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Gall stones in metabolic syndrome- addressing the risks in obese individuals

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Abstract

Significant research has been dedicated in recent years to elucidating the pathophysiologic mechanisms behind gallstone development, but the epidemiology of gallstone disease has received comparatively little focus. Numerous studies have emphasized the correlation between metabolic syndrome and gallstones.

In this study, we found a positive correlation between complicated gall stones and metabolic syndrome. Hence, screening of obese patient or those with PCOS/uncontrolled diabetes, should be introduced in the protocol for facilitate early diagnosis of gall stones.

Keywords: Pain abdomen; Cholecystectomy; Diabetes mellitus; Obstructive jaundice

1. Introduction

Incidence of gallstones is comparatively lower in undeveloped countries than in the western world. Nevertheless, research has indicated that the occurrence of this phenomenon varies throughout the Indian continental region. Gallbladder stones exhibit varying prevalence rates across different geographical locations. In India, the prevalence is estimated to be around 4%, while in the Western world it levels at 10% [1]. The majority of gallstone prevalence studies rely on evidence obtained from autopsy or surgery. [1-3] There are few studies on the occurrence of gallstones in the general population, [4–11], including one conducted inside our nation (India). [12] Evidence has indicated a greater prevalence in the northern region of India, and the factors contributing to this phenomenon have not been thoroughly assessed. The study conducted by Malhotra et al [12] revealed that the frequency in North India was sevenfold more than that among South Indian inhabitants.

Significant research has been dedicated in recent years to elucidating the pathophysiologic mechanisms behind gallstone development, but the epidemiology of gallstone disease has received comparatively little focus. The development of gallstones is associated with several risk factors, but, there is limited study on its link with individuals living in the Indian continent.

The recent designation of India as the diabetic capital of the world provides us with an approximation of the prevalence of metabolic syndrome within its population. Gallstones (GS) are prevalent in the western world (1-6), but there has been a recent rise in their occurrence in India. This can be attributed, in part, to the widespread use of ultrasonography in the past twenty years, as well as changes in socioeconomic structure and other epidemiological factors such as diet. In addition to its potentially life-threatening effects, gallstone disease significantly contributes to healthcare

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expenditures. Appropriate and timely diagnosis and treatment can effectively prevent a significant number of severe and potentially fatal consequences. Early identification of these patients in the normal progression of the disease is of our concern in order to prevent significantly morbid sequelae. The majority of patients are oblivious and so stay asymptomatic indefinitely. Mere fraction of individuals experience symptoms that require medical intervention. The earliest description of the clustering of risk factors for cardiovascular disease, particularly the simultaneous presence of obesity, type 2 diabetes, hyperlipidaemia, and hypertension, was published towards the end of the 20th century. [7,8]

A remarkable surge in the global prevalence of metabolic syndrome has occurred during the last twenty years. Due to its physiological role of bile concentration, the gallbladder is the primary site in the biliary system with the highest likelihood of stone development. [12] While bile supersaturation is a prerequisite for the formation of gallstones, not all individuals with fully saturated bile experience gallstone formation.[13] It is often accepted that diabetes mellitus and cholelithiasis are strongly associated disorders, so a modified glucose metabolism may heighten the susceptibility to developing cholelithiasis in specific individuals.14 Much work has been dedicated in recent years to elucidating the pathophysiological mechanisms underlying the development of gallstones. The significance of serum lipids in the development of cholelithiasis is profound, and in cases of cholesterol gall stones, changes in serum lipids indicate the presence of metabolic syndrome. Empirical evidence indicates that metabolic syndrome could potentially increase the susceptibility to gallstones.[15]

Numerous studies have emphasised the correlation between metabolic syndrome and gallstones[4]. Nevertheless, a recent study has established metabolic syndrome as a risk factor for the development of complex gallstones illness [8]. The significance of this discovery lies in the potential benefits of prophylactic cholecystectomy for individuals with accidental cholelithiasis and metabolic syndrome, as it may help to mitigate the severe consequences of the complex gallstone disease.

A comparative analysis of metabolic syndrome prevalence in uncomplicated and complex gallstone cases was the objective of this investigation.

2. Material and methods

This was a retrospective observational study that was conducted at 2 year period. All patients of gallstone disease who were either managed conservatively (in view of complications) or underwent for surgery.

All patients with proven gall stones will be examined in terms of complete medical history and laboratory examination. Data collection for diagnosis of metabolic syndrome includes Waist Circumference, BP, and lipid and biochemical tests.

