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Frequency of Gallstones in Fatty Liver disease in a Tertiary Care of Suburban Islamabad

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ABSTRACT

Background: Gallstone disease and Non-Alcoholic Fatty Liver Disease (NAFLD) share common etiological pathways. The objective of this study was to determine the frequency of Gallstones and Non-Alcoholic Fatty Liver disease (NAFLD) in patients undergoing abdominal ultrasounds in our hospital and to compare the frequency of Gallstone disease in patients with NAFLD and without NAFLD.

Methodology: This cross-sectional study was carried out at HBS General Hospital, Islamabad from January 2020 till December 2020. Patients undergoing routine ultrasounds in the out-patient department of the hospital were included in the study. Patients having Emergency Ultrasounds, history of Alcohol intake, history of chronic liver disease and pregnant patients were excluded from the study. Data was analysed using Microsoft Excel 2016 and IBM SPSS 22.

Results*:* A total of 689 patients were included with a 3:1 Female to Male ratio. Mean Age was 40.65± 15.610 years. The prevalence of Gallstone disease was found to be 20.9% while that of NAFLD 27.6%. A higher percentage of patients with NAFLD had Gallstones as compared to those who did not have NAFLD (24.2% vs 19.6% respectively) however for overall data, statistical significance was not reached. A statistically significant greater number of young patients with NAFLD had Gallstones as compared to those who did not have NAFLD (50% vs 6%, p<0.001). Mean age was greater in patients who had NAFLD as well as those having Gallstones.

Conclusion: The frequency of Gallstones was greater in patients with NAFLD as compared to those without NAFLD.

Key words*:* Cholelithiasis, Fatty Liver Disease, Gallstones, Non-Alcoholic, Ultrasonogram

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [2,3,4] Critical analysis and manuscript review; [5,6] Data analysis; Manuscript Editing.

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Introduction

Gallstone formation or Cholelithiasis is a complex process with a number of different causative factors leading to a single common pathway of stone formation. Precipitation of crystalline materials in bile forms a nidus around which further precipitation takes place, eventually resulting in the formation of a stone.[1] The precipitation can be

caused by disturbances in biliary homeostasis which can be as a result of many different factors. Weight, diet, drugs, age, gender, fertility, disease and extent of physical activity have been linked to gall stone disease. Gall stone disease shares these predisposing factors with Non-Alcoholic Fatty Liver Disease.[2]

Non-Alcoholic Fatty Liver Disease (NAFLD) is usually asymptomatic in its initial stages and has a poorly understood etiology.[3] Links have been reported to metabolic syndromes including Diabetes Mellitus, Obesity, Dyslipidemia and hypothyroidism.[4] There is ongoing research into understanding NAFLD. Inflammation in NAFLD can lead to steatohepatitis and ultimately Cirrhosis and Chronic liver disease.[4,5] While treatment of cholelithiasis is cholecystectomy, the treatment of NAFLD is complex and involves life style changes as well as medication.[6]

Due to similar risk factors between the two diseases, there has been a recent interest to determine whether there is a link between the two pathologies,[7] however, literature currently is scarce and controversial[8], with some studies claiming that these two conditions are linked while others declare them independent of each other.[5,9,10] In this study, we aim to determine the frequency of Gallstones as well as NAFLD in our patients and to see if these two diseases are related.[11] This information will help us in better understanding of relationship between these diseases and thus will lead to improved management and improved patient outcomes. We compared our results with other published literature to see whether there is an effect of ethnicity and geography on the frequency of these disease.[12] This study will generate local data and will contribute to improvement in academic as well as clinical knowledge of the two diseases.

Methodology

This descriptive study was carried out at our hospital over a period of one year (i.e. January 2020 till December 2020). Ethical approval was obtained from the affiliated medical college, Ethical committee. Patients undergoing routine ultrasounds in the out-patient department of the hospital were included in the study after informed consent and following the inclusion and exclusion criteria. Patients having emergency ultrasounds, history of alcohol intake, history of chronic liver disease and pregnant patients were excluded from the study. All ultrasounds were performed by consultant radiologists and the data were recorded on the designated proforma. A patient was labelled as having cholelithiasis on ultrasound if he/she had mobile stones casting posterior acoustic shadowing or mobile sludge in the gallbladder. A patient was labelled as having NAFLD on ultrasound if he/she had increased echogenicity or coarsened echo-texture of liver or nodular surface of liver and no clinical or radiological signs of inflammation of liver. NAFLD was graded as follows:

Grade I: diffusely increased hepatic echogenicity but peri-portal and diaphragmatic echogenicity was still appreciable

Grade II: diffusely increased hepatic echogenicity obscuring peri-portal echogenicity but diaphragmatic echogenicity was still appreciable

Grade III: diffusely increased hepatic echogenicity obscuring peri-portal as well as diaphragmatic echogenicity.

