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A Comparative Epidemiological-Pathology Study Regarding the incidence of Gall Ball Stone

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دراسة وبائية مرضية مقارنة حول معدل الإصابة بحصوات المرارة

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Abstract:
This retrospective epidemiological study, conducted at Al Jala Hospital in Benghazi, Libya, from 2020 to 2023, investigated the incidence of gallstone disease in relation to age and gender. The study also included a comparative pathological analysis of normal gallbladder tissue from healthy individuals and abnormal tissue from patients with gallbladder cancer.
A total of 886 patients with gallstones, aged 18 to 65 years, were included in the study. The majority were female (83%), with males making up the remaining 17%. Results demonstrated a strong association between gallstone formation and age, with the highest incidence observed in the 36–45 age group. Notably, a significant increase in cases was also found among younger individuals (18–36 years) in the final year of the study. The gender-specific nature of the disease was evident, with females showing a much higher prevalence of 86% compared to males.
In conclusion, the study affirms that females are more susceptible to gallstone formation than males, and that the incidence of this condition has been rising among younger age groups in recent years. These findings underscore the need for targeted health strategies to address the growing prevalence of gallstone disease, particularly among high-risk populations.

Keywords
Age, gender, cholecystectomy, cholecystolithiasis, normal gallbladder, abnormal gallbladder.

الملخص
هدفت هذه الدراسة الوبائية بأثر رجعي، التي أُجريت في مستشفى الجلاء بمدينة بنغازي، ليبيا، خلال الفترة من 2020 إلى 2023، إلى تقييم معدل حدوث حصوات المرارة وعلاقتها بكل من العمر والجنس .كما شملت الدراسة مقارنة نسيج المرارة الطبيعي المأخوذ من أفراد أصحاء بالنسيج غير الطبيعي المأخوذ من مرضى سرطان المرارة.
بلغ العدد الكلي للمرضى المصابين بحصوات المرارة 886 مريضًا، تراوحت أعمارهم بين 18 و65 عامًا .وكانت الغالبية العظمى من المرضى من الإناث (83%)، بينما شكل الذكور نسبة 17 .%أظهرت النتائج وجود ارتباط واضح بين تكوّن الحصوات والعمر، حيث تركزت معظم الحالات في الفئة العمرية 36-45 عامًا .ومن الجدير بالذكر أن الدراسة لاحظت زيادة ملحوظة في معدل الإصابة بين الفئات الأصغر سنًا (18-36 عامًا) خلال السنة الأخيرة من الدراسة .كما تبين أن الحصوات ذات طبيعة نوعية مرتبطة بالجنس، حيث كانت نسبة الإصابة بين الإناث أعلى بكثير (86%) مقارنة بالذكور.
وخلصت الدراسة إلى أن الإناث أكثر عرضة للإصابة بحصوات المرارة من الذكور، وأن معدلات الإصابة قد شهدت ارتفاعًا بين الفئات العمرية الأصغر في السنوات الأخيرة .وتؤكد هذه النتائج على ضرورة وضع استراتيجيات صحية موجهة لمواجهة الانتشار المتزايد لمرض حصوات المرارة، وخاصة بين الفئات السكانية الأكثر عرضة للخطر.

الكلمات المفتاحية: العمر، الجنس، استئصال المرارة، حصوات المرارة، دراسة نسيجية للمرارة طبيعية وغير طبيعية.