The files of all adult patients aged 18 yrs and above with history of gallstone disease presenting to Surgery OPD and Emergency OPD were included. Those with history of prior abdominal surgery, with other associated abdominal conditions, suspected gall bladder malignancy and with bleeding diathesis were excluded.

2.1. Statistical analysis

The data will be analyzed with SPSS 26.0.1.1 software (SPSS Inc., Chicago, IL, USA). Chi square test was used to detect statistical significance and a p-value of <0.05 was taken as significant.

3. Results

This study included 100 patients with gall stone disease to evaluate the incidence of MeTs. The mean age of the study population was 38.11 +/- 21.01 years. Most common age group as 31-40 years, followed by 21-30 years. Male to female ratio was 0.3:1, with 70% of the study population comprising of females. This corroborated with the most common risk factors of gall stones- the female gender, in reproductive age group and obese.

The mean duration of abdominal symptoms such as pain abdomen, jaundice and vomiting was 7.88 +/- 3.56 months. There was a significant correlation between age and duration of symptoms (The f-ratio value is 328.3433. The p-value is < 0.001.)

All patients presented with complaints of pain abdomen, which is the most common symptom associated with gall stone disease, when symptomatic . hen we observed the abdominal examination signs, we noted that tenderness in the abdomen was the most common finding.

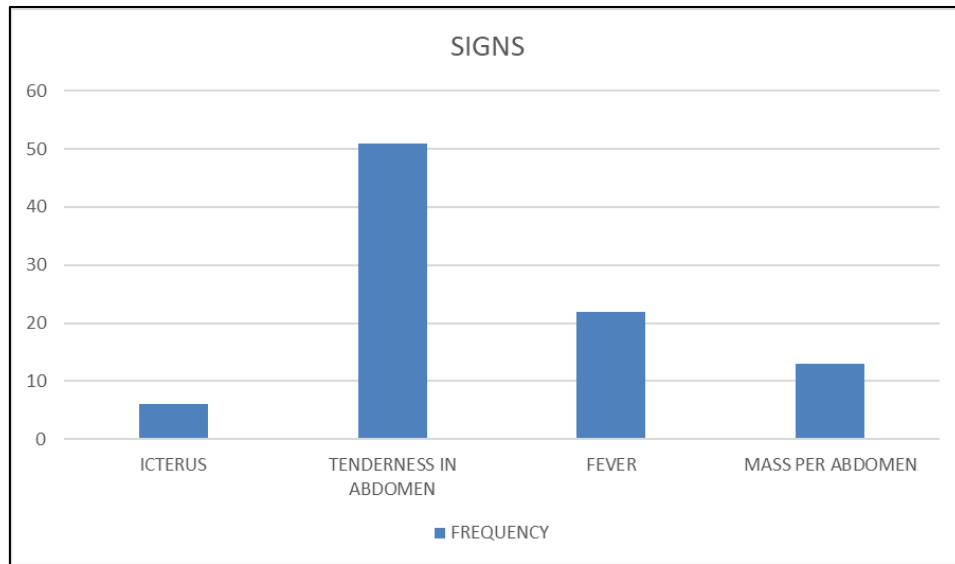


Figure 1 Signs noted in the study population

Table 1 Correlation of Age, BMI and WC

VARIABLES	AGE	BMI	WC
N	100	100	100
$\sum X$	2829	1727.3	6284
Mean	43.5231	26.5738	96.6769
$\sum X^2$	133867	46911.01	621512
Std.Dev.	12.9544	3.9726	14.7871

We observed a significant correlation between the age of the study participants, BMI and WC. The f-ratio value is 648.53866. The p-value is $< .00001$. The result is significant at $p < .05$.

