Gallbladder diseases detected by ultrasound and correlated risk factors

Sahar Ahmed MAHDI[1], Israa JAAFAR[2]

[1]Department of Radiologic Techniques, Turath University College, Baghdad, Iraq
[2]College of Dentistry, Al-Esraa University Baghdad, Iraq

ABSTRACT

Background. Gallbladder diseases are relatively common, most of which are asymptomatic, others may be presented with right hypochondriac pain. Obesity, metabolic syndrome, long-term fasting, rapid weight reduction, bariatric surgery and drugs are associated with bile stasis and hence participate in gallstone formation. The study aimed to determine the variety of gallbladder disease detected by ultrasound in Iraqi patients.

Methods. This study involved a randomly selected sample of 100 men and 100 women who attended the ultrasound clinic at Emamein Kadhimein Medical City for abdominal ultrasonography for various reasons in a period of 8 months (Oct 2022-Jul 2023). Data about age, sex, risk factors and symptoms were collected from those who had ultrasound features of gallbladder diseases.

Results. It was found that gallbladder diseases are more common in women (23% of all examined women) than men (11% of all examined men). The most affected age groups are between 40-49, the percentage of women affected in this age group is 30.47% and men 12%. Most of the cases were without symptoms. The most common ultrasound finding is gallstones, where the percentage of affected women reached 82.6% and the affected men 81.8%.

Conclusion. Ultrasound has a valuable role in screening, detection and follows up of gallbladder diseases. It is safe, available and cost-effective examination. Gallbladder diseases particularly gall stones are relatively common in Iraqi population, being more common in middle age women with clear association with obesity and multiparty among other risk factors. Most of patients were asymptomatic others presented with symptoms like abdominal pain.

INTRODUCTION

Gallbladder is an organ related to the digestive system, situated in the right hypochondrium. It has 3 parts: fundus, body and neck. Bile produced by the liver is concentrated and stored in the gallbladder [1]. Cholelithiasis is gallstones and is a condition in which the gallbladder develop stones made of bile, bilirubin, and cholesterol. Most of the time, these stones have no symptoms and are only found accidentally. Ultrasound is the best diagnostic tool for identifying gallstones.

Gallstones are treated according to their symptoms. Risk factors of cholelithiasis include: female gender and pregnancy resulting in stasis. Obesity, metabolic syndrome, long-term fasting, rapid weight reduction, bariatric surgery and some drugs (estrogens, fibrates, and somatostatin analogs) all are associated with bile stasis and hence participate in gallstone formation and genetic also has a role. Abdominal ultrasound is the principal imaging modality of choice in diagnosing and evaluating gallstone-related disease, and other imaging techniques, are magnetic resonance imaging (MRI) or com-

puted tomography (CT). However, these techniques have been found to be helpful when ultrasonography results are inconclusive [2].

Acute cholecystitis is main consequence of cholelithiasis and accounts for 3-10% of all patients complaining of abdominal discomfort and is a frequent reason for hospital admission. The main risk factor, which accounts for up to 95% of cases, is cholelithiasis. A series of events occur in acute calculus cholecystitis: The gallbladder neck or cystic duct being blocked by a gallstone then bile stasis causes mucosal chemical damage by bile salts that results in an inflammatory reaction. Reactive mucus production causes distention and elevated intraluminal pressure which will lead to restricted blood supply to the gallbladder wall (gallbladder hydrops) leading to thick edematous wall. Around 66% of patients acquire secondary bacterial infections, further complications include: gangrenous cholecystitis (most common 20%), gallbladder perforation (5%), emphysematous cholecystitis, pericholecystic abscess, cholecystoenteric fistula and less likely complication are vascular (gallbladder hemorrhage, portal vein thrombosis, cystic artery pseudoaneurysm). The sonographic Murphy sign combined with cholelithiasis is the most sensitive US finding in acute cholecystitis. Pericholecystic fluid and gallbladder wall thickening (>3 mm) are both secondary findings [3].

