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Sonographic Association Between Fatty Liver And Gall Bladder Stones In Females With Metabolic And Hormonal Risk Factors

Habib Ur Rehman
Lecturer, Faculty of Allied Health Sciences, The Superior University, Lahore
Email: habiburrehman7915@gmail.com
Zoha Khan
BS Medical Imaging Technologist, Faculty of Allied Health Sciences, The Superior University, Lahore Email: zoharahim0000@gmail.com
Saba Nawaz
BS Medical Imaging Technologist, Faculty of Allied Health Sciences, The Superior University, Lahore Email: nawazsaba596@gmail.com
Zaheer Qamar
BS Medical Imaging Technologist, Faculty of Allied Health Sciences, The Superior University, Lahore Email: zaheerqamar30@gmail.com
Niaz Ahmed
BS Medical Imaging Technologist, Faculty of Allied Health Sciences, The Superior University, Lahore Email: niazahmedniazahmed996@gmail.com
Kiran Shakeel
Lecturer, Institute of Health Sciences, Khwaja Fareed University of Engineering & Information Technology Email: kiran.shakeel@kfueit.edu.pk

Author Details

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Corresponding E-mail & Author*:
Habib Ur Rehman
Email:habiburrehman7915@gmail.com

Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) and gallstone disease are increasingly prevalent conditions worldwide, particularly among females with metabolic and hormonal disturbances. Both disorders share common risk factors such as obesity, insulin resistance, dyslipidemia, and hormonal imbalance, suggesting a possible association. However, limited data are available regarding their relationship in females with specific metabolic and endocrine risk factors.

Objective: To determine the sonographic association between fatty liver and gallbladder stones in females with metabolic and hormonal risk factors.

Methods: A cross-sectional study was conducted on 220 female patients presenting with metabolic and hormonal risk factors. Data were collected on demographic characteristics, medical history (including diabetes and PCOS), lifestyle factors, and laboratory investigations such as lipid profile. Ultrasound imaging was performed to assess liver status (fatty liver grading) and gallbladder findings (presence or absence of gallstones). Statistical analysis was conducted to assess the association between fatty liver and gallstone disease.

Results: The results indicate that metabolic factors such as diabetes and obesity significantly influence both fatty liver and gallbladder stone formation. Hormonal imbalance represented by FSH/LH ratio also plays a significant role. These findings

support the hypothesis that fatty liver and gallbladder stones share common metabolic and hormonal risk factors in females.
Conclusion: The coexistence of fatty liver disease and gallbladder stones reflects an underlying metabolic-hormonal burden, and comprehensive screening of at-risk female populations is strongly recommended to reduce long-term hepatobiliary complications.

Introduction

Fatty liver disease and gallbladder stones are among the most frequently encountered hepatobiliary disorders in contemporary clinical practice, and their global prevalence has increased significantly over the past few decades. This rise is largely attributed to rapid changes in lifestyle and dietary behavior, urbanization, and the increasing burden of metabolic disorders worldwide. These conditions are now widely recognized as important public health concerns because of their progressive nature and their potential to cause serious complications, including chronic liver disease, biliary obstruction, metabolic dysfunction, and reduced quality of life. In addition, the growing incidence of obesity and type 2 diabetes mellitus has further amplified the burden of these disorders, making them a significant challenge for healthcare systems, particularly in low- and middle-income countries (1).

Non-alcoholic fatty liver disease (NAFLD) is characterized by the excessive accumulation of triglycerides within hepatocytes in individuals who consume little or no alcohol. It represents a spectrum of liver abnormalities ranging from simple steatosis to more advanced conditions such as non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. NAFLD is widely regarded as the hepatic manifestation of metabolic syndrome and is closely associated with insulin resistance, central obesity, dyslipidemia, hypertension, and impaired glucose metabolism. The pathogenesis of NAFLD is multifactorial and involves increased hepatic uptake of free fatty acids, enhanced de novo lipogenesis, reduced mitochondrial fatty acid oxidation, and impaired lipid export from hepatocytes. These metabolic disturbances contribute to hepatic fat accumulation, oxidative stress, inflammation, and progressive liver injury. If left untreated, NAFLD may progress to advanced fibrosis, cirrhosis, and even hepatocellular carcinoma, thereby significantly increasing morbidity and mortality (2).

Similarly, gallbladder stones, also known as cholelithiasis, represent one of the most common disorders of the biliary system. Gallstones usually develop due to alterations in bile composition, gallbladder motility, and cholesterol metabolism. Cholesterol stones account for the majority of cases and occur when bile becomes supersaturated with cholesterol, leading to crystal precipitation and eventual stone formation. Multiple factors contribute to gallstone formation, including increased hepatic cholesterol secretion, reduced bile acid synthesis, impaired gallbladder emptying, and biliary stasis. In addition to cholesterol stones, pigment stones may also develop due to increased bilirubin levels, particularly in conditions such as hemolytic disorders or chronic liver disease (3).

