

Prevalence of Non Alcoholic Fatty Liver Disease with Gall Stone Disease in Rural Population in Government Medical College, Azamgarh, Up

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Abstract

Introduction: Gallstone disease is a major public health problem worldwide, particularly in adult population. Incidence of gallstone disease shows considerable geographical and regional variations. Its occurrence has been found to be at least 6% in the adult population of North India. The rate of gall bladder diseases are more common among females than males. Gall bladder disease are more common in the Northern and Northeastern states of Uttar Pradesh, Bihar, Orissa, West Bengal and Assam. Risk factors for gall bladder disease include diet, obesity, multiparity and chronic infections including Salmonella typhi and paratyphi and Helicobacter pylori.

Materials and Methods: This cross-sectional study was done in the department of surgery from June 2017 to May 2019 in Govt Medical College, Azamgarh. And patients from all over the state are being referred & treated in this hospital. A total of 300 patients of ultrasound proven cholelithiasis admitted in hospital for cholecystectomy, underwent Fibroscan in the department of Gastroenterology and were evaluated to establish relationship between cholelithiasis and NAFLD.

Results: This study, was conducted from 1st of June 2017 to May 31st 2019, included 300 patients who came to surgery or gastroenterology OPD with ultrasonography proven cholelithiasis (gall stone disease). Out of 300 patients in the study 240 (80%) patients were females and 60 (20%) were male respectively. Patient's ranged from 22 to 80 years of age with an average age of 44.3 yrs. (SD-11.9). Maximum numbers of patients were in the age group of 31-50 yrs. constituting 57.5% of the total study population. Age wise distribution showed 43 patients (14.3%) in age group 18-30 years, 76 (25.3%) patients in age group 31-40 yrs., 96 (32%) patients in age group 41-50 yrs., 51(17%) patients in age group 51-60 yrs., 30 (10%) patients in age group 61-70 yrs., and 4 (1.4%) patients in age group >70 years.

Conclusion: There is a high prevalence of NAFLD in patients of gall stone disease in azamgarh population. Most of the patients of NAFLD with gall stones had mild degrees of steatosis. Fibrosis was present in 27% patients of NAFLD with gall stone disease. Patients of gall stone disease with NAFLD had a higher mean BMI, TG, T. Ch, steatosis and fibrosis levels than gall-stone disease patients without NAFLD.

Key Words: NAFLD, BMI, TG, Fibrosis.

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I. Introduction

Gallstone disease is a major public health problem worldwide, particularly in adult population. Incidence of gallstone disease shows considerable geographical and regional variations. Its occurrence has been found to be at least 6% in the adult population of North India. The rate of gall bladder diseases are more common among females than males. Gall bladder disease are more common in the Northern and Northeastern states of Uttar Pradesh, Bihar, Orissa, West Bengal and Assam. Risk factors for gall bladder disease include diet, obesity, multiparity and chronic infections including Salmonella typhi and paratyphi and Helicobacter pylori.

Although the gold standard for diagnosis and staging NAFLD is liver biopsy. Liver biopsy has inherent limitations because of risks and life threatening complications, sample size and sampling variability which

render liver biopsy a less than ideal gold standard.(3) Ultrasound is commonly used to screen for hepatic steatosis, but its limitations include suboptimal sensitivity as well as specificity for the detection of mild steatosis & operator dependence. Hence it is not ideal for detecting the early stages of NAFLD.(4) Transient elastography (fibroskan) is a new, user friendly, noninvasive test. TE for the evaluation of cirrhosis has shown validity and excellent diagnostic accuracy in chronic hepatitis C & B, alcoholic liver disease, primary biliary cholangitis and after liver transplant. It has high sensitivity and specificity in mild to moderate steatosis and fibrosis.

Thus, this study is possibly the first attempt to study the prevalence of NAFLD in patients with gall stone disease by using transient elastography in Himalayan population of the Indian subcontinent, which represents a distinct geographic, environmental and diet consuming entity than the rest of the Indian subcontinent.

II. Materials And Methods

This cross-sectional study was done in the department of surgery from June 2017 to May 2019 in Govt Medical College, Azamgarh. And patients from all over the state are being referred & treated in this hospital. A total of 300 patients of ultrasound proven cholelithiasis admitted in hospital for cholecystectomy, underwent Fibroskan in the department of Gastroenterology and were evaluated to establish relationship between cholelithiasis and NAFLD.

Inclusion Criteria

Were aged 18 years or above, diagnosed gall bladder stone disease on screening ultrasonography for right hypochondriac pain or biliary pain who underwent cholecystectomy.

