



# Analysis of the Incidence of Risk Factors for Cholelithiasis in Patients Younger than 40 Years Who Underwent Cholecystectomy at the Ricardo Baquero Gonzalez Hospital

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## Research Article

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## Abstract

**Objective:** This study analyzes the incidence of risk factors for the development of cholelithiasis in patients younger than 40 years who underwent cholecystectomy.

**Methods:** Retrospective study.

**Results:** showed that the sample was 151 patients; 70% are female and 30% male. 41% of patients have an age under 40 years old. In the risk factors, 42% of patients had family history of gallstone, 40% of the women in the sample use oral contraceptives and 40% of the patients are overweight.

**Conclusion:** this study concluded that the cases of cholelithiasis are appearing at younger ages, than they used to be before. There was a high incidence of cases of gallstones in those women who used oral contraceptives or other hormonal contraceptives. In addition, the investigation observed an increase of incidence of gallstones in patients who are not within the risk groups, such as women younger of 40 years, in normal weight and with few pregnancies.

**Keywords:** Cholelithiasis; Gallstone; Risk factors; Gallbladder

## Introduction

Cholelithiasis is one of the main problems that affect millions of people in the world. Gallbladder stone formation is the result of a complex interaction between genetic and non-genetic factors [1]. The gallbladder is an organ in the form of an oval sac whose function is to store and concentrate bile, which subsequently passes through the cystic duct towards the main bile duct and then to the second portion of the duodenum. It measures between 7

to 10 cm long and can store between 30-50 cc of bile [2]. Bile contains between 90% and 95% water, along with bilirubin, cholesterol, bile acids and electrolytes [3,4]. Most people with cholelithiasis are asymptomatic, presenting an annual risk of 2 - 4% to develop symptoms and 0.7 - 3% to develop complications, while those who are symptomatic present complications in 30%, the most frequent being acute cholecystitis, pancreatitis, cholangitis, choledocholithiasis [2]. Gallstones constitute one of the disorders of the digestive system that are most frequently treated in primary care,

with cholecystectomy being the most common surgical intervention. Geographically, there are notable differences in the incidence of this pathological entity, due to environmental and dietary causes. As for the types of gallstones, these can be pigmentary or cholesterol, although there are also mixed stones. Sometimes the expression "bile sludge" is also used to refer to particles with a diameter of less than 2mm<sup>3</sup>. There are 3 types of stones that can develop in the gallbladder or in the bile duct, cholesterol stones being 75% and pigment stones 25%, black being 20% and brown being 5% [1]. Risk factors can be genetic and non-genetic. It's very important to know the interaction between metabolic alterations, lifestyle and genetic factors for the development of gallstones in order to take preventive actions, to reduce its incidence and complications. The main risk factors are mentioned and briefly described below [4].

- Age: Increases with age.
- Gender: Predominantly female.
- Race: Higher prevalence in Caucasians and people of Hispanic origin.
- Body Mass Index:  $\geq 30\text{kg}/\text{mt}^2$ .
- Weight Reduction:  $>1.5\text{ kg}/\text{week}$ . Pregnancy.
- Diseases Of The Ileum: Crohn's disease and ileal resection.
- Diabetes Mellitus: Type 1 and 2.
- Organ Transplant: Kidney and bone marrow.

### Drugs

Oral contraceptives, Ceftriaxone; Bezafibrate; Somatostatin analogues [5,6].

Gallstones were a pathology that mainly affected adult women, around 40 to 50 years old. Currently, an increased incidence of gallstones has been observed in younger people [7]. For this reason, the authors wondering why, even though the risk factors for its development remain the same, a marked increase in the incidence is being seen in patients younger than 40 years.

### Methods

A retrospective study design during the period, from 1 January 2019 to 15 December 2021, was conducted at the Dr. Ricardo Baquero Gonzalez hospital, Caracas, Venezuela. The objective of the research was to analyze the incidence of risk factors for the development of gallstones in patients younger than 40 years who underwent cholecystectomy. For a population of 365 medical records of patients who underwent open or laparoscopic cholecystectomy, the sample consisted of 151 medical records of patients younger than 40 years. The exclusion criteria were those medical records

of patients  $\geq 40$  years. As study variables were considered risk factors classified as: age, sex, weight, use of tobacco, pre-existing pathologies, fiber and saturated fat intake and in women the use of oral contraceptives and the number of pregnancies. Variable definition

- Age: Expressed in years.
- Gender: Corresponds to the sex of the patient.
- Weight: Expressed in the normal, overweight and obese categories, according to the body mass index (BMI).
- First-Line Family Factors: Understood family history of gallstones. Use of tobacco.
- Pre-Existing Pathologies: Pathologies such as liver cirrhosis or diabetes mellitus.
- Diet: Measured in terms of the frequency of consumption of saturated fat and fiber.
- Use of Oral Contraceptives: Collects the frequency of patients who refer to their use.
- Number of Pregnancies: It is the number of times the patient was pregnant.