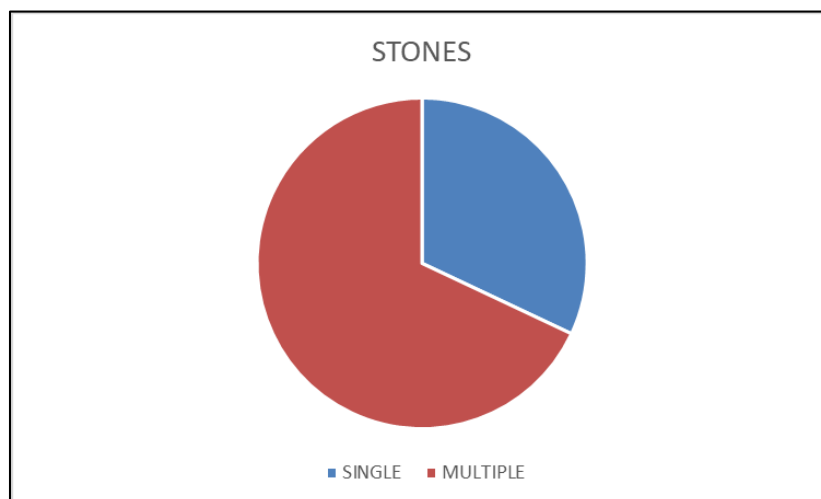


Figure 2 Presence of single or multiple stones

In this study, majority of the patients had multiple gall stones.

Table 2 Correlation of metabolic syndrome with complicated gall stone disease

Metabolic syndrome	Complicated gall stone disease (43)	Uncomplicated gall stone disease (57)	Odd ratio at 95% confidence interval	P value
Present	29	24	OR 3.986 (CI: 2.142-6.872)	<0.001
Absent	14	86		

The most common finding on USG in the present study was an oedematous gall bladder with multiple stones within.

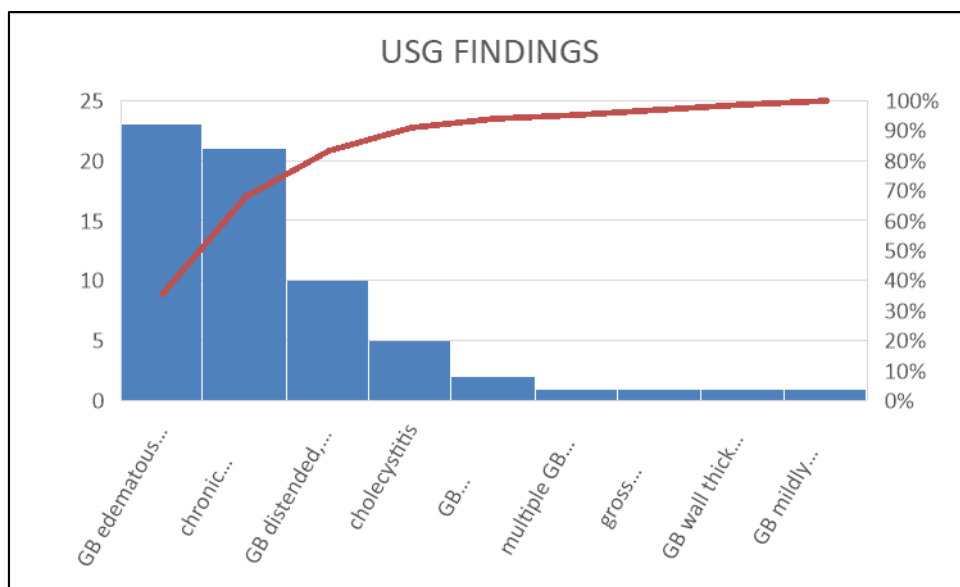


Figure 3 USG findings

The most common finding noted intraoperatively was adhesions in the Calot’s triangle, with 34 have moderate adhesions, while 27 had severe adhesions. This often obscures the anatomy, and can lead to a subtotal cholecystectomy.

The most common complication was post-operative pain with a mean duration of post-op stay 6.08 +/- 5.88 days

Table 3 Correlation of metabolic syndrome with other parameters

Components of metabolic syndrome	Complicated gall	Uncomplicated gall	Odd ratio at 95% confidence interval	P value
DERANGED LIPID PROFILE (n=92)	30	22	OR 1.031 (CI: 1.064-1.045)	0.71
METABOLIC SYNDROME FRC II AND III	27	17	OR 0.90 (CI: 0.504-1.605)	0.834
Fasting plasma glucose ≥100 mg/dl or previously diagnosed as type 2 DM	28	12	OR 2.800 (CI: 1.609 to 4.874)	< 0.001

4. Discussion

In contemporary times, the prevalence of obesity and metabolic syndrome is rapidly rising in India and other South Asian countries, leading to increased rates of illness and death caused by cardiovascular disease and type 2 diabetes mellitus. Timely identification of metabolic syndrome is crucial to minimise the likelihood of problems which arise from the disease. (13)Recent study suggests that metabolic syndrome may provide an increased risk of developing (11,12) disease. There is empirical evidence to substantiate the notion that the formation of gallstones is a manifestation of

metabolic syndrome. The basis for this data is in the correlation between gallstone disease and dyslipidaemia, obesity, diabetes, and hyperinsulinemia.^{14, 15}

The objective of this study was to ascertain the potential correlation between complicated gallstone disease and metabolic syndrome. Both the CGSD and UGSD groups exhibited similar age and gender distributions among the broader population. The observed change did not reach statistical significance.