Recent studies suggest that fatty liver disease and gallbladder stones may share common metabolic and pathophysiological pathways. Metabolic syndrome, characterized by central obesity, hypertension, hyperglycemia, and dyslipidemia, plays a major role in the development of both conditions. Insulin resistance is considered a key linking mechanism, as it promotes hepatic lipid accumulation while simultaneously increasing bile cholesterol secretion and altering gallbladder motility. Furthermore, chronic low-grade inflammation, altered adipokine secretion, and oxidative stress are believed to contribute to the coexistence of NAFLD and cholelithiasis. These metabolic abnormalities create favorable conditions for both hepatic steatosis and gallstone formation, suggesting a strong interrelationship between the two disorders (4).

Females are particularly vulnerable to hepatobiliary disorders due to hormonal and physiological factors. Estrogen increases hepatic cholesterol synthesis and promotes its secretion into bile, leading to cholesterol supersaturation and increased risk of gallstone formation. Progesterone reduces gallbladder contractility by relaxing smooth muscle, leading to bile stasis and facilitating gallstone formation. Hormonal fluctuations during pregnancy, menopause, and hormone therapy further influence lipid metabolism and may increase susceptibility to both fatty liver disease and gallbladder stones. Additionally, the use of oral contraceptives and hormone replacement therapy has been associated with an increased risk of gallstone formation, further emphasizing the role of hormonal factors in females (5)(9).

Lifestyle-related factors also play a significant role in the development of these disorders. Increased body mass index, sedentary lifestyle, unhealthy dietary habits, and abnormal lipid profiles contribute to metabolic imbalance and insulin resistance. Diets rich in saturated fats, refined carbohydrates, and low fiber intake are particularly implicated in the development of NAFLD and gallstones. Rapid urbanization and changing socioeconomic conditions have increased the consumption of high-calorie diets while reducing physical activity levels, particularly in developing countries. South Asian populations have shown a higher prevalence of metabolic syndrome and related hepatobiliary disorders, emphasizing the importance of region-specific research. Genetic predisposition may also influence susceptibility, as certain individuals are more prone to lipid metabolism disorders and insulin resistance (6).

Ultrasonography plays an essential role in the diagnosis and evaluation of hepatobiliary diseases. It is a non-invasive, cost-effective, and widely available imaging modality that enables the detection of hepatic steatosis and gallbladder stones with considerable accuracy. Ultrasound imaging allows assessment of hepatic echogenicity for grading fatty liver disease and visualization of gallstones as echogenic structures with posterior acoustic shadowing. In addition to diagnosis, ultrasonography is useful for monitoring disease progression and evaluating treatment response. Because abdominal ultrasound examinations are commonly performed in clinical practice, they provide an effective means to evaluate the coexistence of hepatic and gallbladder abnormalities (10).

Moreover, early detection and timely management of these conditions are crucial to prevent complications. Lifestyle modification, including weight reduction, dietary changes, and increased physical activity, remains the cornerstone of management for both NAFLD and gallstone disease. In selected cases, pharmacological therapy and surgical interventions such as cholecystectomy may be required. Understanding the association between fatty liver disease and gallbladder stones is therefore essential for improving patient outcomes and guiding preventive strategies (11).

In conclusion, fatty liver disease and gallbladder stones are closely linked hepatobiliary conditions with shared metabolic risk factors and pathophysiological mechanisms. Their increasing prevalence, particularly among females and in developing regions, highlights the need for comprehensive research and early diagnostic approaches. Ultrasonography is a valuable tool for detecting and assessing these disorders, enabling integrated evaluation in routine clinical practice (12).

Problem Statement:

Despite the growing body of literature on fatty liver disease and gallbladder stones individually, the relationship between these two conditions remains incompletely understood. Although several studies suggest that they share common metabolic risk factors such as obesity, insulin resistance, and dyslipidemia, the exact nature, direction, and strength of their association remain unclear. Some evidence points to a bidirectional relationship, in which each condition may predispose to the other; however, findings are often inconsistent due to variations in study design, sample size, and population characteristics. Furthermore, many existing studies have focused on

general populations without specifically examining gender differences or evaluating the influence of hormonal factors, thereby limiting the applicability of their conclusions to specific high-risk groups (13).

Females appear to have a higher prevalence of both fatty liver disease and gallbladder stones due to hormonal influences and reproductive factors; however, limited research has investigated the combined effects of metabolic and hormonal risk factors in female populations. Hormonal variations across different life stages—such as puberty, pregnancy, and menopause—may significantly alter lipid metabolism, insulin sensitivity, and biliary physiology, yet these aspects are often underexplored in current research. In addition, the interaction between exogenous hormonal exposure, such as oral contraceptives or hormone replacement therapy, and metabolic risk factors remains inadequately addressed. This creates a gap in understanding how these combined influences contribute to the development and coexistence of hepatobiliary disorders in women (14).

Another important concern is the scarcity of locally relevant data, particularly in developing regions where the prevalence of metabolic disorders is rising rapidly. South Asian populations, in particular, are known to have a higher susceptibility to insulin resistance, central obesity, and dyslipidemia, even at lower body mass index levels. Despite this increased risk, there is a lack of well-structured, region-specific studies that explore the coexistence of fatty liver disease and gallbladder stones, especially among females. Most available data are derived from Western populations, which may not accurately reflect the genetic, environmental, and lifestyle factors influencing disease patterns in South Asian communities (15).