Introduction

Gallstones represent one of the leading causes of gastrointestinal disorders in patient's both the United States and globally. They can result in chronic pain as well as intermittent discomfort. The formation of gallstones is influenced by a combination of metabolic, environmental, and genetic factors and cancer, with their composition varying based on the underlying causes of disease. Gallstones are often mobile and can obstruct the cystic duct, impeding bile flow and causing biliary colic. Prolonged obstruction of the cystic duct can lead to gallbladder inflammation and potential bacterial infiltration. When gallstones enter the bile duct, they may cause biliary obstruction, resulting in symptoms such as jaundice, abdominal pain, and cholangitis; blockage of the common bile duct can lead to pancreatitis [11]. Cholesterol is the primary constituent of the most prevalent type of gallstone, while black stones are composed of calcium bilirubinate. In contrast, brown stones, which form in the presence of bacterial or parasitic infections, contain a mixture of calcium phosphate or palmitate, cholesterol, and bile [12]. Cholesterol stones are frequently found in individuals with diabetes and other metabolic disorders, whereas black stones are associated with inflammatory diseases like Crohn's disease and are often observed in patients with parasitic or bacterial infections and biliary strictures [13]. Gallstones are a major risk factor for gallbladder cancer, but few persons with stones experience development of tumors. Gallstones are a major risk factor for gallbladder cancer, but few persons with stones experience development of tumors .(14). Ultra sound is the preferred method for diagnosing gallstones, although they can also be detected using computed tomography (CT), magnetic resonance imaging (MRI), and, depending on their calcium content, even x-rays. The treatment for gallstones varies based on the severity of the condition and the symptoms presented. Laparoscopic cholecystectomy is considered the standard care for patients suffering from recurrent biliary colic or acute cholecystitis [15]. Gallstones are prevalent among both genders, with a higher incidence in women compared to men (5.41% versus 4.85%). The age-standardized prevalence of all gallstone types increases with age, from 1.05% in those aged 18–30 to 11.6% in those aged 70 and older [16][17]. Furthermore, the demand for cholecystectomy in pediatric patients has risen significantly over the past two decades, with approximately 34 pediatric patients diagnosed with gallbladder stones, averaging 14.1 years of age (ranging from 6 to 18 years), some of whom underwent laparoscopic cholecystectomy due to cholelithiasis (17) (18). The objective of this study is to explore the relationship between age, gender, and the incidence of gallstones among patients, as well as to anticipate future occurrences of these conditions. As well as the comparing between the normal tissue of the gallbladder from normal individual and the abnormal tissue from gallbladder cancer patients.

Patients and Method

This study utilized data from Al Jalla Hospital in Benghazi. Patient files from individuals diagnosed with gallstones between 2021 and 202 3were collected. The diagnoses were confirmed through ultrasound and other examinations across various age groups. A total of 886 cases of gallstones and they were identified as age group and gender group, with incomplete data excluded from the analysis. The collected data were analyzed using SPSS version 21, which incorporates with a significance threshold set at $p<0.05$. The statistical analysis aimed to determine the relationship between age, gender, and the incidence of gallstones among the patients. Finally, the data were further analyzed statistically to predict the likelihood of gallstones based on the patient data from recent years.

Results

1-In 2020, the total number of patients was 143 (Tables 1 and 3). Approximately 60.1% of these cases were in the 36 to 46 age group (Table 2), and the majority of patients were female, at about 86% (Tables 4 and 5). It is notable that 74 females in the 36-65 age group had gallbladder stones (Table 5).

Table 1 Age Statistics of Patients in 2020.

Statistical Measure	Value
N, Valid	143
N, Missing	0
Mean	1.6713
Median	2.0000
Mode	2.00
Std. Deviation	0.54095
Variance	0.293
Range	2.00
Minimum	1.00
Maximum	3.00

Table 2 The table shows the number of patients in different age (2020)

age					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-35	52	36.4	36.4	36.4
	36-45	86	60.1	60.1	96.5
	46-65	5	3.5	3.5	100.0
	Total	143	100.0	100.0	

Table 3 The statistical analysis of mean, median and Stender deviation of gender (2020).

Statistics		
gender		
N	Valid	143
	Missing	0
Mean		1.8671
Median		2.0000
Mode		2.00
Std. Deviation		.34062
Variance		.116
Range		1.00
Minimum		1.00
Maximum		2.00

Table 4 The table shows the number of patients in both genders (2020).