Long-term gallbladder inflammation is referred to as chronic cholecystitis. It is almost always observed in conjunction with cholelithiasis (95%), which is resultant of dysmotility or intermittent cystic duct or gallbladder neck obstruction. Although most patients are asymptomatic, some may have recurrent biliary colic or acute cholecystitis. Known complications include gallbladder cancer, gallstone ileus, and concurrent acute cholecystitis. Gallbladder wall thickening and cholelithiasis are the most often seen imaging features. Pericholecystic inflammation is typically absent, and the gallbladder may be swollen or contracted [4].

Gallbladder cancer refers to primary epithelial malignancies that arises from the gallbladder, with the majority (90%) being adenocarcinomas and the other 10% being squamous cell carcinomas. Despite its rarity, gallbladder adenocarcinoma is the most prevalent primary biliary carcinoma and the fifth most common gastrointestinal cancer. Usually affects women with long-standing cholecystolithiasis, (>60 years of age, F:M ratio = 4:1) and, usually asymptomatic unless they are advanced. Ultrasound can depict focal or diffuse gallbladder wall irregular thickening, a focal intraluminal mass, or a massive mass lesion that replaces the whole gallbladder on imaging. Tumor's margins are frequently irregular and ill-defined, with heterogeneous predominantly low echogenicity. Hyperechoic areas with posterior acoustic shadowing might be observed, prob-

ably representing gallstones or gallbladder wall calcifications commonly known as porcelain gallbladder. It is not unusual to have tumors with some degree of invasion of neighboring structures or metastasis [5].

Gallbladder cholesterolosis is a benign asymptomatic condition results from localized or diffuse accumulation of cholesterol esters and triglycerides within the gallbladder wall. Ultrasound may show hyperechoic foci within the gallbladder wall sometimes with comet tail artifact shadowing [6].

Adenomyomatosis of the gallbladder is another benign usually asymptomatic condition in which there is focal or diffuse hyperplasia of the gallbladder wall. It is a relatively common and may be associated with gallstones and pancreatitis. Ultrasound may show diffuse, focal or annular mural thickening which sometimes difficult to be distinguished from gallbladder malignancy. Adenomyomatosis may be associated with cholesterolosis (33%) giving the combined ultrasound features of both conditions; thickening of gallbladder wall with comet-tail artifact arising from echogenic intramural foci of accumulated cholesterol crystals within the intramural diverticula known as Rokitansky-Aschoff sinuses [7].

The study aimed to determine the variety of gallbladder disease detected by ultrasound in Iraqi patients, to estimate the relation between gallbladder diseases and various factors and to determine symptoms with which patients having gallbladder disease commonly presented.

METHODS

This study involved randomly selected sample of 100 men and 100 women who attended the ultrasound clinic at Emamein Kadhimein medical city for abdominal ultrasonography for various reasons for a period of 8 months (Oct 2022-Jul 2023). Data about age, sex, risk factors and symptoms were collected from those who had ultrasound features of gallbladder diseases.

For proper ultrasound examination of gallbladder, patient need to fast for 8 hours preceding the examination as gallbladder contracts after eating resulting in difficult visualization. If necessary, only water can be taken. If the symptoms are acute, examination is conducted regardless fasting. In Infants – if clinical condition permitting – nothing by mouth is given for 3 hours preceding the examination.

A curvilinear transducer (large footprint abdominal probe, 2.5 to 5.0 MHz) is the typical probe with best penetration and best visualizes bile ducts. Examination starts with the Patient in supine position, switching to left lateral decubitus or upright may be needed in difficult cases. Images may be improved with deep inspiration as it decreases rib shadowing. Gallbladder should be scanned in both axes (short and long axis). Careful

evaluation of gallbladder neck is mandatory as a small stone can be easily missed especially in supine position.