Exclusion Criteria

Were clinical, radiological or biochemical evidence of choledocholithiasis, evidence of gall stone induced pancreatitis, pregnancy, patients with significant alcohol addiction >25 g/day, patients not willing to participate or on hepatotoxic drugs.

Data Collection

Data was recorded and baseline demographic data of all study patients including - Age, Sex, height, weight, BMI (body mass index), blood pressure were recorded. GPE (general physical examination) and systemic examination was done. All routine and relevant investigations to exclude secondary causes of fatty liver including estimation of blood glucose, HbA1c, complete hemogram, renal function tests, ALT, AST, total and direct bilirubin, CRP, thyroid function tests, total protein and albumin and lipid profile, Hep B, Hep C., HIV serology, serum ceruloplasmin and ANA were done. The patients with investigations suggestive of alternative diagnosis were excluded.

The lab. investigations included estimation of blood glucose, HbA1c, complete hemogram, renal function tests, SGOT, SGPT, total and direct bilirubin, CRP, thyroid function tests, total serum proteins, serum albumin and lipid profile. Abdominal USG examination of the subjects was performed using a 3.5 MHz transducer and the presence of gallstones was determined.

NAFLD was diagnosed based on value of CAP (controlled attenuation parameter) on transient elastography (fibroskan), simultaneously degree of fibrosis was assessed based on liver stiffness measurement (LSM) value on transient elastography. Based on CAP value steatosis was graded as S0, S1, S2, S3 and fibrosis was graded as, F0-F1, F2, F3 and cirrhosis. Minimum cut-off value for diagnosing NAFLD was 214 dB/m. Minimum fibrosis significant was taken as F2 or more i.e. LSM value >7.5 kPa.

The finding of Fibroskan were interpreted as: S0 (no fatty liver), $S \geq 1$ ($\geq 10\%$ of hepatocytes with fat), the CAP cut-off values ranged from 214 to 289 dB/m, with a 64%-91% sensitivity and 64%-94% specificity; for $S \geq 2$ ($\geq 33\%$ hepatocytes with fat), the CAP cut-off values ranged from 255 to 311 dB/m, with a 57%-96% sensitivity and 62%-94% specificity; finally, for S3 ($\geq 66\%$ hepatocytes with fat), the CAP cut-off values ranged from 281 to 310 dB/m with a 64%-100% sensitivity and 53%-92% specificity. S1, S2, S3 were graded as mild, moderate and severe NAFLD respectively. The adjusted values were taken as: S0, if CAP score is <214, S1, if CAP score is (215-255), S2, if CAP score is (256-312), and S3, if CAP score is > 312 dB/m. And F0-F1 i.e. no to mild fibrosis if LSM score was between 2.5 and 7.5 kPa, F2 i.e. moderate fibrosis if LSM score was between 7.5- 10 kPa, F3 i.e. severe fibrosis if LSM score was between 10-14 kPa and F4 i.e. cirrhosis if LSM score is >14 kPa. Significant fibrosis was taken as F2 and above.

Statistical Analysis

All numerical data were expressed as mean with standard deviation (SD). All the statistical tests were done using Excel/SPSS software. Discrete and continuous variables were compared using Pearson's coefficient,

Chi square test and Student t-test as appropriate. Multiple comparisons were made using ANOVA. A p value <0.05 was taken as statistically significant.

III. Results

This study, was conducted from 1st of June 2017 to May 31st 2019, included 300 patients who came to surgery or gastroenterology OPD with ultrasonography proven cholelithiasis (gall stone disease). Out of 300 patients in the study 240 (80%) patients were females and 60 (20%) were male respectively. Patient's ranged from 22 to 80 years of age with an average age of 44.3 yrs. (SD-11.9). Maximum numbers of patients were in the age group of 31-50 yrs. constituting 57.5% of the total study population. Age wise distribution showed 43 patients (14.3%) in age group 18-30 years, 76 (25.3%) patients in age group 31-40 yrs., 96 (32%) patients in age group 41-50 yrs., 51(17%) patients in age group 51-60 yrs., 30 (10%) patients in age group 61-70 yrs., and 4 (1.4%) patients in age group >70 years.