Gender					
		Frequeny	Percent	Valid Percent	Cumulative Percent
Valid	male	19	13.3	13.3	13.3
	female	124	86.7	86.7	100.0
	Total	143	100.0	100.0	

Table 5 The comparison between the number of patients of male and female (2020)

age * gender Crosstabulation				
Count				
		Gender		Total
		male	female	
age	18-35	7	45	52
	36-45	12	74	86
	46-65	0	5	5
Total		19	124	143

2- In 2021, the total number of patients was 321 (Tables 6 and 8). There was a notable increase in the number of patients across all age groups. The percentages for the age groups were 30%, 62.3%, and 7.2%, respectively (Table 7). Females continued to have a high incidence, with approximately 83.5% of cases (Table 9). A notable finding was that 172 females in the 36-45 age group had gallbladder stones (Table 10).

Table 6 The statistical analysis of mean, median and standard deviation of age (2021)

Statistics		
age		
N	Valid	321
	Missing	0
Mean		1.9003
Std. Error of Mean		.13531
Median		2.0000
Mode		2.00
Std. Deviation		2.42436
Variance		5.878
Range		43.00
Minimum		1.00
Maximum		44.00

Table 7 The table shows the number of patients in different ages (2021).

age					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-35	97	30.2	30.2	30.2
	36-45	200	62.3	62.3	92.5
	46-65	23	7.2	7.2	99.7
	44.00	1	.3	.3	100.0
	Total	321	100.0	100.0	

Table 8 The statistical analysis of mean, median and standard deviation of gender (2021)

Statistics		
gender		
N	Valid	321
	Missing	0
Mean		1.8349
Std. Error of Mean		.02076
Median		2.0000
Mode		2.00
Std. Deviation		.37186
Variance		.138
Range		1.00
Minimum		1.00
Maximum		2.00

Table 9. The table shows the number of patients of male and female (2021).

gender					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	53	16.5	16.5	16.5
	female	268	83.5	83.5	100.0
	Total	321	100.0	100.0	

Table 10 The compressing between the number of patients of male and females (2021)

age * gender Crosstabulation				
Count				
		Gender		Total
		male	female	
age	18-35	22	75	97
	36-45	28	172	200
	46-65	3	20	23
	44.00	0	1	1
Total		53	268	321

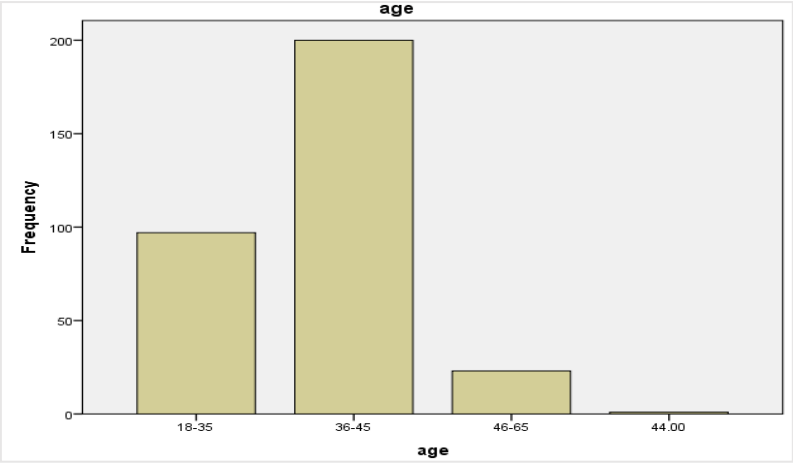

Figure 1 The par chart shows the number of patients in different ages (2021).

