



# An observational study on the association of nonalcoholic fatty liver disease and metabolic syndrome with gall stone disease requiring cholecystectomy



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## H I G H L I G H T S

- Most patients with gallstones have associated NAFLD.
- Metabolic syndrome, NAFLD, gallstones share common factors.
- We recommend health education and lifestyle modification in gall stone patients.
- Majority first degree relatives of gall stone patients had gallstones.
- First degree relatives of patients had gallstones and this relation was more pronounced patients who had associated NAFLD.

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## A B S T R A C T

**Objective:** Recognition of Non alcoholic fatty liver disease (NAFLD) and metabolic syndrome in patients with gallstones undergoing laparoscopic or open cholecystectomy, along with it we will also study the life style of patients with gall stones.

**Background:** Patients with gallstones have associated NAFLD, with concurrent metabolic syndrome and these ailments share similar factors for example obesity, hypertriglyceridemia and diabetes mellitus. Factors like body mass index, gender, raised lipid levels, use of contraceptives and alcohol and having diabetes, physical inactiveness, multiparous women, water with excessive iron content, metabolic syndrome, and NAFLD are accountable factors for gallstones formation.

**Methodology:** This was a case series done at Surgical Unit 1 of Civil Hospital Karachi. Selective samples of 88 patients were included. Duration was 3 months. We included both sexes with ultrasound proof of gall stone irrespective of cholecystitis. Excluded patients with history of seropositive viral hepatitis, auto-immune and wilson's disease. As these conditions can act as a confounder to our variables.

**Results:** Nafld was present in 62.5%(n = 55) while 28.4% (n = 25) had metabolic syndrome. 26.94% had BMI less than 18, 32.12 had BMI between 18 and 25 and majority had BMI greater than 25 i.e in 40.93%. Of all 46.6% had a family history of cholelithiasis. Gallstone patients with NAFLD reported about their first degree relative being suffering from cholelithiasis at a significant p-value of 0.034 while this was not significant in cases of metabolic syndrome and the p -value was 0.190.

**Conclusion:** We found association of metabolic syndrome with gallstones and NAFLD. Non alcoholic fatty liver was highly prevalent in our study subjects. Huge percentage of first degree relatives of gall stone patients had gallstones and this relation was more pronounced patients who had associated NAFLD.

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## 1. Introduction

Non alcoholic fatty liver disease (NAFLD) has the prevalence of 15%–20%. It is the amassing of fats in the hepatic tissue without significant alcohol intake that result in hepatic steatosis [1]. NAFLD includes a broad range of liver conditions including plain fattiness

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in hepatic tissue which is static to progressive steatohepatitis that may progress to cirrhotic changes and hepatic carcinoma [2–4]. NAFLD contributes as the commonest cause that leads to cirrhosis and approximately 22% of NAFLD progresses to cirrhosis as reported by studies. Currently there is no medical remedy to stop this progression or to reverse the cirrhotic condition. However weight reduction is the mainstay of preventing cirrhosis in NAFLD patients [5]. Non alcoholic fatty liver disease happens in two phases. First triglycerides get accumulated in liver without hepatic damage and later on hepatic damage takes place. Lipid peroxidation and oxidative stress are the understood noxious pathologies [6,7].

Patients with gallstones have associated NAFLD, with concurrent metabolic syndrome and these ailments share similar factors for example obesity, hypertriglyceridemia and diabetes mellitus [8].

Gallstone forms by the precipitation of calcium, bilirubin, cholesterol mucous and proteins. It is one of the commonest ailments presenting to surgical units. A study reported an incidence of 9.03% [9]. Nearly 75% of the patients with gall stones are symptomless [10].

Factors like body mass index, gender, raised lipid levels, use of contraceptives and alcohol and having diabetes [11,12], physical inactiveness [13], multiparous women [14], water with excessive iron content [15], metabolic syndrome [16], and NAFLD [1] are accountable factors for gallstones formation.