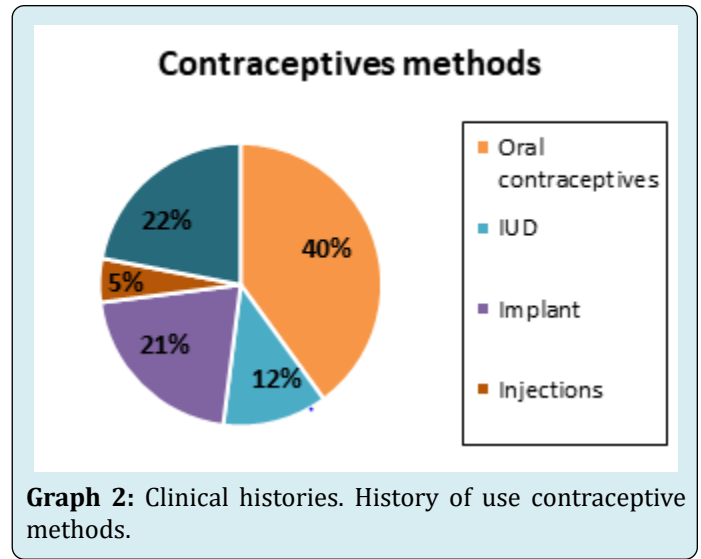
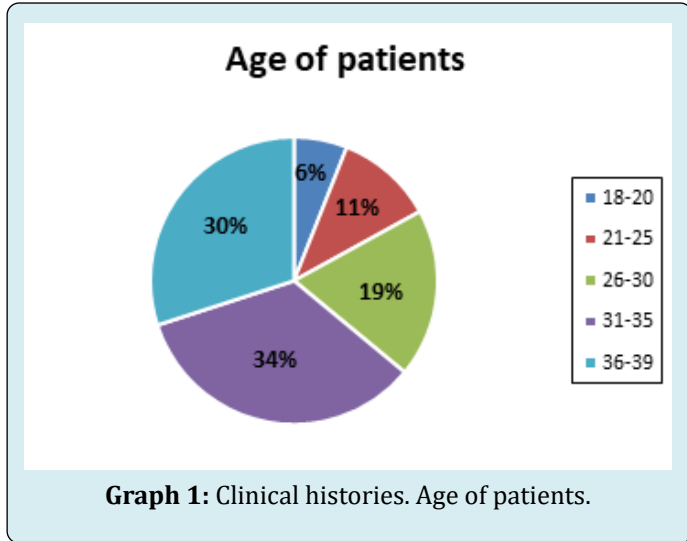
The data was classified considering the variables defined for the investigation. The data was processed using the Microsoft Excel program, for which different tables were created taking the study variables as criteria. The data analysis was using the Excel formula's function, the absolute frequency (ni), its percentage and its graphic representation were determined for the different variables of the study. Descriptive statistics were used for data analysis, considering those variables that presented a higher absolute frequency. Being a descriptive work and incidence of certain factors, no statistical correlation was made to establish its relative risk in the appearance of gallstones.