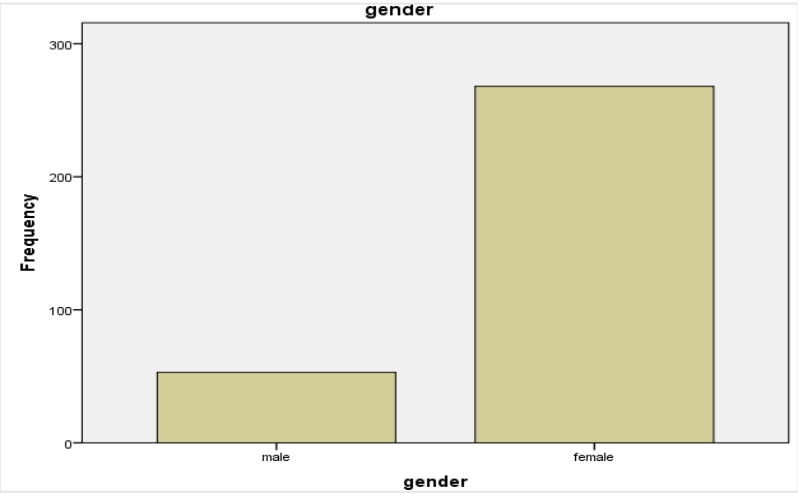

Figure 2 The par chart shows the comparison between the number of patients of male and female (2021).

3- In 2022, there was a gradual decrease in the number of patients. However, it was recorded that the percentage of the disease increased in different age groups: 18-35 (36.9%), 36-45 (36.9%), and 46-65 (23.3%). As illustrated in the table, females had the highest percentage (80.6%) (Table 13). It is notable that 88 females in the 18-35 age group had gallbladder stones (Table 16).

Table -12. The statistical analysis of mean, median and Stender deviation of age (2022)

Statistics		
age		
N	Valid	279
	Missing	0
Mean		1.9857
Std. Error of Mean		.08766
Median		2.0000
Mode		1.00[a]
Std. Deviation		1.46413
Variance		2.144
Range		21.00
Minimum		1.00
Maximum		22.00
a. Multiple modes exist. The smallest value is shown		

Table 13 The table shows the number of patients of different ages (2022).

age					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-35	103	36.9	36.9	36.9
	36-45	103	36.9	36.9	73.8
	46-65	65	23.3	23.3	97.1
	more than 65	7	2.5	2.5	99.6
	22.00	1	.4	.4	100.0
	Total	279	100.0	100.0	

Table 14 The statistical analysis of mean, median and standard deviation of gender (2022)

Statistics		
gender		
N	Valid	279
	Missing	0
Mean		1.8065
Std. Error of Mean		.02370
Median		2.0000
Mode		2.00
Std. Deviation		.39579
Variance		.157
Range		1.00
Minimum		1.00
Maximum		2.00

Table 15 The comparison between the number of patients of male and female (2022).

gender					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	54	19.4	19.4	19.4
	female	225	80.6	80.6	100.0
	Total	279	100.0	100.0	

Table 16 The comparison between the number of patients of age and gender (2022).

age * gender Crosstabulation				
Count				
		gender		Total
		male	female	
age	18-35	15	88	103
	36-45	20	83	103
	46-65	16	49	65
	more than 65	2	5	7
	22.00	1	0	1
Total		54	225	279

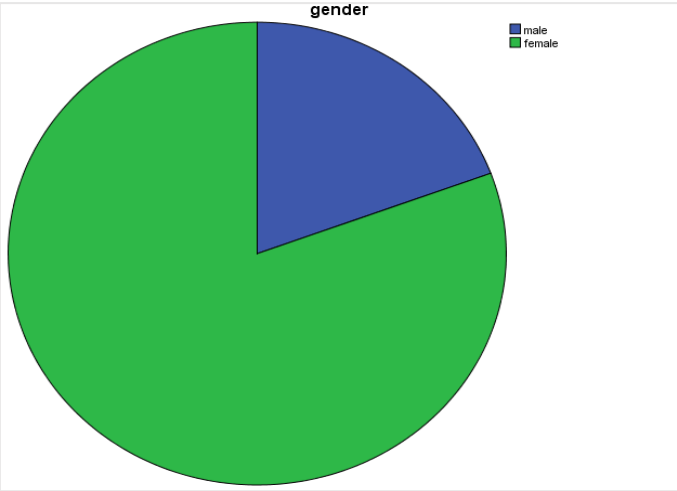

Figure 3 The pie chart shows the comparison between the number of patients of male and female (2022).