The presence of three or more of the following five factors is defined as the Metabolic Syndrome by Adult Treatment Panel III (ATP III) criteria. [17,18]: (1) hypertriglyceridemia: (higher TG) greater than 150 mg/dL; (2) abdominal obesity e waist girth in men greater than 90 cm and in women greater than 80 cm (3) lower HDL-C: serum HDL-C less than 40 mg/dL in men and <50 mg/dL in women; (4) hyperglycemia: fasting plasma glucose greater than 100 mg/dL or DM history (including medical record or self-reported). (5) elevated blood pressure (systolic blood pressure greater than 130 mmHg or diastolic blood pressure greater than 85 mmHg or hypertension history (including medical record or self-reported).

The study will be a paradigm to identify the presence of Non alcoholic fatty liver disease (NAFLD) and metabolic syndrome in patients with gallstones undergoing laparoscopic or open cholecystectomy along with it we will also study the life style of patients with gall stones. Also role of metabolic syndrome in pathophysiology of Non alcoholic fatty liver disease and gallstone will be identified as well as their interrelation.

## 2. Objective

Recognition of Non alcoholic fatty liver disease (NAFLD) and metabolic syndrome in patients with gallstones undergoing laparoscopic or open cholecystectomy, along with it we will also study the life style of patients with gall stones.

## 3. Methodology

This was a case series done at Surgical Unit 1 of Civil Hospital Karachi. Selective samples of 88 patients were included in this which was calculated by [www.OpenEpi.com](http://www.OpenEpi.com) taking the population size of 95 at 95% CI and 3% margin of error [19]. Duration was 3 months. Institutional review board approval for research proposal was also taken from Dow University Of Health Sciences with reference id of IRB-748/DUHS/Approval/2016/240. Random sampling was done. We included both sexes with ultrasound proof of gall stone irrespective of cholecystitis. Excluded patients with history of seropositive viral hepatitis, autoimmune and wilson's disease. As these conditions can act as a confounder to our variables.

After signing a consent all the relevant data was collected on a proforma. To make the liver ultrasound report more authentic and to pick up NAFLD more critically a well experience sonographer was given the duty to see the participants of our research. All data collected data was entered and analyzed via SPSS-20.

## 4. Results

Analysis of the data showed 37.5% (n = 33) were males and 62.5% (n = 55) were females. The mean age of the participants was  $36.40 \pm 12.97$ . Majority were married (78.4%). 37.5% belonged to the rural areas while 62.5% were from urban areas. A huge percentage (45.5%) had history of addiction Beatle nut chewing was reported by 40.5% and smoking in 5%. 39% drink un-boiled water. 38.77% reported taking oral contraceptive pills. About 38.6% had abdominal surgery in the past.

Table 1 is representing the education statuses our participant which is showing a very less literacy rate. Most of our participants had no exercise habit as shown by Table 2.

26.94% had BMI less than 18, 32.12 had BMI between 18 and 25 and majority had BMI greater than 25 i.e. in 40.93%. The mean weight was 65.7 and standard deviation of  $\pm 15.6$  the mean height was 1.6 m and standard deviation of 0.109 m. Abdominal circumference came out to be  $87.5 \pm 5.8$ .

Of all 46.6% had a family history of cholelithiasis. Gallstone patients with NAFLD reported about their first degree relative being suffering from cholelithiasis at a significant p-value of 0.034 while this was not significant in cases of metabolic syndrome and the p-value was 0.190.

As far as the parity is concerned 90.73% were multipara. Systolic BP was greater than 130 in 55.30% and diastolic BP was greater than 85 in 56.69%.

Nafld was present in 62.5% (n = 55) while 28.4% (n = 25) had metabolic syndrome.

The patients with metabolic syndrome had a co morbid of hypertension and diabetes at a p-values of 0.001. and 0.00, respectively which were highly significant.