### Results

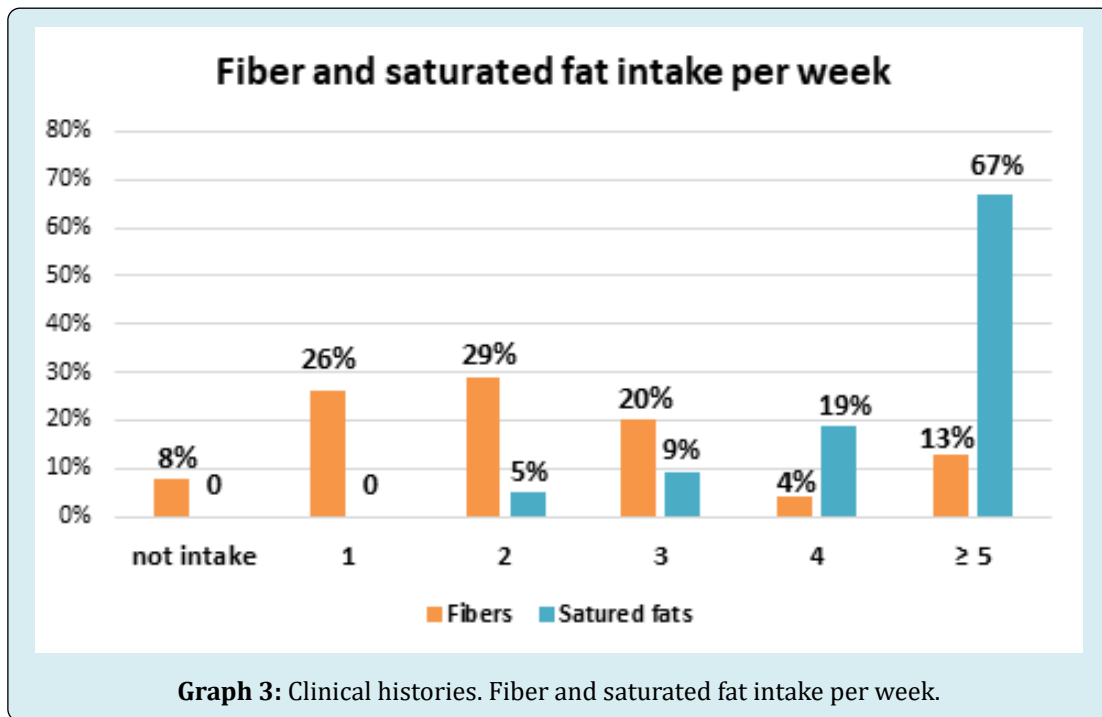
For a sample of 151 patients, the investigation showed the following results. 70% of gallstone cases occurred in female patients, while only 30% of cases occurred in male. Regarding the age of the patients in the sample, the study indicated that 41% were younger than 40 years. Incidence between 31 and 35 years were 34%, while 30% were between 36 and 39 years. The remaining 36% were patients  $\leq 30$  years. The rest of the population for 59% was  $\geq 40$  years Graph 1.

On the other hand, it was found that 46% of patients with gallstones had a normal weight and 40% of them had overweight. Finally, the remaining 14% of the patients had obesity. The results showed that 58% of the patients did not report a family history of gallstones, while 42% did report any family history. About toxic habits, it was found that 21% of patients consume tobacco. On the other hand, 79%

of patients do not report having harmful habits. Finally, no cases of diabetes mellitus or liver cirrhosis were detected. The investigation showed that 40% of the patients with gallstones have a history of using oral contraceptives. On the other hand, 38% of the patients used non-oral contraceptive methods and 22% of the patients did not use any contraceptive method Graph 2.

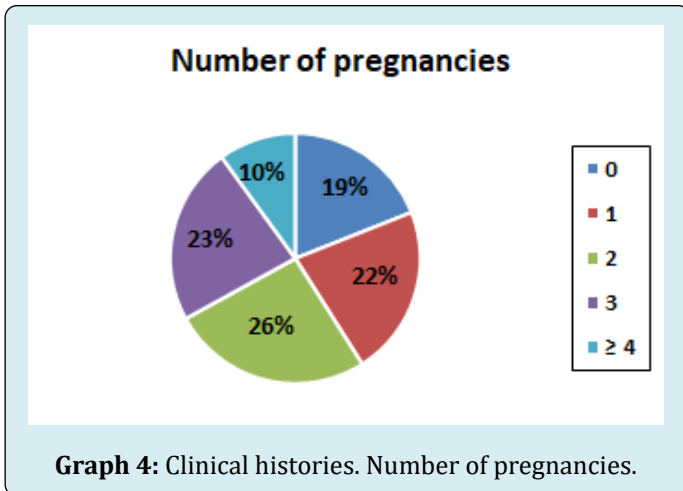


The results showed that only 13% of the patients consumed fiber five times or more a week, while 79% of the patients did so between one and four times a week, the remaining 8% reported not eating fiber. See graph 3. This study obtained as result that 67% of the patients consumed saturated fats five or more times per week, the remaining 33% consumed them between one and four times per week. None of the patients reported not consuming them Graph 3.