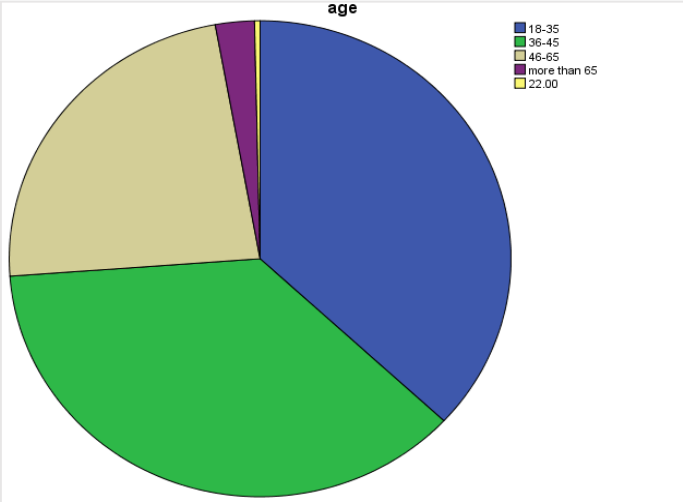

Figure 4 The pie chart shows the number of patients of different ages (2022).

4- In 2023, the total number of patients was approximately 143. Table 18 shows an increase in the number of patients in the 18-35 and 46-65 age groups, at 41.3% and 24.5%, respectively (Figure 5). However, there was a clear decrease in the number of females to 32.6% in 2023. It is noteworthy that the number of females with gallbladder stones increased to approximately 52 cases in the 18-35 age group (Table 19) (Figure 6).

Table 17 The statistical analysis of mean, median and standard deviation of gender (2023)

Statistics			
		age	gender
N	Valid	143	143
	Missing	0	0
Mean		1.8601	1.8601
Std. Error of Mean		.06990	.02911
Median		2.0000	2.0000
Mode		1.00	2.00
Std. Deviation		.83583	.34806
Variance		.699	.121
Range		3.00	1.00
Minimum		1.00	1.00
Maximum		4.00	2.00

Table 18 The table shows the number of patients in different ages (2023).

Age					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-35	59	41.3	41.3	41.3
	36-45	47	32.9	32.9	74.1
	46-65	35	24.5	24.5	98.6
	more than65	2	1.4	1.4	100.0
	Total	143	100.0	100.0	

Table 19 The table shows the number of males and females (2023).

age * gender Crosstabulation				
Count				
		gender		Total
		male	female	
age	18-35	7	52	59
	36-45	7	40	47
	46-65	5	30	35
	more than65	1	1	2
Total		20	123	143

Table 20 The comparison between ages and gender in 2023.

Gender					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	20	14.0	14.0	14.0
	female	123	86.0	86.0	100.0
	Total	143	100.0	100.0	