The patient with NAFLD had hypertension and diabetes as a co morbid at a p-values of 0.89 and 0.336, respectively. There is no gender related association of metabolic syndrome nor NAFLD as shown by Figs. 1 and 2.

Patients with the presence of metabolic syndrome had higher mean SGPT level i.e. 86.96 as compared to patients with absent metabolic syndrome (48.09) at a p-value of 0.005. The triglyceride levels in patients with presence metabolic syndrome was higher (mean = 162.5200) and the p value was 0.00 and HDL was significantly low (mean = 98.3600) at a p value of 0.001 (Tables 3 and 4).

Patients with presence of nafld were found to have deranged SGPT and SGOT (Means = 74.4182 and 75.7273) as compared to the ones with absent of nafld at a p value of 0.002 and 0.006 respectively. (Tables 5 and 6).

## 5. Discussion

A nation wide survey conducted in America revealed a very high

**Table 1**  
Education status.

	Frequency	Percent
Illiterate	27	30.7
School	39	44.3
Undergraduate	20	22.7
Graduate	2	2.3
Total	88	100.0

**Table 2**  
Exercise habit of participants.

	Frequency	Percent	Valid Percent	Cumulative Percent
No	71	80.7	80.7	80.7
Rarely	2	2.3	2.3	83.0
Once A Week	2	2.3	2.3	85.2
Twice A Week	2	2.3	2.3	87.5
Yes, Often	11	12.5	12.5	100.0
Total	88	100.0	100.0	

prevalence of cholelithiasis i.e. 13.9%–26.7% in women and 5.3%–8.9% in men under the domain of third National Health and Nutrition Examination Survey [20]. In Pakistan, the prevalence of gallstone is still not known. However in India which is the neighbouring country to Pakistan with similar geography and ethnicity had a study on 5100 and 1448 people with and without symptoms of gallstones. They had gallbladder ultrasonography that showed noteworthy figures of prevalence of 5.59% in women and 1.99% in males [21]. Our study showed this trend as well, as most (62.5%) of the gallstone patients were females. There is a general conjecture that sex hormones and cholesterol metabolism have possible interrelation [16]. This makes a point to ruminate on how sex is implicated in cholesterol stones formation. Most of the studies suggest female predominance when it comes to the prevalence of gallstones along with it the likelihood of being at risk for stone formation [20–22]. On contrary, Liu CM et al. denied gender relation to gallstones [23]. The mean age of the participants was  $36.40 \pm 12.97$  and this was in line with the results of study by Lirussi F. et al. that indicated an existence of high age relation with cholelithiasis more astounded in women [22]. Liu CM et al. explained since people with high age had been more exposed to a pile of chronic factors like alcohol intake, hyperlipidemia and diabetes mellitus (DM), hence they are more prone to gallstone development due to manifestation of decreased motility of gallbladder [23].

Chen LY et al. [16] while discussing gallstone formation phenomenon also favored the theory of hyperlipidemia, decreased motility of gall bladder being overweight and insulin resistance as

culprit factors of cholelithiasis pathology. According to him separation of crystals of cholesterol from supersaturated bile is the prime event. Phospholipids and bile acids makes cholesterol more soluble and prevents its precipitation. Phospholipid transfer protein (PLTP) transfers lipids from low-density lipoproteins to high-density lipoproteins. In hyperlipidemia, haptoglobin inhibits PLTP and results in reversal of cholesterol transport. Cholesterol transporter ABCG5-G8 and phospholipid floppase ABCB4 polymorphisms makes one vulnerable to gallstone risk [16]. Protein kinase(PKC $\beta$ ) is also considered as a major physiological regulator of lipids [16].

A huge percentage (45.5%) of our participants had habit of addiction. Of all 5% had smoking addiction. Diehl et al. [24] argued about role of smoking in stone formation as nicotine would probably raises the lithogeneity of the bile. Beate nut chewing was very commonly seen in our study and 40.5% had its addiction which is much higher than another study which reported a figure of 16.6% in the neighbouring country India [25].