Moreover, inconsistencies in diagnostic criteria and imaging techniques further complicate the interpretation of existing evidence. While ultrasonography is widely used to detect hepatic steatosis and gallstones, variations in operator expertise and reporting standards may affect diagnostic accuracy and comparability across studies. There is also limited emphasis on assessing the severity of fatty liver disease in relation to gallstone formation, which could provide deeper insights into disease progression and correlation (16).

The lack of comprehensive and focused evidence regarding the coexistence of fatty liver disease and gallbladder stones in females highlights a significant gap in current knowledge. Understanding this association is particularly important, as early identification of individuals at risk may help prevent disease progression and associated complications. Investigating their sonographic association, along with identifying key metabolic and hormonal predictors, may contribute to improved screening protocols, targeted prevention strategies, and more effective clinical management of hepatobiliary diseases in women (17).

Therefore, this study aims to evaluate the sonographic association between fatty liver disease and gallbladder stones in females, while accounting for relevant metabolic and hormonal risk factors. By addressing existing gaps in the literature and focusing on a specific high-risk population, this research seeks to provide more precise and clinically relevant insights into the interrelationship between these two common hepatobiliary conditions (18).

Rationale of this Study:

Fatty liver disease and gallbladder stones are common hepatobiliary disorders that are increasingly associated with metabolic conditions such as obesity, insulin resistance, and dyslipidemia. Recent studies suggest that both diseases may share similar metabolic and pathophysiological mechanisms; however, the exact relationship between them remains unclear. Although several studies have investigated these conditions individually, limited research has explored their coexistence, particularly in female populations. Females are more susceptible to hepatobiliary disorders due to hormonal influences that affect cholesterol metabolism, bile composition, and

gallbladder motility. Despite this increased risk, few studies have specifically examined the combined role of metabolic and hormonal factors in the development of both fatty liver disease and gallbladder stones in women.
Furthermore, there is limited locally relevant data in South Asian populations, where metabolic disorders are rapidly increasing. Ultrasonography provides a safe and reliable method for detecting both hepatic steatosis and gallbladder stones. Therefore, this study aims to evaluate the sonographic association between fatty liver disease and gallbladder stones in females to improve understanding, early detection, and preventive management of these hepatobiliary disorders.

Material and Methods:
Multicenter hospital-based observational study (multicenter cross-sectional design of consecutive patients undergoing abdominal ultrasound in participating radiology departments). The study was conducted at different hospitals and clinics in Rahim Yar Khan. 4 to 6 months after the approval of the synopsis. Consecutive sampling of all eligible women referred for abdominal ultrasound at each participating center during the recruitment period until the target sample size (220) is reached. Samples was selected consecutively by including all eligible female patients who meet the inclusion criteria during the study period. Inclusion criteria was 1.Female age ≥18 years. 2.Referred for abdominal ultrasound at participating centers. 3.Able and willing to provide written informed consent. The exclusion criteria was 1.Known chronic liver disease other than NAFLD (e.g., viral hepatitis B/C, autoimmune hepatitis, Wilson's disease). 2.History of prior cholecystectomy. 3.Currently pregnant. 4.Known malignancy or terminal illness. 5.Incomplete clinical or laboratory data despite attempts at retrieval. Equipments are ultrasound Machine, using a curvilinear abdominal transducer (typically 3-5 MHz). Scanning technique includes All participants will undergo abdominal ultrasound after a fasting period of at least 6–8 hours to ensure adequate gallbladder distension and optimal visualization of hepatobiliary structure for better and accurate diagnosis for the study. Scanning protocols are ultrasound examinations will be performed using a standardized protocol, including assessment of liver echogenicity for fatty liver grading and evaluation of the gallbladder for the presence of stones or sludge. Scanning will be performed with a convex transducer (3–5 MHz), and images will be obtained in multiple planes. All sonographic evaluations will be conducted by trained sonographers following uniform criteria, and a random subset of scans will be reviewed by a senior radiologist to ensure reliability.

Statistical Analysis:
Linear regression analysis was applied to examine the effect of metabolic and hormonal risk factors on fatty liver and gallbladder stones among female participants. Independent variables included diabetes status, body mass index (BMI), cholesterol level, and FSH/LH ratio, while dependent variables were fatty liver and gallbladder stones diagnosed through ultrasonography. The strength of association was assessed using R-square values, which measured the percentage variation explained by each predictor. ANOVA was used to determine overall model significance through F-statistics, while regression coefficients were used to determine the direction and magnitude of association. A p-value less than 0.05 was considered statistically significant.
The regression findings demonstrated that diabetes ($p=0.0098$), BMI ($p<0.001$), and FSH/LH ratio ($p=0.0027$) were significant predictors of fatty liver, whereas cholesterol showed a non-significant association ($p=0.0736$). For gallbladder stones, diabetes ($p=0.0032$), BMI ($p=0.0342$), cholesterol ($p=0.0070$), and FSH/LH ratio ($p=0.0324$) were all statistically significant predictors. These findings suggest that

both metabolic dysfunction and hormonal imbalance contribute significantly to the development of fatty liver and gallstones in females.