Features to look for on ultrasound examination of gallbladder are:

- Ultrasound Murphy's Sign (tenderness on compression of gallbladder with the probe).
- Thickened gallbladder wall (>3 mm).
- Changed wall echogenicity (may be decreased in acute cholecystitis, increased in chronic cholecystitis, calcification is seen in porcelain gallbladder, intramural hypoechoic or anechoic diverticula may be seen in adenomyomatosis, intramural echogenic foci can be seen in cholesterolosis with or without comet tail v – shaped artifact).
- Pericholecystic fluid.
- Gallstones are echogenic and when >3mm result in shadowing, mobility with changing patients position need to be checked especially if found in gallbladder neck as it may predict impending Cholecystitis within ensuing days.
- An echogenic non – mobile shadow may indicate polyp and it is usually non – shadowing unless calcified. A large ill-defined shadow is considered as a mass which may break through the wall extending to the surrounding liver tissue if malignant.
- Gallbladder sludge is a common finding especially with long standing decreased oral intake [8].

RESULTS

Total patients with gallbladder disease, including those with surgically removed gallbladder, were 34(17%), 11 males (11% of total males, 5.5% of the total sample) and 23 females (23 % of total females, 11.5% of the total sample). Age groups are shown in Table 1.

The presence of possible associated risk factor including obesity, hypertension as well as female parity was determined in patients with gallbladder disease as shown in Table 2. Chi-Square test was acceptable by significance level (0.116), that means the affected of possible risk factors on genders are weak.

TABLE 2. *Possible risk factors for gender*

%	Females	%	Males	Possible risk factors
78.3	18	63.6	7	Obesity
17.4	4	27.3	3	Hypertension
21.7	5	18.2	2	Diabetes
56.5	13	0	0	Multiparty (>5)
Pearson Chi-Square=5.903; P=0.116				

Using Odds Ratio and Relative Risk test

Most of the affected patients were asymptomatic, in others the presenting symptoms were dyspepsia, abdominal pain, few had fever and jaundice as seen in Table 3 below. Chi-Square test for symptoms with Gender, which its value non-significance (0.981).

TABLE 3. *Presenting symptom by males and females*

%	Females	%	Males	Symptoms
43.5	10	54.5	6	Non
17.4	4	18.2	2	Dyspepsia
21.7	5	18.2	2	Abdominal pain
8.7	2	9	1	Fever and Jaundice
Pearson Chi-Square=0.178; P=0.981				

Using Odds Ratio and Relative Risk test

Ultrasound finding of the diseased gallbladder included gall stones, thickened wall, polyp or mass and removed diseased gallbladder as shown in Table 4 below. Chi-Square test for Ultrasound Finding with Gender, which its value non-significance (0.833).

TABLE 4. *Ultrasound finding by males and females*

%	Female	%	Male	Ultrasound finding
82.6	19	81.8	9	Gall stones
8.7	2	18.2	2	Thick wall
4.3	1	9	1	Polyp or mass
13	3	9%	1	Removed gallbladder
Pearson Chi-Square=0.869; P=0.833				

Using Odds Ratio and Relative Risk test

TABLE 1. *Age group, males and females, males and females with diseased gallbladder and its percentage*

%	Females with diseased gallbladder	Females	%	Males with diseased gallbladder	Males	Age group
0	0	2	0	0	0	0-9
11.1	1	9	0	0	4	10-19
10	2	20	9	1	11	20-29
23.5	4	17	5.5	1	18	30-39
30.4	7	23	12	3	25	40-49
27.7	5	18	11.1	3	27	50-59
42.8	3	7	22.2	2	9	60-69
25	1	4	16.6	1	6	70 +
23	23	100	11	11	100	Total

DISCUSSION

This study included an ultrasound examination of 200 abdominal cases in Emamein Kadhimein medical city for a period of 8 months (Oct 2022-Jul 2023). It was found that more women suffer from gallbladder disease than men, as the percentage of affected women is 23% out of 100 cases, whereas men are affected in 11% of 100 cases. The most affected age groups are between 40-49. The percentage of women affected in this age group is 30.47% and men 12%. Most of the cases were without symptoms. The most common disease is gallstones, where the percentage of affected women reached 82.6% and the affected men 81.8%. Many other studies in different countries agreed with our study. A study in the United States examined 286731 persons from the community over an 8-year period and detected 7110 cases of gallbladder illnesses, the majority of which were gallstones, 95% in comparison with other diseases, and they tended to be more common in women [9].