None of our study participant had alcoholism habit. Alcohol consumption counts as a contributing factor for gallstone formation [11,12]. In oppose to this there is a study that says that intake of small to moderate amount of alcohol lowers the biliary cholesterol saturation index and thus act as protective [26].

In this study 39% used to drink un-boiled water. Unisa S et al. also noticed the drinking of water from unsafe source was common in gallstone patients [21]. 38.77% reported taking oral contraceptive pills which is a known risk factor for cholelithiasis [11,12].

Our study results were also in coherence with another series in matter of educational status as most of the participants were found to have low education [21]. As per Table 2 most of the study participants had inactive lifestyle. Physical inactiveness is a well known factor accounted for gallstones [13].

About 38.6% had abdominal surgery in the past. A with retrospective study design showed that major abdominal surgery can result in acceleration of stone formation. However this needs to be confirmed through a prospective research so that prophylactic measures could be taken [27].

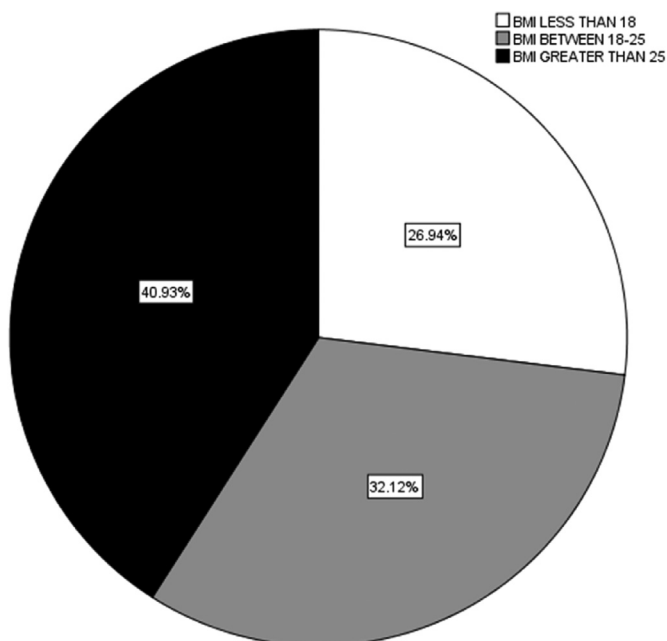
Majority (40.93%) of our participants had a BMI greater than 25 (Fig. 1), nevertheless the mean of abdominal circumference came out to be greater as well i.e.  $87.5 \pm 5.8$ . Our results in terms of BMI are quite different from another study that reported 80% of patients had normal BMI and that was no different than control group [25]. Obese women are slightly higher risk of stone formation as compared to women with ideal BMI especially when talking about cholesterol gallstone [24]. The observation of Trotman has brought the fact into light that pigment GS and with cholesterol GS patients had no differences in their BMIs [28].

Our results show 46.6% of the first degree relatives of the patients also had cholelithiasis and this trend was also in assertion as proved by another study [29]. This point leads to contemplate a strong reason to screen the first degree relatives for gallstones.

Out of all 90.73% our participants were multipara. Parity has been accounted as one of the significant factors for GS(14). Sarin et al. [30] mentioned about 94% of patients were multiparous in his study outcome.

A previous study made the fact apparent that the obese patients with an Asian lineage had raised diastolic blood pressure. Our study out came in the same harmony, as diastolic BP was greater than 85 in 56.69%. Moreover the Systolic BP was also greater than 130 in 55.30%. Reason being people with hypertension may have more sympathetic nerve activities that may probably decrease bowel movements [31].