Results:

A total of 220 female participants were included in this study to determine the sonographic association between fatty liver and gallbladder stones in females with metabolic and hormonal risk factors. Ultrasound was used to diagnose fatty liver and gallbladder stones. Metabolic risk factors included diabetes mellitus, BMI, and cholesterol levels, while hormonal risk factor included FSH/LH ratio.

Regression analysis was performed to determine the impact of each independent variable on fatty liver and gallbladder stones separately. The findings revealed significant associations between diabetes, BMI, hormonal imbalance (FSH/LH ratio), fatty liver, and gallbladder stones.

Multiple R	0.1739							
R Square	0.0302							
Adjusted R-Square	0.0258							
Standard Error	0.3194							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*	*Significance F*			
Regression	1.0000	0.6932	0.6932	6.7970	0.0098			
Residual	218.0000	22.2340	0.1020					
Total	219.0000	22.9273						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	0.9397	0.0718	13.0953	0.0000	0.7983	1.0811	0.7983	1.0811
Diabetes	0.1135	0.0435	2.6071	0.0098	0.0277	0.1993	0.0277	0.1993

Table 1 Impact of Diabetes on Fatty liver

The regression analysis demonstrated a statistically significant association between diabetes and fatty liver ($p = 0.0098$). The model was significant ($F = 6.79$, $p < 0.05$), indicating that diabetes is a predictor of fatty liver. The regression coefficient ($\beta = 0.1135$) shows a positive association, suggesting that patients with diabetes are more likely to have fatty liver.

Diabetes showed a significant association with Fatty liver disease ($p = 0.0098$); therefore, it supports the Alternative Hypothesis (H1).

Table 2 Impact of BMI on Fatty liver

Multiple R	0.3359							
R Square	0.1128							
Adjusted R Square	0.1088							
Standard Error	0.3055							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*	*Significance F*			
Regression	1.0000	2.5866	2.5866	27.7223	0.0000			
Residual	218.0000	20.3406	0.0933					
Total	219.0000	22.9273						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.7457	0.1210	14.4328	0.0000	1.5073	1.9841	1.5073	1.9841
BMI	0.0213	0.0041	5.2652	0.0000	0.0293	0.0134	0.0293	0.0134

A simple linear regression was conducted to examine the impact of BMI on fatty liver condition. The results show that the model is statistically significant ($F = 27.7223$, $p < 0.001$), indicating that BMI is a meaningful predictor of fatty liver outcomes. The coefficient for BMI is positive and significant ($\beta = 0.0213$, $p < 0.001$), suggesting that each one-unit increase in BMI is associated with a small increase in fatty liver score. BMI showed a significant association with fatty liver ($p = 0.0000$); therefore, it supports the Alternative Hypothesis (H1).

Multiple R	0.1209							
R Square	0.0146							
Adjusted R Square	0.0101							
Standard Error	0.3219							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*	*Significance F*			
Regression	1.0000	0.3349	0.3349	3.2317	0.0736			
Residual	218.0000	22.5924	0.1036					
Total	219.0000	22.9273						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.3797	0.1471	9.3792	0.0000	1.0898	1.6697	1.0898	1.6679
Cholesterol	0.0012	0.0007	1.7977	0.0736	0.0026	0.0001	0.0026	0.0001

Table 3 Impact of FSH/LH ratio on Fatty liver

A simple linear regression was conducted to assess the impact of the FSH/LH ratio on fatty liver condition.The coefficient for the FSH/LH ratio is positive and significant (β = 0.0797, p = 0.0027), showing that higher FSH/LH ratios are associated with a slight increase in fatty liver score.

However, the overall effect is small, suggesting that fatty liver is influenced by multiple other biological and metabolic factors beyond this ratio.

FSH/LH ratio showed a significant association with fatty liver (p = 0.0027); therefore, it supports the Alternative Hypothesis (H1).

Multiple R	0.2017							
R Square	0.0407							
Adjusted R Square	0.0363							
Standard Error	0.3176							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*	*Significance F*			
Regression	1.0000	0.9326	0.9326	9.2436	0.0027			
Residual	218.0000	21.9947	0.1009					
Total	219.0000	22.9273						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.0509	0.0308	34.1346	0.0000	0.9903	1.1116	0.9903	1.1116
FSH/LH ratio	0.0797	0.0262	3.0403	0.0027	0.0280	0.1313	0.0280	0.1313

Table 4 Impact of Cholesterol on Fatty liver

A simple linear regression was conducted to examine the impact of cholesterol on fatty liver condition. The results show that the model is statistically significant (F = 3.2317, p = 0.0736), indicating that cholesterol have a significant effect on fatty liver in this study. The model also has very low explanatory power (R^2 = 0.0146). The coefficient for cholesterol is positive (β = 0.0012), suggesting a slight increase in fatty liver score with increasing cholesterol levels; however, this relationship is statistically significant (p = 0.0736). The 95% confidence interval includes zero, further confirming the absence of a significant association. Overall, cholesterol appears to have a good and significant impact on fatty liver condition in this dataset. Cholesterol shows a significant association with fatty liver (p = 0.0736); therefore, it supports the Alternative Hypothesis (H1).