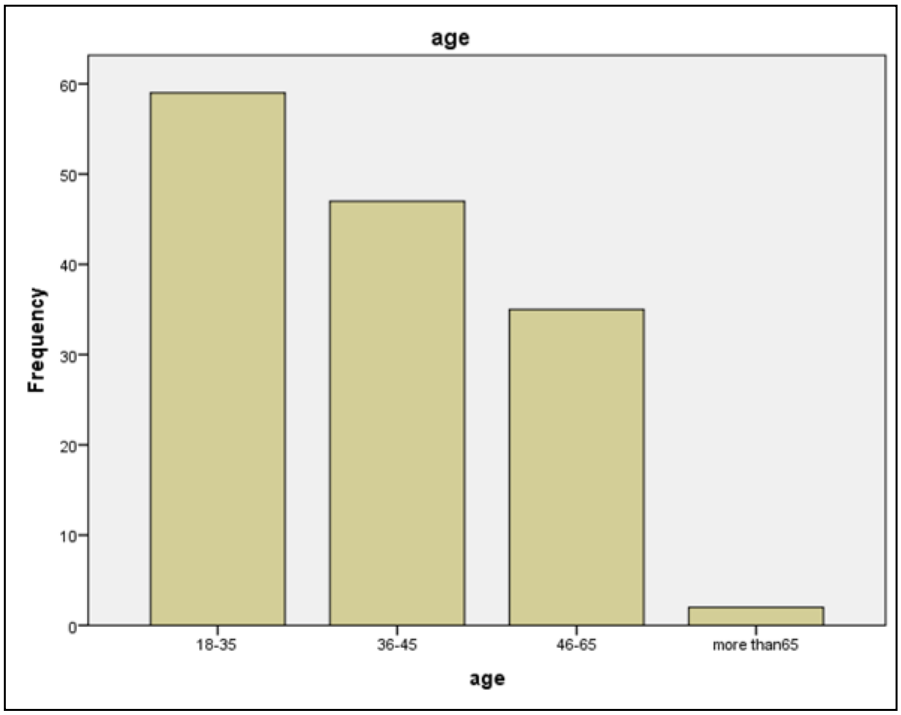

Figure 5 The par chart shows a comparison between the number of patients and age.

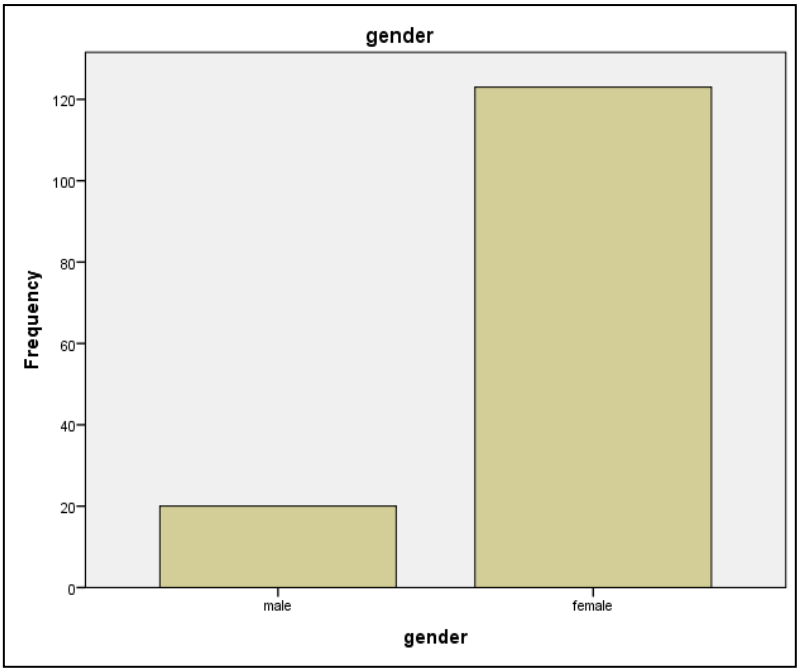

Figure 6 The figure shows the compression between the number of patients and gender.

5-The comparative study between the normal tissue of the gallbladder and abnormal tissue of gallbladder (gallbladder cancer)

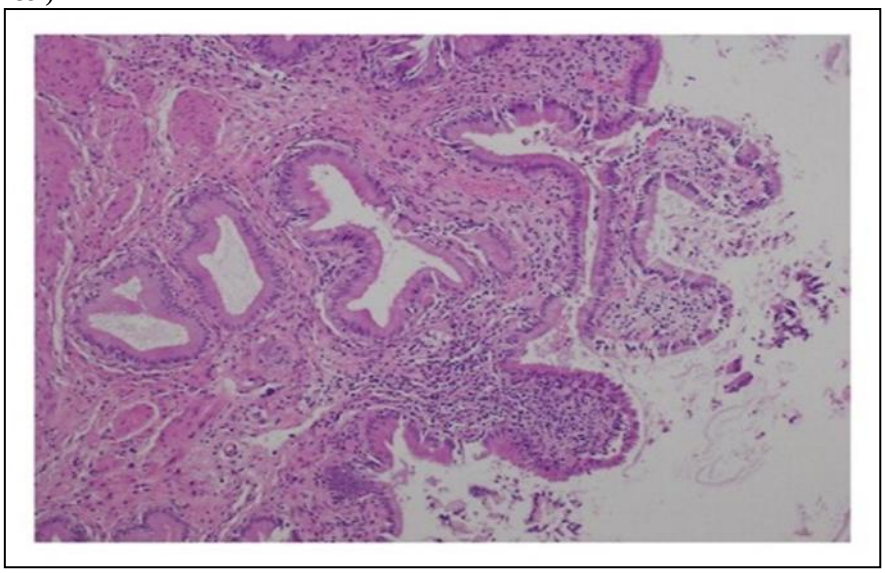

Figure 7 shows the normal gallbladder H&E.