Patients with gallstones have associated NAFLD, with concurrent metabolic syndrome and these ailments share similar factors for example obesity, hypertriglyceridemia and diabetes mellitus



**Fig. 1.** BMIs of the study participants.

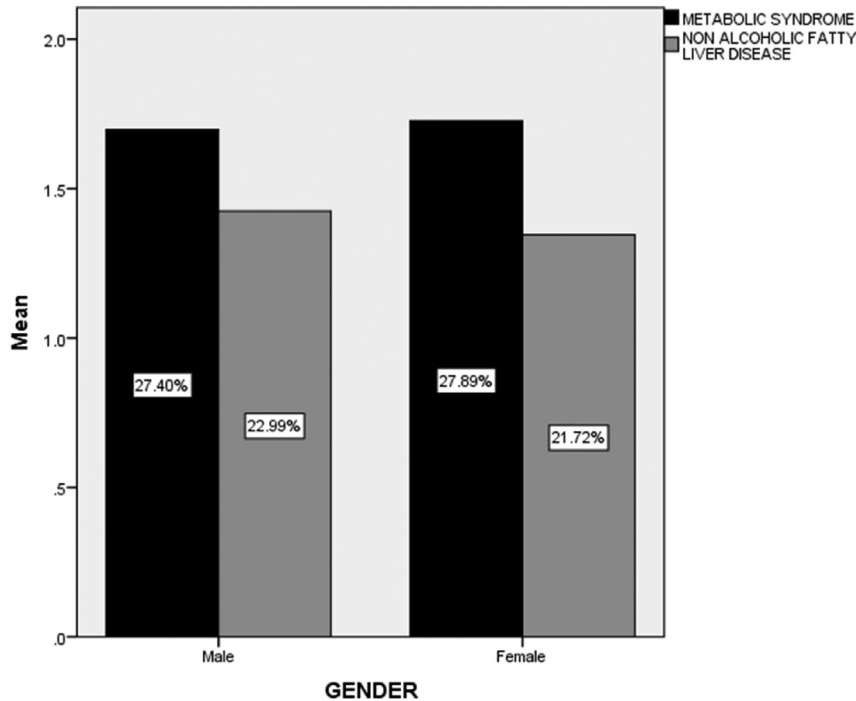


Fig. 2. Gender wise ratios of Metabolic Syndrome and Non Alcoholic Fatty Liver Disease Occurrences among the participants.

Table 3  
Analysis of presence of metabolic syndrome relation status with SGPT, SGOT, BILIRUBIN, FBS, TRIGLYCERIDE and HDL.

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Minimum
						Lower Bound	Upper Bound		
SGPT	Yes	25	86.9600	83.20931	16.64186	52.6129	121.3071	7.00	333.00
	No	63	48.0952	43.48627	5.47875	37.1434	59.0471	7.00	300.00
	Total	88	59.1364	59.73604	6.36788	46.4795	71.7932	7.00	333.00
SGOT	Yes	25	75.0400	88.94637	17.78927	38.3247	111.7553	8.00	333.00
	No	63	55.5238	52.64484	6.63263	42.2654	68.7822	8.00	300.00
	Total	88	61.0682	65.08382	6.93796	47.2782	74.8581	8.00	333.00
Total BILIRUBIN	Yes	25	1.9088	3.45250	0.69050	0.4837	3.3339	0.25	15.70
	No	63	1.3695	3.29433	0.41505	0.5399	2.1992	0.10	23.80
	Total	88	1.5227	3.32898	0.35487	0.8174	2.2281	0.10	23.80
Fasting plasma glucose level(FBS)	Yes	25	108.5600	37.12937	7.42587	93.2337	123.8863	75.00	200.00
	No	63	102.4286	17.19688	2.16660	98.0976	106.7595	75.00	180.00
	Total	88	104.1705	24.47012	2.60852	98.9857	109.3552	75.00	200.00
TRIGLYCERIDE level	Yes	25	162.5200	37.79453	7.55891	146.9192	178.1208	81.00	215.00
	No	63	115.6190	45.58028	5.74258	104.1398	127.0983	51.00	210.00
	Total	88	128.9432	48.24038	5.14244	118.7220	139.1643	51.00	215.00
SERUM HDL	Yes	25	98.3600	26.59085	5.31817	87.3838	109.3362	32.00	150.00
	No	63	121.5556	27.50354	3.46512	114.6289	128.4822	50.00	175.00
	Total	88	114.9659	29.06570	3.09841	108.8075	121.1243	32.00	175.00