Multiple R	0.1976							
R Square	0.0391							
Adjusted R Square	0.0346							
Standard Error	0.4899							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*	*Significance F*			
Regression	1.0000	2.1266	2.1266	8.8604	0.0032			
Residual	218.0000	52.3234	0.2400					
Total	219.0000	54.4500						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.2374	0.1101	11.2408	0.0000	1.0205	1.4544	1.0205	1.4544
Diabetes	0.1988	0.0668	2.9766	0.0032	0.0672	0.3303	0.0672	0.3303

Table 5 Impact of Diabetes on Gallbladder Stones

A simple linear regression was conducted to examine the impact of diabetes on gallbladder stones. The results show that the model is statistically significant (F = 8.8604, p = 0.0032), indicating that diabetes has a significant association with gallbladder stones. However, the model has low explanatory power (R^2 = 0.0391),

meaning diabetes explains only 3.91% of the variation in gallbladder stone occurrence. The coefficient for diabetes is positive and statistically significant (β = 0.1988, p = 0.0032), suggesting that the presence of diabetes is associated with an increase in gallbladder stone risk or score. The 95% confidence interval [0.0672, 0.3303] supports the reliability of this positive relationship. Overall, diabetes appears to have a significant but modest effect on gallbladder stones, while other factors may also contribute to their development.

Diabetes showed a significant association with gallbladder stones (p = 0.0032); therefore, it supports the Alternative Hypothesis (H2).

Multiple R	0.1429							
R Square	0.0204							
Adjusted R Square	0.0159							
Standard Error	0.4946							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*		*Significance F*		
Regression	1.0000	1.1113	1.1113	4.5422		0.0342		
Residual	218.0000	53.3387	0.2447					
Total	219.0000	54.4500						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.9613	0.1959	10.0135	0.0000	1.5753	2.3474	1.5753	2.3474
BMI	0.0140	0.0066	2.1312	0.0342	0.0269	0.0011	0.0269	0.0011

Table 6 Impact of BMI on Gallbladder stone

A simple linear regression was conducted to examine the impact of BMI on gallbladder stones. The results indicate that the model is statistically significant (F = 4.5422, p = 0.0342), suggesting that BMI has a significant association with gallbladder stones. However, the model explains only 2.04% of the variation in gallbladder stone status (R^2 = 0.0204), indicating low explanatory power. The coefficient for BMI is positive and statistically significant (β = 0.0140, p = 0.0342), indicating that an increase in BMI is associated with a slight increase in gallbladder stone score. The 95% confidence interval [0.0269, 0.0011] confirms the significance of this relationship. Overall, BMI has a statistically significant but weak effect on gallbladder stones, and other contributing factors are likely involved.

BMI showed a significant association with gallbladder stones (p = 0.0342); therefore, it supports the Alternative Hypothesis (H2).

Multiple R	0.1815							
R Square	0.0329							
Adjusted R Square	0.0285							
Standard Error	0.4915							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*		*Significance F*		
Regression	1.0000	1.7937	1.7937	7.4260		0.0070		
Residual	218.0000	52.6563	0.2415					
Total	219.0000	54.4500						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	2.1553	0.2246	9.5970	0.0000	1.7127	2.5979	1.7127	2.5979
Cholesterol	0.0029	0.0011	2.7251	0.0070	0.0050	0.0008	0.0050	0.0008

Table 7 Impact of Cholesterol on Gallbladder stones

A simple linear regression was conducted to examine the impact of cholesterol on gallbladder stones. The results show that the model is statistically significant (F = 7.4260, p = 0.0070), indicating that cholesterol has a significant association with gallbladder stones. However, the model has low explanatory power (R^2 = 0.0329), meaning cholesterol explains only 3.29% of the variation in gallbladder stone status.

The coefficient for cholesterol is positive and statistically significant (β = 0.0029, p = 0.0070), suggesting that increasing cholesterol levels are associated with a slight

increase in gallbladder stone score. The 95% confidence interval [0.0050, 0.0008] confirms the significance of this relationship.
Cholesterol showed a significant association with gallbladder stones (p = 0.0070); therefore, it supports the Alternative Hypothesis (H2).

Multiple R	0.1443							
R Square	0.0208							
Adjusted R Square	0.0163							
Standard Error	0.4945							
Observations	220.0000							
			ANOVA					
	df	*SS*	*MS*	*F*		*Significance F*		
Regression	1.0000	1.1345	1.1345	0.6387		0.0324		
Residual	218.0000	53.3155	0.2446					
Total	219.0000	54.4500						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	1.6242	0.0479	33.8832	0.0000	1.5297	1.7186	1.5297	1.7186
FSH/LH ratio	0.0879	0.0408	2.1538	0.0324	0.1638	0.0075	0.1683	0.0075

Table 8 Impact of FSH/LH ratio on Gallbladder stones

A simple linear regression was conducted to examine the impact of the FSH/LH ratio on gallbladder stones. The results indicate that the model is statistically significant (F = 0.6387, p = 0.0324), suggesting that the FSH/LH ratio has a significant association with gallbladder stones. The coefficient for the FSH/LH ratio is positive and statistically significant (β = 0.0879, p = 0.0324), indicating that an increase in the FSH/LH ratio is associated with a slight increase in gallbladder stone score. Overall, the FSH/LH ratio has a statistically significant but weak effect on gallbladder stones, while other factors likely contribute more strongly to their development.
FSH/LH ratio showed a significant association with gallbladder stones (p = 0.0324); therefore, it supports the Alternative Hypothesis (H2).