The mean BMI of the study population was 25.7(SD-3.7), with a range from 16.5 to 36.3. Mean LFT's of the study population were found to be within normal limits, in which, mean total bilirubin of the study population was 0.77 mg % (SD-0.5), with a range from 0.1 mg% to 4.8 mg%, and mean conjugated bilirubin was 0.24 mg% (SD 0.20), with a range from 0.01 mg% to 0.96 mg%. Mean ALT of the study population was 34.9 U/L(SD-16.7), with a range from 10 U/L to 111 U/L. Mean AST of the study population was 33.5 U/L(SD-20.1), with a range from 15 U/L to 205 U/L. Mean ALP of the study population was 103.4 U/L (SD-45.5) with a range from 43 U/L to 370 U/L.

Mean total cholesterol of the study population was 179.3 mg/dL (SD-40.5) with a range from 100 mg/dL to 287 mg/dL. Mean triglycerides of the study population were 71.6 mg/dL (SD-71.6), with a range from 32 mg/dL to 474 mg/dL. Mean HDL of the study population was 48.8 mg/dL (SD-13.1), with a range from 24 mg/dL to 119 mg/dL. (table-1) In this study, significant liver steatosis, suggestive of NAFLD was found in 189 patients, i.e. 63%, however 111 patients i.e. 37% did not have significant steatosis suggestive of NAFLD, calculated on the basis of CAP value. Those with significant steatosis suggestive of NAFLD were graded as 90(30%) mild steatosis (S1), 62(20.6%) moderate steatosis (S2) and 37 (12.4%) severe steatosis (S3). Similarly, fibrosis was calculated on the basis of LSM score and it was found that 79 patients, i.e. 26.3% had significant fibrosis (basic cut-off value for significant fibrosis was taken as >7.5 kPa) and 221 patients did not have significant fibrosis.

S.No	Variable	GSD without NAFLD (Mean)	GSD with NAFLD (Mean)	P Value
1	Age	43.5	44.8	0.43
2	TOT, Bilirubin	0.76	0.77	0.538
3	Conj, Bilirubin	0.27	0.22	0.335
4	ALT	31.4	37.0	0.018
5	AST	30.3	35.5	0.143
6	ALP	105.0	102.4	0.431
7	TG	139.2	180.0	<0.001
8	HDL	49.6	48.3	0.499
9	LDL	97.6	105.7	0.086
10	Total Cholesterol	169.2	185.4	0.005
11	Steatosis	175.3	271.5	<0.001
12	Fibrosis	4.3	7.8	<0.001

Table 1: Comparison of Various Parameters in Gall Stones Patients with and without NAFLD

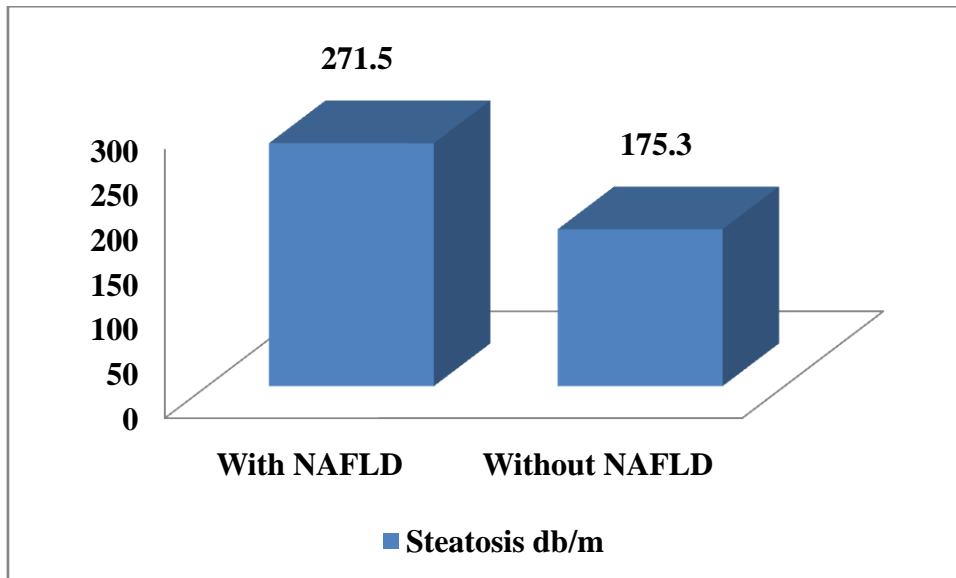


Figure 1: Comparison of Mean Value (CAP dB/m) of Steatosis in Patients of Gall Stone Disease with and without NAFLD