[8]. The patients with metabolic syndrome had a co morbid of hypertension and diabetes at a p-values of 0.001. and 0.00, respectively which were highly significant. The patient with NAFLD had hypertension and diabetes as a co morbid at a p-values of 0.89 and 0.336, respectively.

The existing association between cholelithiasis and metabolic syndrome has never been studied before 2005. Afterwards Mendez-Sanchez et al. [32] presented the first report which showed a very strong association among the two entities. The author was so much fascinated my that association that led him to conclude “ .... gallstone disease may be a part of metabolic syndrome.”The established association was later on got confirmed by studies with a large sample sizes [16,33]. Ata N et al. indicated

prophylactic surgery in patients with metabolic syndrome for gallstones [33]. In our study 28.4% had metabolic syndrome.

Metabolic syndrome has the prevalence of 25% in Europe [34] and 10–19% in Asia [35]. The contributing factors for metabolic syndrome include sedentary lifestyle, genetic predisposition Specific macronutrients, and higher intake of total energy. Pakistan has prevalence of 18%–46%. About 46%–75% diabetic patients suffers metabolic syndrome [35].

I-Ching Lin et al. reported difference in the means of HDL-C, BMI, TG, systolic B.P, diastolic B.P, fasting blood glucose and age between gallstone and non gallstone groups [36]. These facts are also evident by our results more in patients with metabolic syndrome (Table 3 and 4). The mean TG was high i.e 162.52 with standard deviation

**Table 4**  
Anova for metabolic syndrome status with SGPT,SGOT,BILIRUBIN,FBS,TRIGLYCERIDE and HDL.

ANOVA				Sum of Squares	df	Mean Square	F	Sig.
SGPT	Between Groups	(Combined)		27033.975	1	27033.975	8.203	0.005
		Linear Term	Unweighted	27033.975	1	27033.975	8.203	0.005
			Weighted	27033.975	1	27033.975	8.203	0.005
	Within Groups		283416.389	86	3295.539			
	Total		310450.364	87				
SGOT	Between Groups	(Combined)		6816.917	1	6816.917	1.621	0.206
		Linear Term	Unweighted	6816.917	1	6816.917	1.621	0.206
			Weighted	6816.917	1	6816.917	1.621	0.206
	Within Groups		361706.674	86	4205.892			
	Total		368523.591	87				
Total BILIRUBIN	Between Groups	(Combined)		5.205	1	5.205	0.467	0.496
		Linear Term	Unweighted	5.205	1	5.205	0.467	0.496
			Weighted	5.205	1	5.205	0.467	0.496
	Within Groups		958.937	86	11.150			
	Total		964.142	87				
Fasting plasma glucose level	Between Groups	(Combined)		672.855	1	672.855	1.125	0.292
		Linear Term	Unweighted	672.855	1	672.855	1.125	0.292
			Weighted	672.855	1	672.855	1.125	0.292
	Within Groups		51421.589	86	597.925			
	Total		52094.443	87				
TRIGLYCERIDE level	Between Groups	(Combined)		39369.619	1	39369.619	20.760	0.000
		Linear Term	Unweighted	39369.619	1	39369.619	20.760	0.000
			Weighted	39369.619	1	39369.619	20.760	0.000
	Within Groups		163091.097	86	1896.408			
	Total		202460.716	87				
Serum HDL	Between Groups	(Combined)		9629.582	1	9629.582	12.966	0.001
		Linear Term	Unweighted	9629.582	1	9629.582	12.966	0.001
			Weighted	9629.582	1	9629.582	12.966	0.001
	Within Groups		63869.316	86	742.666			
	Total		73498.898	87				

**Table 5**  
Analysis of presence OF NON alcoholic fatty liver disease status relation with SGPT,SGOT,BILIRUBIN,FBS,TRIGLYCERIDE and HDL.