The cross-section in normal gallbladder from normal individual, Mucosal Layer: Lined by simple tall columnar epithelium with a smooth brush border (microvilli) on the luminal surface. Underlying lamina propria contains loose connective tissue with sparse inflammatory cells and a vascular network .No Muscularis Mucosae or Submucosa. Unlike other GI organs, the gallbladder mucosa rests directly on the muscular layer .Laminar Smooth Muscle Layer (Muscularis Externa). Randomly arranged smooth muscle bundles with intervening collagen and elastic fibers .Outer Layers: a. Areas attached to the liver are covered by dense connective tissue (adventitia); free surfaces have a thin serosa with mesothelium .Absence of Pathologic Features: No inflammatory infiltrates, mucosal ulceration, edema, or fibrosis .No Rokitansky–Aschoff sinuses or cholesterol-laden macrophages (Figure- 7)

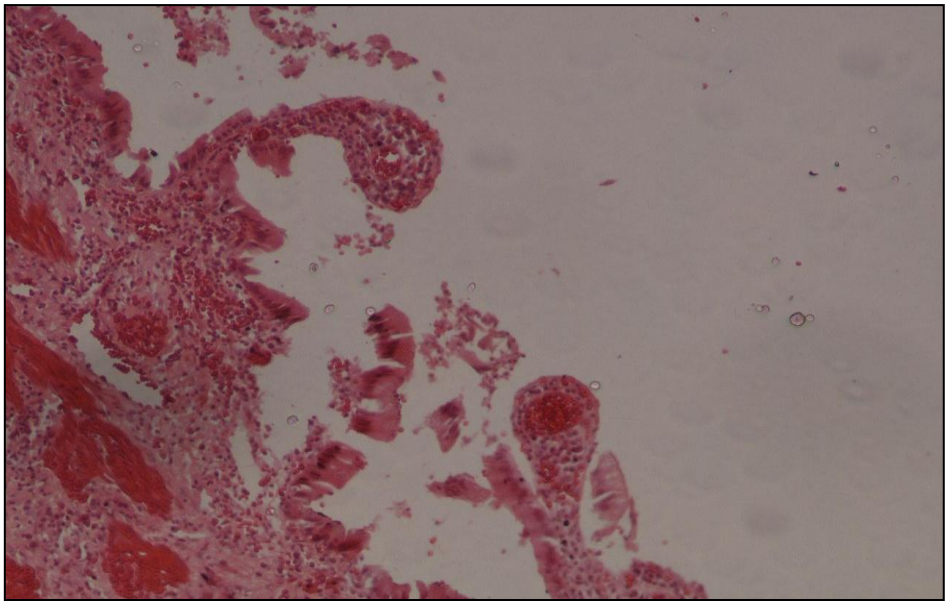

Figure 8 shows the anormal gallbladder(H&E).

In the cross-section, the abnormal gallbladder from patient who has gallbladder cancer shows that the epithelium has disrupted architecture, surface erosion, mucosal ulceration. inflammatory infiltrates; there is dense leukocyte infiltration in the mucosa and lamina propria, and minimally scattered lymphocytes. Muscular Layer; possible thickening or fibrosis, thin regular smooth muscle bundles. It is clear that are edema, capillary congestion and fibrosis (Figure-8).

Discussion

The current study was designed to study the relationship between age and gender and gallbladder stones in different populations from eastern Libya. Previous studies reported that risk factors affect the development of gallbladder disease, biliary diseases and the survival rate in people who are diagnosed with gall diseases and biliary diseases. Due to burden of gallbladder diseases and biliary diseases effected on the health service, this study spot light about the risk factors such as age and gender and as well as the prediction of incidence of disease to apply new strategies to limit the epidemiology of the disease.