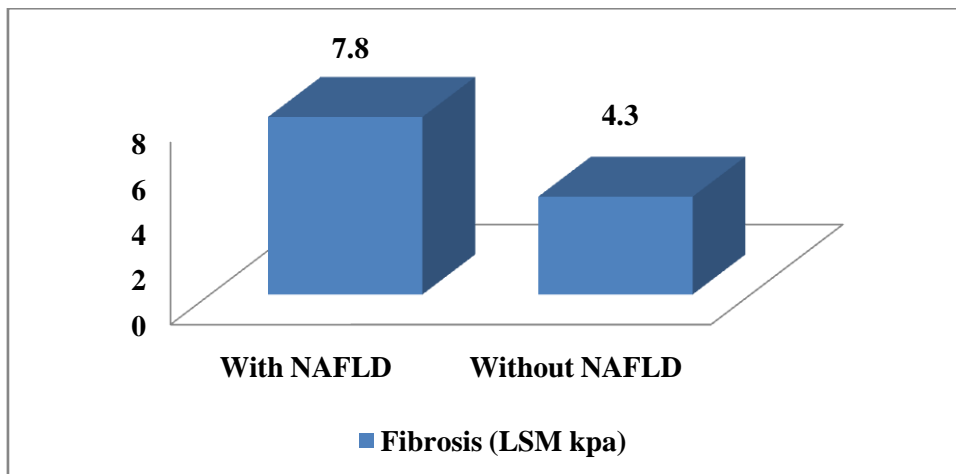


Figure 2: Comparison of Mean Value (kPa) of Fibrosis in Patients of Gall Stone Disease with and without NAFLD

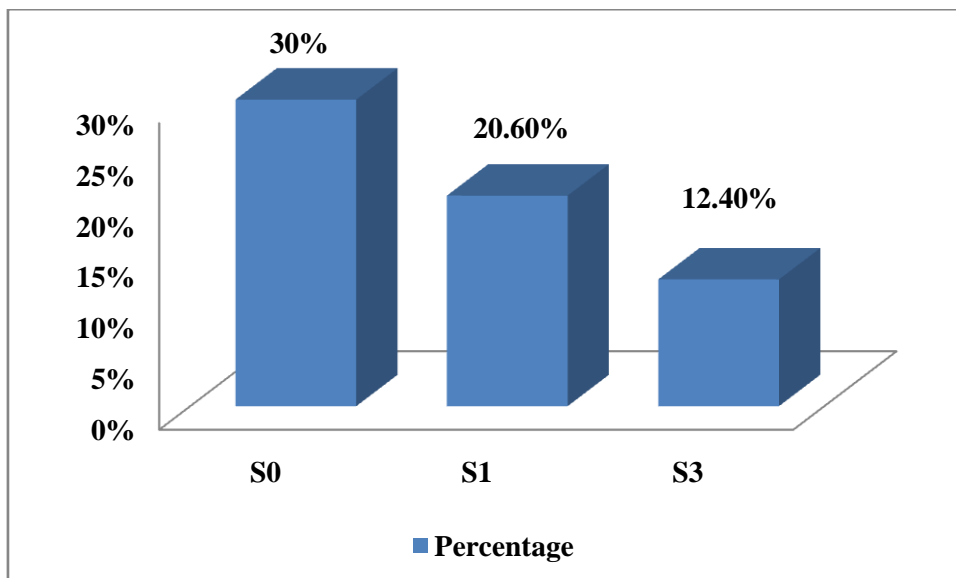


Figure 3: Grades of Steatosis in Patients of NAFLD with Gall Stone Disease

Fibrosis was graded as F0-F1, F2, F3 and cirrhosis i.e. no-to insignificant fibrosis, moderate fibrosis, severe fibrosis and cirrhosis, based on the cut-off values and out of 300 patients, 221 (73.7%) patients had no to insignificant fibrosis(f0-f1), 51 (17%) patients had moderate fibrosis, 14 (4.6%) patients had severe fibrosis and 7(2.4%) patients had cirrhosis on TE (fibrosan). In this study, patients of gall stone disease with NAFLD and patients without NAFLD were compared and it was found that: Mean age of patients with NAFLD was found to be 44.8 yrs., and without NAFLD was 43.5 yrs. with a p-value of 0.43. Thus, no significant association was found between age and NAFLD in patients with gall stone disease. Mean number of male patients, with NAFLD were 80.7 and without NAFLD were 79.0. Similarly, the mean number of females with NAFLD were 19.3 and without NAFLD were 21.0, with a p-value of 0.771. Thus, no significant association was found between sex and NAFLD in patients with gall stone disease.