The results showed that 19% of patients reported never have been pregnant, 22% of them were pregnant once and 26% twice. On the other hand, 23% of the women were

pregnant 3 times and the remaining 10% had four or more pregnancies Graph 4.



**Graph 4:** Clinical histories. Number of pregnancies.

## Discussion

There have been multiple works and investigations about the risk factors of gallstones in the world. The results of such investigations could depend on the place and population studied. Age and female sex are important risk factors for cholelithiasis, with a difference in prevalence between women and men younger than 50 years, greater than 2 to 3 times, as compared to adults over 50 years, which is less than 2 times [5]. Salman M, et al. found that 85% of young patients with cholelithiasis were female [7]. This result is similar to our study, which allows the authors to conclude that women have a higher risk of gallstones. Even though age is an important risk factor for gallstones [5]. The authors observed a significant increase in the incidence of cholelithiasis in patients younger than 40 years in Venezuela, in compared with study conducted in Argentina, by Palermo M, et al. where showed that only 27% of patients were in that age range [8]. It should be noted that in our study the highest incidence of cases occurred after thirty years of age. Obesity is an established risk factor for cholesterol stones, probably due to increased cholesterol synthesis and secretion [5]. In our study, obesity was not a determining factor to increase the risk of gallstones, because the highest incidence was in patients with normal BMI and overweight. In study by Salman M, et al. in Pakistan where young people with cholelithiasis were studied, it was obtained that 35% of them were normal BMI and 54% were overweight [7]. Therefore, authors concluded that in young patients there wasn't a direct relationship between weight and gallstones development.

Genetic plays an important role in the development of gallstones in patients with family history [5,7,8]. It's has been studied that the mutation of the hepatic ABCG8 transporter increases the risk [5]. In the study by Salman M, et al. Obtained a ratio of 2.7:1 in people with a family history of first-line gallstones, thus favoring genetic theories for

gallstones [7]. Results that is similar to our findings showing that approximately one of two cases had a family history of gallstone. Liver cirrhosis and diabetes mellitus are risk factors for the development of gallstones [5,8]. However, in the present investigation these diseases weren't found; findings that do not rule out its relationship with the development of gallstones. Tobacco use doubles the risk of disease in men [8]. This study concluded that there is a relationship between tobacco consumption and cases of gallstones. On the other hand, the patients in this investigation did not refer to chronic alcohol consumption.

In the specific case of female patients, research reports a significant association between oral contraceptives with progesterin or in combination with estrogen-progesterone and the development of cholelithiasis [5,9]. Although this study is not of a correlational type, so it is not possible to affirm that there is a causal relationship between these variables, the high percentage of women who presented gallstones and had a history of using hormonal contraceptive method still alarming, especially oral contraceptive. Research affirms that a diet rich in fiber decreases biliary saturation and shows a protective effect for the development of gallstones, while saturated fats increase the risk of cholelithiasis [10]. For this reason, this research collected related information, but not the amount of fiber and saturated fat intake of the 151 patients in the sample. A significant imbalance was obtained as a result in terms of high consumption of foods rich in saturated fats and low fiber intake. Although this study did not determine the amount of saturated fat intake by patients, the frequency of its consumption could be considered as high. Pregnancy as a risk factor for cholelithiasis increases with the frequency and number of pregnancies, due to the hormonal effects of estrogen, which increased the secretion of cholesterol into the bile. While progesterone delays gallbladder emptying, with the consequent increase in gallstones formation [5,7,11]. However, in this investigation there wasn't a significant association between the number of pregnancies and cholelithiasis. As a final finding, even though research and literature associate gallstones with some risk factors such as patients age over 40 years, obesity, female, pregnancy, DM, among others [5-8,11]; in this investigation it was possible to observe that an important part of the patients was not within these risk groups. That is a fact that should be considered for future research. This study concluded that the cases of cholelithiasis are appearing at younger ages, than they used to be before. There was a high incidence of cases of gallstones in those women who used oral contraceptives or other hormonal contraceptives. In addition, in young people, obesity was not a determining factor. The study of this pathology in different contexts allows us to understand which are the most important risk factors for developing gallstones of each place.

**Conflict of Interest:** The authors declare that they have no conflict of interest regarding this study.

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