The finding of this study that the gender has strong effect on the incidence of the disease in 2020 the most of patient were females around 86.7% of the total number 143 patient and 13.3 % were males. This agrees with Osuch et al 2020 that reported the patients 504 underwent surgical gallbladder removal, in this group there were 326 (64.7%) female and 178 (35.3%) male patients that participate in their study. Could be the risk factor of gender was powerfully heterogeneous (19) (Osuch et al., 2020).

The finding of 2021 years that rapidly increase of the number of patients approximately 321. Notable that still the most of patient were females who surfing with gallbladder stones (83%) perspective. It was increased the number of patients in age 18-35 from 13.3 to 30.2 about the double during one year. This finding agrees with (20) Spasovski et al 2022 founded that a significant difference between females and males. there was a significant value of progesterone service for female group, and testosterone and IgA in for male group. Could be the influence of the hormonal factor on the intensity and character of the inflammatory changes in both groups. Could be the effect of covid-19 epidemic on the life style of people such as stress and food haplites.

The finding of 2022, there was noteworthy increased the number of patients in both groups, young people and old people. Millennials (age: 25-32 years) and Generation-Z individuals (age: 10-25 years) exhibit a shift in the occurrence of gallbladder diseases, which may be related to changes in lifestyle and genetics. The diagnosis of gallstones in young adults is presently complicated, as the signs and symptoms of biliary tract sickness differ significantly between those under and over 30 years of age (21) (Kazi et al., 2022). The incidence was higher in women than that in men (22) (Song et al., 2022). The increase incidence rate in old strongly agree with (23) Wang et al (2024) that found the increased gallbladder stones with age (age $\geq$70) to 11.6%.

The finding of 2023 shows rapid increase the number of young patients in contrast decreased the number of patients in age 36-46. It could be the fast food and obesity the cause of gallstone in young people, it is agreed with (24) Kim et al (2019) that reported obesity-related factors (BMI, waist size, thigh circumference, and cholesterol, LDL, and HDL levels) correlated with GB disease in the young generation. Females have the high percentage of gallbladder stones incidence that is agree with (25) Bhatti et al (2016) that found Gallstones represent high prevalence disease in adult females more than males and it increases by age. The prediction that the gallbladder

stones will increase in young people is based on patient data from recent years and due to change the lifestyles of young people.
Gallstone cancer was recorded in this study, and histology section shows that there was mucosal ulceration, inflammatory infiltrates, edema, capillary congestion, and fibrosis. Persons with large gallstones were found to be at increased risk for cancer. For those with stone diameters of 2.0 to 2.9 cm, the odds ratio (v stone size <1 cm) was 2.4; for stones 3 cm or larger, the ratio was 10.1 (26). It could be the association of large gallstones with cancer; this should be repeated in a large group to confirm that. As well as managing the gallstones incidence, young people should avoid the epidemiology of cancer. Biliary tract cancers, encompassing gallbladder, extrahepatic bile duct, and ampulla of Vater cancers, are uncommon but often fatal malignancies (27).

Conclusion

The study reveals a general increase in the number of patients with gallstones in recent years. Women, particularly those between the ages of 36 and 45, remain at a higher risk for developing the condition. A significant finding is the notable increase in the incidence of gallstones among younger people, specifically those between the ages of 18 and 35. This growing epidemiological problem in both younger and older populations highlights the need for improved healthcare and the development of screening programs for individuals at high risk of gallbladder disease. Public awareness campaigns, utilizing media such as television and radio advertisements, are crucial for educating people and teenagers about the health risks associated with poor dietary habits.

Recommendation

- Gallstones are a common occurrence in females; therefore, they should consider annual routine check-ups.
- Young people with obesity should undergo ultrasounds to confirm the presence of gallstones to ensure they receive appropriate treatment.
- Gallstones, regardless of size, should be followed up by a doctor.
- Gallstones can cause various symptoms and may increase the risk of developing gallbladder cancer.

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