Table shows Fatty Liver Regression Summary

Variable	R^2	P-value	Interpretation
Diabetes	0.0302	0.0098	Significant
BMI	0.1128	0.0001	Significant
FSH/LH Ratio	0.0407	0.0027	Significant
Cholesterol	0.0146	0.0736	Non-significant

Table demonstrates the regression analysis showing the impact of metabolic and hormonal risk factors on fatty liver among female participants. Diabetes showed a statistically significant positive association with fatty liver (R^2 = 0.0302, p = 0.0098), indicating that diabetic females had a higher likelihood of developing fatty liver disease. BMI showed the strongest association with fatty liver (R^2 = 0.1128, p < 0.001), suggesting that obesity plays a major role in hepatic fat accumulation.
Similarly, FSH/LH ratio showed a significant positive association (R^2 = 0.0407, p = 0.0027), indicating that hormonal imbalance may contribute to fatty liver development. However, cholesterol also showed a significant relationship with fatty liver (R^2 = 0.0146, p = 0.0736), suggesting that cholesterol alone may not be a major predictor of fatty liver in this study population.

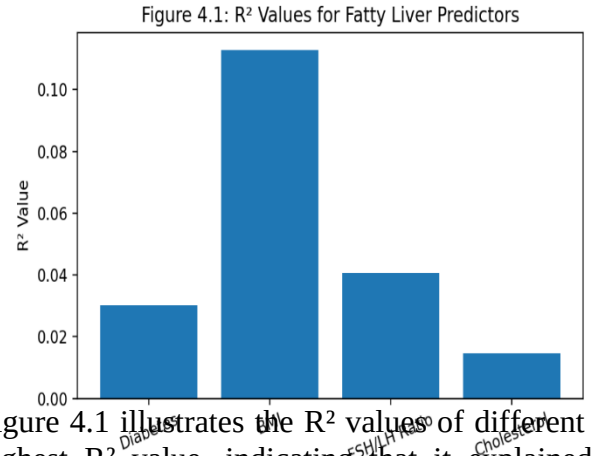

Figure 4.1 illustrates the R^2 values of different predictors of fatty liver. BMI had the highest R^2 value, indicating that it explained the greatest variation in fatty liver occurrence among all studied variables. Diabetes and FSH/LH ratio also contributed significantly, whereas cholesterol showed the least contribution.

Interpretation: BMI showed the strongest association with fatty liver.

Variable	R^2	P-value	Interpretation
Diabetes	0.0391	0.0032	Significant
BMI	0.0204	0.0342	Significant
Cholesterol	0.0329	0.007	Significant
FSH/LH Ratio	0.0208	0.0324	Significant

Table shows Gallbladder Stones Regression Summary

Table presents a regression analysis of metabolic and hormonal factors affecting gallbladder stone formation. Diabetes showed a significant association with gallbladder stones ($R^2 = 0.0391$, $p = 0.0032$), indicating increased stone formation risk among diabetic females. BMI also showed significant association ($R^2 = 0.0204$, $p = 0.0342$), suggesting obesity contributes to gallstone formation. Cholesterol demonstrated a statistically significant relationship ($R^2 = 0.0329$, $p = 0.0070$) which indicates that abnormal lipid metabolism may promote gallstone development. Similarly, FSH/LH ratio showed significant association ($R^2 = 0.0208$, $p = 0.0324$), highlighting the role of hormonal imbalance in gallbladder stone formation.

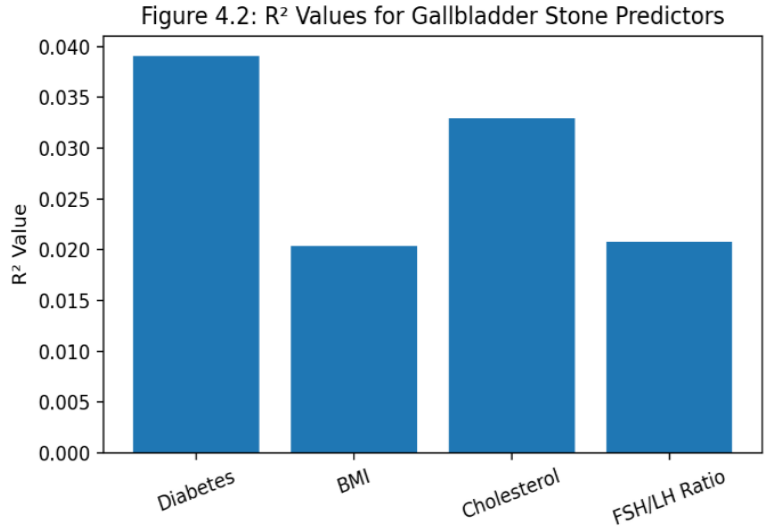

Figure 4.2 shows the R^2 values of predictors associated with gallbladder stones. Diabetes demonstrated the highest predictive contribution followed by cholesterol, while BMI and FSH/LH ratio showed relatively lower but statistically significant contributions.