Another study in the United States comprised 14.2 million women and 6.3 million men aged between 20 to 74 who had gallbladder problems, found that the majority of gallbladder diseases were gallstones [10].

Further research in India on 13 Indian persons, found that 17.8% of women and 17.4% of men have gallstones, with the most afflicted age group being 47 years old or older [11].

A study conducted in Korean Medical Institute included 724,114 persons, revealed that those with gallbladder disorders range in age from 20 to 39 in both men and women. Additional risk factors, such as obesity, have been related to an increased chance of having these disorders [12].

Another study of 1,721 Latino vegetarians found that the incidence of gallbladder illness was higher in females than in males. Alcohol consumption, and a high level of body mass index also contribute to the risk of acquiring these disorders [13].

There are 30 studies in which 4623435 participants were examined. According to these studies, gallbladder diseases are 1.25 times more likely in smokers than nonsmokers [14].

Another study found that obesity is a recognized risk factor for gallstone formation and also raises the likelihood of gallstone complications [15].

One of the research projects involved an ultrasound examination of 318,403 people, 171,276 (53.8%) of whom were men and 147,127 (46.2%) of whom were women, and 27,463 (8.6%) of whom were diagnosed to have gallstone disease. High blood pressure was also found to be substantially related with the likelihood of developing gallbladder disease. Women have a higher link between hypertension and gallstone disease than males [16].

In a nationally representative sample of United States (US) population, an increased incidence of gallstone disease (gallstones or a history of cholecystectomy) was confirmed by ultrasound among individuals with diagnosed diabetes (33.3%) and undiagnosed diabetes (23.3%) and prediabetes (20.8%) compared to people with normal glucose (16.7%). This association was found in all demographic subgroups with regard to both gallstones and cholecystectomy. A review of published epidemiologic studies of ultrasound-detected gallstone disease reveals a very constant connection between gallstone disease and diabetes, regardless of obesity or other common risk factors. Insulin resistance has also been linked to gallstone disease in people who do not have diabetes. Gallstone disease, for example, was 60% more prevalent among women in the highest fasting serum insulin percentile compared to the lowest. Diabetes and gallstone disease may be linked via insulin resistance [17].

A cross-sectional research of gall stone disease using ultrasonography was conducted to determine the prevalence in connection to age at menarche, usage of oral contraceptives, number of pregnancies, miscarriages, deliveries, breastfeeding, age at menopause, and the use of postmenopausal hormone therapy. The random sample included 2301 women of Danish origin who are 30, 40, 50, and 60 years, with 1765 (77%) attending the study. Gall stone illness was linked to an early age at menarche, miscarriages, and multiple deliveries. The use of oral contraceptives was highly related to the development of gall stone in univariate but not in multivariate analysis. Breastfeeding, the age of menopause and the usage of menopausal hormone therapy were also related with gall stones. These determining attributes appeared to be sufficient to explain why women had a higher prevalence of gallstone disease than males [18,19].

CONCLUSIONS

Ultrasound has a valuable role in screening, detection and follows up of gallbladder diseases. It is safe, available and cost-effective examination. Gallbladder diseases particularly gall stones are relatively common in Iraqi population. Gallbladder diseases are more common in middle age women with clear association with obesity and multiparty among other risk factors. Most patients were asymptomatic, while others presented with symptoms like abdominal pain.

Statistical conclusion

The main age group with diseased gallbladder is (40-59) for both males and females. The main possible risk factor is obesity for both males and females. In addition to that, the low possible risk factors are diabetes for

males, and Hypertension for females. Most male and female patients were asymptomatic; the most common presenting symptom is abdominal pain whereas the least is fever and jaundice for both sexes. The most common ultrasound finding with the highest percentage is gallstones for males and females, the least one was polyp or mass for both. Chi-Square test shows that gender has not been affected by (possible risk factors, Symptoms, and ultrasound finding).