Data were analyzed using Microsoft excel 2016 and IBM SPSS 22. Mean and standard deviation was calculated for quantitative data like age. Frequency and percentages was calculated for analysis of qualitative data like gender, presence of gall stones, presence of NAFLD. Stratification was done according to age, gender, presence and absence of gall stones and NAFLD. Chi-square test was used to compare the frequency of NAFLD in patients with and without Gallstones.

Results

We included 689 patients in our study. There was an overwhelming female predominance in our study, n= 524 (76.1%) as compared to n= 165 (23.9%) of male patients. Mean age was 40.65± 15.610 years. Gallstones were found to be 20.9% (n= 144) while that of Fatty liver disease was found to be 27.6% (n= 190). Chi-square test was applied to compare frequencies of presence of gall stones in patients who had Fatty liver disease with those who did not, and it was found, this was not statistically significant. This is illustrated in Table I. Figure I depicts the frequency of different grades of Fatty liver disease found in our patients.

Mean age was compared between patients who had Fatty Liver Disease versus patients who did not have Fatty Liver disease and patients with Gallstones versus patients without Gallstones, using t-test. Mean age was found to be significantly lower in patients who did not have Fatty Liver disease as compared to those who had Fatty liver disease (38.78±16.44 years vs 45.57±11.882 years, p<0.001). A similar finding was noted based on the presence and absence of Gallstones (39.25±15.64 vs 45.94±14.32 years, p<0.001).

Table I: Frequency of Fatty Liver disease in patients according to gender and presence of Gallstones (n=689)

		Non-Alcoholic Fatty Liver Disease		p-value
		Absent	Present	
Gall stones	Absent	401 (58.2%)	144 (20.89%	0.187
	Present	98 (14.22%)	46 (6.67%)	
Gender	Male	110 (15.9%)	48 (6.9%)	0.332
	Female	381 (55.29%)	137 (19.88%	

Stratification was done according to age as well. This yielded results which showed that the frequency of both Gallstones and Fatty Liver disease increased with age. Subgroup analysis of younger patients also revealed that patients who had Fatty Liver were more likely to have gallstones as compared to those who did not have Fatty liver disease (50% vs 6%, p<0.001). Figure II shows frequency of gallstones and Fatty liver disease stratified according to age.

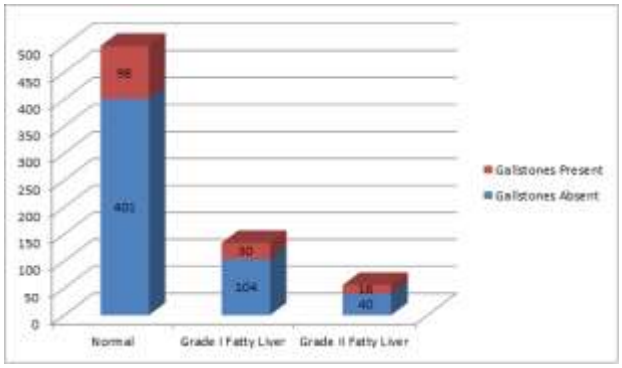

Figure 1: Presence and Absence of gallstones in patients according to grades of Fatty Liver disease

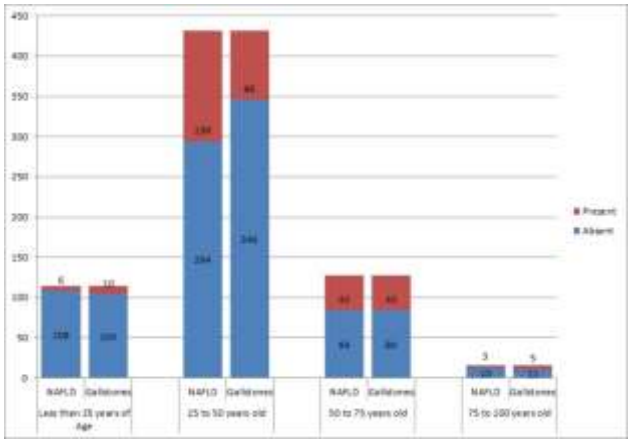

Figure 2: shows frequency of Gallstones and Fatty Liver disease stratified according to age

Discussion

Gallstone disease is one of the most common disease affecting humans. It has a common etiology which has common causative factors with Non-alcoholic Fatty liver disease. The frequency of

Gallstones and NAFLD in our study to be 20.9% (n=144) and 27.6% (n=190) respectively. This demonstrates that both of these diseases are common among our population while NAFLD is slightly more common than gallstones. As these disease have some common etiological pathways, interest has been generated to investigate whether these two disease have other correlations. In our study, we compared the frequency of gallstones in patients having NAFLD and those not having NAFLD and found that although patients having NAFLD had higher frequency of gallstones (NAFLD group= 24% vs non-NAFLD group 19%, p= 0.187), it did not reach statistical significance.