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
SGPT	Yes	55	74.4182	66.67602	8.99059	56.3931	92.4432	12.00	333.00
	No	33	33.6667	33.60215	5.84938	21.7519	45.5815	7.00	200.00
	Total	88	59.1364	59.73604	6.36788	46.4795	71.7932	7.00	333.00
SGOT	Yes	55	75.7273	75.44865	10.17349	55.3306	96.1239	9.00	333.00
	No	33	36.6364	30.41979	5.29541	25.8500	47.4228	8.00	144.00
	Total	88	61.0682	65.08382	6.93796	47.2782	74.8581	8.00	333.00
Total BILIRUBIN	Yes	55	1.7747	3.87796	0.52290	0.7264	2.8231	0.20	23.80
	No	33	1.1027	2.11207	0.36766	0.3538	1.8516	0.10	12.43
	Total	88	1.5227	3.32898	0.35487	0.8174	2.2281	0.10	23.80
Fasting plasma glucose level(FBS)	Yes	55	107.6545	28.66164	3.86473	99.9062	115.4029	75.00	200.00
	No	33	98.3636	13.64006	2.37443	93.5271	103.2002	75.00	130.00
	Total	88	104.1705	24.47012	2.60852	98.9857	109.3552	75.00	200.00
TRIGLYCERIDE level	Yes	55	130.5455	44.92785	6.05807	118.3998	142.6912	51.00	215.00
	No	33	126.2727	53.93415	9.38873	107.1485	145.3969	51.00	210.00
	Total	88	128.9432	48.24038	5.14244	118.7220	139.1643	51.00	215.00
Serum HDL	Yes	55	113.2727	30.01818	4.04765	105.1577	121.3878	32.00	175.00
	No	33	117.7879	27.62444	4.80880	107.9927	127.5831	50.00	160.00
	Total	88	114.9659	29.06570	3.09841	108.8075	121.1243	32.00	175.00

of  $\pm 37.79$  in patients with metabolic syndrome than with no metabolic syndrome at very high significant p-value of 0.00. Similar differences were also seen in HDL among the two groups with a significant p value of 0.001 (Table 4).

Apart from gall stone development there is other various concerns with metabolic syndrome as some studies have reported its association with diabetes, cardiovascular disease chronic kidney disease and nonalcoholic fatty liver disease [37,38]. So, metabolic syndrome hovers as a gigantic health issue globally.

Non alcoholic fatty liver disease (NAFLD) has the prevalence of

15%–20% [1]. It stands among the most common chronic liver conditions and is becoming the center of concern in the world of medicine [39]. During the recent years its occurrence has been shown rising because of dramatically increased rates in obesity, metabolic syndrome and diabetes [1].

The prevalence of NAFLD among outpatients is well established and described in various studies [1,39] while the proportion for hospitalized patients not known [39]. Further more the association of NAFL with other gastrointestinal conditions has not been into talk [39].