REFERENCES

1. https://teachmeanatomy.info/abdomen/viscera/gallbladder/
2. https://www.statpearls.com/ArticleLibrary/viewarticle/22041
3. Radswiki T, Vadera S. Acute cholecystitis. Reference article, Radiopaedia.org. (accessed on 12 May 2022) https://doi.org/10.53347/rID-12084
4. Weerakkody Y, Knipe H. Chronic cholecystitis. Reference article, Radiopaedia.org. (accessed on 12 May 2022) https://doi.org/10.53347/rID-24003
5. Radswiki T, El-Feky M. Gallbladder carcinoma. Reference article, Radiopaedia.org. (accessed on 12 May 2022) https://doi.org/10.53347/rID-12407
6. Weerakkody Y, Jones J. Gallbladder wall cholesterolosis. Reference article, Radiopaedia.org. (accessed on 12 May 2022) https://doi.org/10.53347/rID-52456
7. Ryu Y, Bell D. Adenomyomatosis of the gallbladder. Reference article, Radiopaedia.org. (accessed on 12 May 2022) https://doi.org/10.53347/rID-7056
8. https://fpnotebook.com/mobile/surgery/Rad/GlbldrUltrsnd.htm
9. Wenxiang Li, Jingjia Liang, Wentao Shao, et al, Maternal smoking during pregnancy is risk factor for gallbladder disease in offspring during adulthood: a prospective study from UK Biobank, Annals of Hepatology, Volume 26, 2021.
10. James E Everhart, Meena Khare, Michael Hill, Kurt R Maure, Prevalence and ethnic differences in gallbladder disease in the United States. *Gastroenterology.* 1999;117 (3);632-9.
11. James E Everhart, Fawn Yeh, Elisa T Lee, et al, Prevalence of gallbladder disease in American Indian populations: findings from the Strong Heart Study. *Hepatology.* 2002;35 (6):1507-12.
12. Kim HS, Cho SK, Kim CS, Park JS. Big data and analysis of risk factors for gallbladder disease in the young generation of Korea. *PLoS One.* 2019;14(2):e0211480. https://doi.org/10.1371/journal.pone.0211480
13. Chen YC, Chiou C, Lin MN, Lin CL. The Prevalence and Risk Factors for Gallstone Disease in Taiwanese Vegetarians. *PLoS One.* 2014;9(12):e115145. https://doi.org/10.1371/journal.pone.0115145
14. Papadopoulos V, Filippou D, Mimidis K. Smoking habits and gallbladder disease: a systematic review and meta-analysis study. *Hippokratia.* 2020 Oct-Dec;24(4):147-56. PMID: 35023890; PMCID: PMC8747579.
15. Cruz-Monserrate Z, Conwell DL, Krishna SG. The Impact of Obesity on Gallstone Disease, Acute Pancreatitis, and Pancreatic Cancer. *Gastroenterol Clin North Am.* 2016 Dec;45(4):625-637. http://doi.org/10.1016/j.gtc.2016.07.010. Epub 2016 Oct 13. PMID: 27837777.
16. Zhang Y, Sun L, Wang X, Chen Z. The association between hypertension and the risk of gallstone disease: a cross-sectional study. *BMC Gastroenterol.* 2022 Mar 26;22(1):138. http://doi.org/10.1186/s12876-022-02149-5 PMID: 35346065; PMCID: PMC8961935.
17. Ruhl CE, Clark JM, Everhart JE. Liver and Gallbladder Disease in Diabetes. In: Cowie CC eds.. Diabetes in America. 3rd ed. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018 Aug. Chapter 26. PMID: 33651558.
18. https://scholar.google.ca/
19. Mahdi SA, Kareem TF, Abdullah DF. Preterm detection of congenital anomalies by ultrasound and correlation with possible associated risk factors. *Wiad Lek.* 2022;75(1 pt 2):268-274.