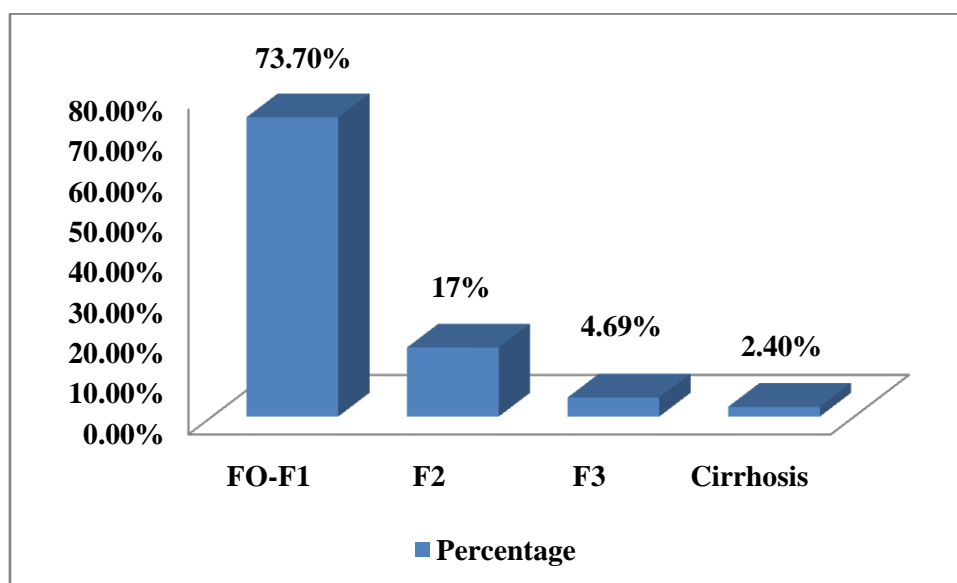


Figure 4: Grades of Fibrosis in Studied Patients

IV. Discussion

Non-alcoholic fatty liver disease (NAFLD) has a prevalence of 15%–20% in the general population. In our study NAFLD as detected by CAP value on TE, was present in 63% patients of GSD. The higher prevalence of NAFLD in our patients than the general population, suggest a possible association between NAFLD and gall stone disease. Similar higher prevalence of NAFLD has been reported in other studies which are in consonance with this study. Koller et al [8] found higher prevalence of GSD among patients with NAFLD versus those without NAFLD (47% vs. 26%, respectively). While, Farah et al from Pakistan reported the prevalence of NAFLD in 62.5% patients with gall stones disease. Higher prevalence of NAFLD in patients with gall stone disease is due to sharing of common risk factors like body mass index, gender, raised lipid levels, use of contraceptives, alcohol and having diabetes, physical inactiveness, multiparous women, water with excessive iron content & metabolic syndrome.

Most of the patients in our study population had mild severity of steatosis (S1 i.e. 30%), this is in contrast to other studies which found that there is a greater degree of steatosis among patients with NAFLD and gallstones. Francazani et al. including 524 Italian patients with biopsy-proven NAFLD found a GSD prevalence of 20% with NASH prevalence being significantly higher in patients with GSD, as compared to patients without GSD (77% vs. 56%).

In our study, we found that fibrosis was present in 26.5% of patients and the mean fibrosis score was higher (7.8 kPa) in patients with NAFLD than those without NAFLD (4.3 kPa) with a significant p-value of <0.001. Thus, we come to a result that fibrosis present in GSD with NAFLD is severe as compared to gall stone disease patients without NAFLD. The result of one series showed about 10% of the gallstone patients at the time of diagnosis had NAFLD progression to fibrosis which was biopsy proven. NAFLD contributes as the commonest cause that leads to cirrhosis, portal hypertension and hepatic cancer and it has been estimated that approximately 22% of NAFLD progresses to cirrhosis. One of the studies justified for performing liver biopsy for the detection of NAFLD during cholecystectomy and that series captured more NAFLD in patients who undergone biopsies than those with simple ultrasound findings and liver function tests. Thus we claim that fatty female of febrile age needs fibrosan to rule out gall stones disease.

V. Conclusion

There is a high prevalence of NAFLD in patients of gall stone disease in azamgarh population. Most of the patients of NAFLD with gall stones had mild degrees of steatosis. Fibrosis was present in 27% patients of NAFLD with gall stone disease. Patients of gall stone disease with NAFLD had a higher mean BMI, TG, T. Ch, steatosis and fibrosis levels than gall-stone disease patients without NAFLD.

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