Interpretation:
Diabetes showed the strongest relationship with gallbladder stones.
BMI contributed most strongly towards fatty liver, while diabetes contributed most strongly towards gallstones.
Overall, the results indicate that metabolic factors such as diabetes and obesity significantly influence both fatty liver and gallbladder stone formation. Hormonal imbalance represented by FSH/LH ratio also plays a significant role. These findings support the hypothesis that fatty liver and gallbladder stones share common metabolic and hormonal risk factors in females.

Discussion:
The present study was conducted to determine the sonographic association between fatty liver disease and gallbladder stones in females with metabolic and hormonal risk factors. A total of 220 female participants were assessed using ultrasonography along with evaluation of metabolic variables such as diabetes, BMI, cholesterol, and hormonal imbalance represented by FSH/LH ratio. The findings of this study demonstrate that both metabolic and hormonal factors significantly contribute to the development of fatty liver disease and gallbladder stones, supporting the hypothesis that these hepatobiliary disorders share common pathophysiological mechanisms (1).
The results revealed that diabetes mellitus showed a statistically significant positive association with fatty liver disease ($p = 0.0098$). This finding is consistent with previous studies indicating that insulin resistance and hyperglycemia contribute to hepatic fat accumulation by increasing lipolysis, free fatty acid influx to the liver, and impaired glucose metabolism. Diabetes is widely recognized as a major component of metabolic syndrome, and its role in NAFLD progression has been extensively documented. In the current study, diabetic females showed a greater likelihood of developing fatty liver, reinforcing the concept that impaired glucose homeostasis is an important predictor of hepatic steatosis (4).
Body Mass Index (BMI) demonstrated the strongest association with fatty liver among all studied variables ($R^2 = 0.1128$, $p < 0.001$). Obesity is known to increase the accumulation of adipose tissue, which promotes insulin resistance, chronic inflammation, and lipid dysregulation. These metabolic disturbances facilitate excessive triglyceride deposition in hepatocytes, leading to fatty liver development. The significant role of BMI observed in this study is in agreement with international research showing obesity as one of the most important risk factors for NAFLD. Therefore, weight management should be considered a major preventive strategy for reducing fatty liver prevalence in females (2).
Hormonal imbalance, represented by FSH/LH ratio, was also significantly associated with fatty liver ($p = 0.0027$). This finding suggests that endocrine disturbances may influence hepatic metabolism, possibly through alterations in insulin sensitivity, ovarian function, and fat distribution. Hormonal disorders such as polycystic ovarian syndrome (PCOS), menopause-related endocrine changes, and altered reproductive hormone levels may increase susceptibility to hepatic steatosis. The significance of FSH/LH ratio in this study highlights the importance of considering hormonal factors when evaluating hepatobiliary disorders in women (15).

Cholesterol also show a statistically significant association with fatty liver disease (p = 0.0736). Although dyslipidemia is generally considered a contributing factor to NAFLD. This suggests that cholesterol alone may not independently predict fatty liver in this specific population (5).

Regarding gallbladder stones, diabetes mellitus again demonstrated a significant positive association (p = 0.0032), indicating that diabetic females had a higher likelihood of gallstone formation. This is likely due to insulin resistance-induced changes in bile composition, increased hepatic cholesterol secretion, and impaired gallbladder motility. These findings align with previous evidence suggesting that metabolic syndrome predisposes individuals to cholelithiasis (8).

BMI was also significantly associated with gallbladder stones (p = 0.0342), supporting the role of obesity in gallstone formation. Increased body fat contributes to cholesterol supersaturation in bile and reduced gallbladder emptying, thereby facilitating stone development. Although the predictive strength was weaker than for fatty liver, the significance remains clinically important (16).

Unlike its relationship with fatty liver, cholesterol showed a statistically significant association with gallbladder stones (p = 0.0070). This finding supports the established mechanism that abnormal cholesterol metabolism directly contributes to cholesterol gallstone formation through bile supersaturation. Therefore, cholesterol appears to be a more relevant predictor for gallstone disease than for fatty liver in this study (23).

The FSH/LH ratio also showed a significant association with gallbladder stones (p = 0.0324), further emphasizing the influence of hormonal disturbances on gallbladder physiology. Female hormonal factors such as estrogen and progesterone are known to affect cholesterol metabolism and gallbladder motility, which may explain the increased prevalence of gallstones in women (5).

Overall, the findings suggest that fatty liver disease and gallbladder stones are interconnected conditions sharing several common metabolic and hormonal risk factors. Diabetes, obesity, and hormonal imbalance were significant predictors for both disorders, while cholesterol was specifically more influential for gallbladder stone formation. These results support previous literature proposing a shared metabolic basis for NAFLD and gallstone disease (1).

