

Abdominal ultrasound is considered the most common used method of diagnosis of the presence of gallstones as it has the sensitivity of 90–95% [49,50]. Many other methods are used but are less frequent than abdominal ultrasound such as Computed Tomography (CT), Endoscopic Retrograde Cholangiopancreatography (ERCP), hepatobiliary iminodiacetic acid (HIDA) scan, or Magnetic Resonance Cholangiopancreatography (MRCP). Also, sometimes blood tests can be useful in the diagnosis of such cases [51–54].

Symptomatic gallstones are treated by the surgical removal of the gallbladder either laparoscopically, or by an open cholecystectomy [55,56].

Gallstones are divided into many types in the medical literature but mainly divided into three categories based on their cholesterol content; cholesterol gallstones, which represent 75% of all gallstones with a yellow color and are mostly composed of cholesterol, pigmented gallstones representing 20% of all gallstones and are usually black or brown in color, and mixed composition stones representing 5% of gallstone types [59–62].

A publication entitled “A comparative study of gallstones from children and adults using FTIR spectroscopy and fluorescence microscopy” by Kleiner et al., studied the chemical characteristics of gallstones obtained from 21 children and 67 adults. The stones that went under FTIR spectroscopy varied in color, shape, and size, but the emphasis was on the composition of black, brown and green stones. In the study green stones were described as being similar to white stones in having a very high content of cholesterol [63].

Stoner et al. published a case report named “Pearl-White Gallstones Causing Choledocholithiasis” in 2018; the authors presented a rare case of white gallstones retrieved from the common bile duct during ERCP that involved sphincterotomy and balloon extraction. The reasons behind the bizarre white color of the stones and their chemical components were not discovered [64]. Our chemical analysis showed that pearl-white gallstones are composed mainly of cholesterol (99.6%) mixed with a small amount of calcium carbonate (0.4%).

## 5. Conclusion

Pearl-white gallstones are very rarely encountered. Our study found that these stones are composed mainly of cholesterol just like other types of gallstones. The cause and pathogenesis of such stones is not reported yet in literature. So, further attention should be focused on such entities.

### Source of funding

None.

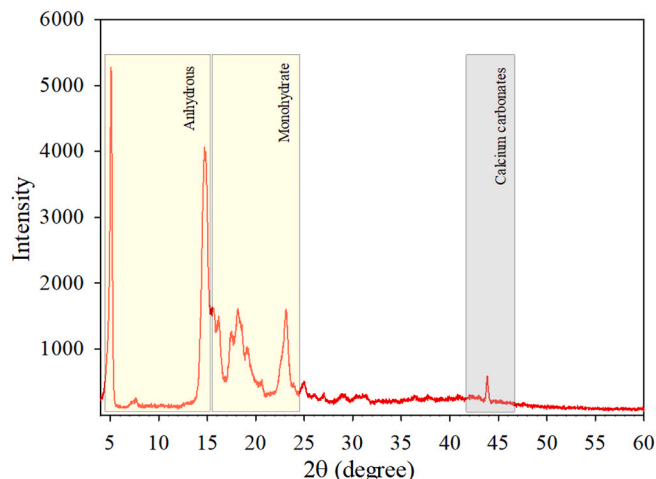


Fig. 4. XRD analysis for the gallstones.

## Ethical approval

Ethical approval for case reports and case series are waived according to the ongoing regulations of Yarmouk university.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal on request.

## Author contributions

R.D and A.A: Case report design and patient medical and surgical care.

R.D and S.A and M.A and F.H: Wrote the initial draft of the case report.

S.A.K and S.A and M.A: FTIR and XRD analysis of the stones.

R.D and A.A: revised the manuscript.

All authors read and approved the content of the submitted case report.

## Research registration

This case report is not eligible for obtaining a research registry since it only contains a report of a known entity with no new surgical or medical interventions.

## Guarantor

Mohammad Araydah.

## Availability of data and materials

All data related to the outcome are included in the manuscript. Mentioned video can be found in the supplementary materials.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

All authors declare that they have no conflict of interest.

## Acknowledgments

We want to thank our patient for consenting to the publication of the article.

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