**Table 6**  
Anova for NON alcoholic fatty liver disease status WITH,SGOT,BILIRUBIN,FBS,TRIGLYCERIDE HDL.

ANOVA				Sum of Squares	df	Mean Square	F	Sig.
SGPT	Between Groups	(Combined)		34251.648	1	34251.648	10.665	0.002
		Linear Term	Unweighted	34251.648	1	34251.648	10.665	0.002
			Weighted	34251.648	1	34251.648	10.665	0.002
	Within Groups			276198.715	86	3211.613		
SGOT	Between Groups	(Combined)		31517.045	1	31517.045	8.043	0.006
		Linear Term	Unweighted	31517.045	1	31517.045	8.043	0.006
			Weighted	31517.045	1	31517.045	8.043	0.006
	Within Groups			337006.545	86	3918.681		
Total BILIRUBIN	Between Groups	(Combined)		9.314	1	9.314	0.839	0.362
		Linear Term	Unweighted	9.314	1	9.314	0.839	0.362
			Weighted	9.314	1	9.314	0.839	0.362
	Within Groups			954.828	86	11.103		
Fasting plasma glucose level	Between Groups	(Combined)		1780.370	1	1780.370	3.043	0.085
		Linear Term	Unweighted	1780.370	1	1780.370	3.043	0.085
			Weighted	1780.370	1	1780.370	3.043	0.085
	Within Groups			50314.073	86	585.047		
TRIGLYCERIDE level	Between Groups	(Combined)		376.534	1	376.534	0.160	0.690
		Linear Term	Unweighted	376.534	1	376.534	0.160	0.690
			Weighted	376.534	1	376.534	0.160	0.690
	Within Groups			202084.182	86	2349.816		
Serum HDL	Between Groups	(Combined)		420.473	1	420.473	0.495	0.484
		Linear Term	Unweighted	420.473	1	420.473	0.495	0.484
			Weighted	420.473	1	420.473	0.495	0.484
	Within Groups			73078.424	86	849.749		
	Total			73498.898	87			

In our study NAFLD was present in 62.5%. Moreover patients with NAFLD had a deranged and raised SGPT and SGOT levels (Table 5 and 6). The means were raised in NAFLD patients i.e 74.41 and 75.72 respectively as compared to the ones with no NAFLD. The P-values were significant i.e. 0.002 and 0.006 respectively. Our results are in accordance with another study with similar objective [29]. However presence of normal ranges of liver enzymes does not exclude NAFLD as rectified by some other series [19,40]. Mofrad et al. as reported a NAFLD spectrums with normal values of ALT in retrospective series. The result of one series showed about 10% of the gallstone patients at the time of diagnosis had NAFLD progressed to fibrosis which was biopsy proven.

NAFLD contributes as the commonest cause that leads to cirrhosis, portal hypertension and hepatic cancer [5] and it has been estimated that approximately 22% of NAFLD progresses to cirrhosis [5]. One of the study 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 [19]. We would like to mention here that this case series was done according to PROCESS Guidelines [41].

## 6. Conclusion

Non alcoholic fatty liver was highly prevalent in our study subjects. Based on our study results we recommend health education and implementation of lifestyle modification when patients present with gall stone disease requiring cholecystectomy as many of them could have NAFLD which may eventually progress to cirrhosis. We also found association of metabolic syndrome with gallstones and NAFLD. A huge percentage of first degree relatives of gall stone patients had gallstones and this relation was more pronounced patients who had associated NAFLD. A huge percentage of

first degree relatives of gall stone patients had gallstones and this relation was more pronounced patients who had associated NAFLD.

## Strengths and limitations of this study

The study helped to enlighten the possible link between gallstone disease, NAFLD and MS which are top-line discussion topics nowadays. Many pertinent evidences were discussed along with the possible theories behind as their explanations. Not only this, we also discussed how outcomes of the study can help in future interventions. We also discussed if we could control MS and NAFLD occurrences we can minimize gallstone disease and respective surgery. And this all can help in decreasing the morbidity, mortality of gallstone and the complications due to its surgery.

## Ethical approval

Yes.  
IRB-748/DUHS/Approval/2016/240.

## Sources of funding

None.

## Author contribution

Dr.Qamaruddin Baloch and Zahid Ali Memon did all the surgeries.  
Dr.Farah and Iqra did data collection.  
Everybody contributed in writing and thinking process.

## Conflicts of interest

None.

## Guarantor

Professor Qamaruddin Baloch, Farah Ahmed.

## Research registration unique identifying number (UIN)

It was an observational study.

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