From a clinical perspective, the coexistence of fatty liver and gallbladder stones in females should prompt healthcare professionals to assess patients comprehensively for metabolic syndrome, obesity, endocrine abnormalities, and lifestyle factors. Ultrasonography proved to be an effective diagnostic tool for simultaneously identifying both hepatic steatosis and gallbladder pathology, making it highly valuable in routine screening of high-risk females (18).

This study contributes valuable regional data, particularly for South Asian female populations, where metabolic syndrome and hormonal disturbances are increasingly prevalent. It emphasizes the need for early detection, lifestyle interventions, and preventive management strategies to reduce the burden of hepatobiliary diseases (24).

Comparison with other studies:

The findings of the present study are largely consistent with previously published literature regarding the association between non-alcoholic fatty liver disease (NAFLD) and gallbladder stone disease. The significant association observed between diabetes mellitus and fatty liver disease supports the findings of Lu et al. (2021) and Ahmed et al. (2017), who reported that insulin resistance and impaired glucose metabolism are major contributors to hepatic fat accumulation and progression of NAFLD. Similarly, the current study demonstrated that diabetes was significantly associated with gallbladder stone formation, which is in agreement with previous research suggesting that hyperinsulinemia increases cholesterol secretion into bile and impairs gallbladder motility, thereby promoting gallstone development. The strong association between BMI and fatty liver disease observed in this study is also supported by Kim et al.

(2019) and Kong et al. (2023), who identified obesity as one of the most important predictors of hepatic steatosis. Increased adiposity contributes to chronic inflammation, altered lipid metabolism, and insulin resistance, all of which facilitate liver fat accumulation. Furthermore, the significant relationship between BMI and gallbladder stones found in the present study corresponds with findings reported by Portincasa et al. (2023), who demonstrated that obesity increases biliary cholesterol saturation and predisposes individuals to gallstone formation. The association between hormonal imbalance, represented by the FSH/LH ratio, and both hepatobiliary disorders is also supported by previous studies that highlighted the influence of female hormones on lipid metabolism, gallbladder contractility, and insulin sensitivity. Lyu et al. (2022) reported that hormonal disturbances may significantly affect metabolic homeostasis and increase susceptibility to both fatty liver disease and gallstone formation in women. However, unlike some previous studies that reported a strong association between dyslipidemia and NAFLD, the present study did not find a statistically significant relationship between cholesterol levels and fatty liver disease. This discrepancy may be attributed to differences in sample characteristics, dietary patterns, genetic factors, and population demographics. Nevertheless, cholesterol showed a significant association with gallbladder stones, which is consistent with the established pathophysiological mechanism of cholesterol supersaturation in bile leading to gallstone formation. Overall, the results of this study strengthen existing evidence that fatty liver disease and gallbladder stones share common metabolic and hormonal risk factors and may represent interconnected manifestations of underlying metabolic dysfunction in females.

Limitations:

Despite providing valuable insights into the association between fatty liver disease and gallbladder stones in females, this study has several limitations that should be considered when interpreting the findings. First, the cross-sectional study design limits the ability to establish a causal relationship between metabolic and hormonal risk factors and the development of hepatobiliary disorders. Since exposure and outcome variables were measured simultaneously, it is not possible to determine the temporal sequence of events. Second, the study was conducted in selected hospitals and clinics of Rahim Yar Khan, which may limit the generalizability of the findings to other populations, regions, or ethnic groups. Third, the sample size of 220 participants, although adequate for statistical analysis, may not fully represent the diversity of female populations with varying socioeconomic and clinical characteristics. Fourth, ultrasonography, while being a safe, non-invasive, and widely accepted diagnostic modality, has inherent limitations in detecting mild hepatic steatosis and may be influenced by operator experience and patient-related factors. Advanced imaging techniques such as MRI-based fat quantification or liver biopsy were not utilized due to practical and ethical considerations. Additionally, certain potentially relevant variables, including dietary intake, genetic predisposition, duration of diabetes, medication history, and detailed reproductive hormonal profiles, were not comprehensively evaluated. These factors may have influenced the observed associations. Finally, the study focused exclusively on female participants, which prevents direct comparison with male populations. Future longitudinal multicenter studies with larger sample sizes, broader geographical representation, and more comprehensive metabolic and hormonal assessments are recommended to further clarify the causal pathways linking fatty liver disease and gallbladder stones.

Conclusion:

This study concludes that there is a significant sonographic association between fatty liver disease and gallbladder stones in females with metabolic and hormonal risk factors. BMI, diabetes mellitus, cholesterol levels, and hormonal imbalance (FSH/LH

ratio) were key predictors, with BMI showing the strongest association with fatty liver and diabetes with gallbladder stones. The findings suggest that both conditions share common metabolic and endocrine pathways. Ultrasonography proved to be a reliable, non-invasive tool for simultaneous evaluation. Early screening of high-risk females and timely lifestyle, metabolic, and hormonal interventions are recommended to reduce future hepatobiliary complications.

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Declaration:
I declare that this article is my original work and has not been submitted or published elsewhere.

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