Singh K et. al in their study described the prevalence of NAFLD in 101 patients undergoing cholecystectomy for gallstones.[4] The gender distribution and mean age in their study is comparable to our study as their study also had a female predominance (75% female patients vs 25% male patients) and mean age was close to the mean age in our study (42.37±13.21 years in their study). The prevalence of NAFLD on Ultrasound in their study was found to be 34.7%, keeping in mind that they only included patients who were undergoing Cholecystectomies for cholelithiasis in their study, while in our study this was found to be 31.9% (n=46 out of 144 patients who had Gallstones). The similarities in our data might be explained by relatively close geographical location as their study was carried out in Chandigarh, India. The diet and eating habits of both these regions are also quite similar because of a shared culture before the creation of Pakistan and India.

Li X and Gao P in their cross-sectional study carried out in China included 897 patients.[9] They found that the prevalence of gallstone disease was similar in men and women. They also reported that younger patients who had Fatty Liver disease had a higher frequency of gallstone disease as compared to young patients who did not have Fatty liver disease. They also found that the frequency of gallstones increased with age. A similar finding was also noted in our study, as the frequency of gallstones increased with age, with the prevalence at 8.7% in Patients younger than 25 years old, 19.9% in 25-50 years old, 33.8% in 50-75 years old and 31% in patients older than 75 years. We also found that the frequency of gallstones in patients younger than 25 was higher in NAFLD group as compared to non-NAFLD group. This finding is in line with the finding of Li X and GaoP, that in young patients, Fatty Liver disease may be a risk factor for developing Gallstone disease. This may be due to the common etiological factors associated with both diseases as well as a probability that those young patients who have NAFLD also have dysfunctional bile homeostasis leading to the development of Gallstones.

Another study done by Qiao Q et. al in China described the correlation between gallstones and NAFLD in their population.[13] They found that the prevalence of NAFLD was significantly higher in patients having Gallstones as compared to those without gallstones (58.98% vs 46.58%, p <0.001). Although we found a similar finding, our results did not reach statistical significance (31.9% in Gallstone group vs 26.4% in Non-Gallstones group, p = 0.187). This might be due to the difference in sample size of the two studies as well as geographical and demographic factors. Qiao Q et. al included 7583 subjects in their study, whereas our study had a sample size of 689 patients, which is roughly 10% of their sample size. An increase in the sample size also raises the possibility of detecting a statistically significant difference between the frequency of NAFLD in patients with Gallstones and those without Gallstones.

In our results, although the frequencies of NAFLD and Gallstones appeared to be greater in patients who had the other disease, this was not found to be statistically significant, apart from young patients. One of the possible deductions might be that our sample size was underpowered to detect the difference between the groups.[13] Previously published literature demonstrates that there is a

relationship between these two diseases having common causes and etiological pathways.[14]

Arrese M[15] stated that there is a complex but definite relationship between fatty liver & gall stone disease, whether the patient takes alcohol or not. Hung MC et al calculated the relationship between gall stones and number of metabolic risk factors including lipid profile, ultrasound scan findings and weight of the patient[16]. His team showed invariably increased incidence of gall stones in fatty liver and obese patients.

Chang Y et al conducted a study in Korea concluding that increased non-invasive fibrosis markers of NAFLD were positively associated with an increased Frequency of gallstones in a graded and dose-responsive manner (p-value <0.01). This large-scale cohort study of young and middle-aged individuals demonstrated a bidirectional association between NAFLD and GD. NAFLD and its severity were independently associated with an increased incidence of gallstones.[17]

Another study published in World Journal of Gastrointestinal Pathophysiology has proposed that gall stones and cholecystectomy are risk factors for non-alcoholic fatty liver disease.[18] Similar results were shown by summart U et al[19] from Thailand.

Kakati D from US found out that NAFLD does not worsen the symptoms or disease progression[20].

Conclusion

The frequency of Gallstones was greater in patients with NAFLD as compared to those without NAFLD, but it was not statistically significant.

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