A fundamental basis for extensive study in public health programs is the correlation between obesity and a variety of diseased conditions. The impaired capacity of blood insulin to efficiently exert its impact on the metabolism of carbs and fats is a result of abdominal obesity induced by obesity. The manifestation of this phenomena is believed to be a precursor to the onset of diabetes in individuals diagnosed with type II diabetes. The resistance shown by the cells of an obese patient to insulin is also accountable for the dysfunction of the cardiovascular system, leading to the final deterioration of the cardiovascular system [9]. The proposal of the metabolic syndrome, also referred to as syndrome X, the deadly quartet, and insulin resistance syndrome, arose from the correlation observed between diabetes and cardiovascular disease, along with several metabolic abnormalities, and the association between the latter two and obesity [10]. Among the several criteria used to determine if an individual is experiencing metabolic syndrome, the National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) is the most commonly used assay [11].

A study conducted by Ahmed et al found that the ages of individuals with severe and uncomplicated gallstone disease were similar. Specifically, the average age in the former group (n = 52) was 42.42 +/- 12.15 years, while in the latter group (n = 50) it was 39.24 +/- 10.41 years. The results of our study were consistent with this finding.

The study conducted by Kumar N et al revealed that the average age of individuals with difficult gall bladder conditions was 47.2 +/- 13.2 years, whereas cases without complications had an average age of 46.7 +/- 13.8 years. The statistical analysis revealed no significant difference between the two groups (p 0.54). Although our analysis revealed a significantly greater mean age, there was no significant difference between the groups. The study conducted by Peswani et al revealed that the average age of the patients was 56.18 years, which was similar to the average age of 54.42 years in the control group. The proportion of cases in the 60-70 years age group was 40%, compared to 36% in the control group. An international study conducted by Zhu et al in the urban Chinese population found that the mean age of 873 participants who experienced gallstone episodes was 47.34 ± 14.04 years old for males and 48.43 ± 14.19 years old for females. This value is determined to be greater than the results obtained in our investigation.

This study included a sample size of 30 males and 70 females. An investigation conducted by Kumar N et al revealed that the female to male ratio was 8.2:1 in the CGSD group and 4:1 in the UGSD group. Within a study conducted by Peswani et al, 72 of the cases were female, while 70 of the controls were also female. This is consistent with the results of the current study, as well as research conducted internationally. In the current investigation, the Area Under Curve (AUC) for WC and TG was determined to be 0.54. This value suggests that the AUC is both sensitive and specific in recognising the severity of patients' clinical conditions. (The AUC values vary between 0.5 and 1.0, where a value of 0.5 suggests that the test is equivalent to chance in accurately differentiating between those with diseases and those without diseases.) In a study conducted by Peswani et al., the objective was to determine the occurrence of METS in patients with both uncomplicated and complex gall stone disease. The researchers observed that the criterion met more than 3/5, and identified this in 16 out of the 100 Controls and 36 out of the cases/complicated gall stone cases, which was a far greater percentage. (Statistical significance 0.023) Among the 220 patients studied by Kumar N et al, 145 individuals had a blood HDL-C level below 30mg/dl in men and 35mg/dl in women. Among the 145 patients, 80 (55.2%) had CGSD and 65 (44.8%) had UGSD. Statistically significant hyperglycaemias (fasting plasma glucose levels ≥100 mg/dl or prior diagnosis of type 2 DM) were observed in the CGSD group compared to the UGSD group (60 patients and 33 patients respectively, p value <0.001). Cholelithiasis, also referred to as gallstones, is a highly common surgical condition worldwide. However, the occurrence and frequency of these cases differ across different geographical areas. An estimated 10 to 15 percent of the population in the United States is afflicted by the condition [12]. Although exact statistics for the population of Pakistan are not available, a local study approximates that the surgical incidence stands at 9.03% [13]. A separate study conducted in India, situated in close proximity, likewise indicates that the occurrence of the disease is almost same among their population [14]. In addition to ethnicity, genetics, age, female gender, obesity, dyslipidaemia, rapid weight loss, complete parenteral feeding, and socioeconomic status, the aetiology of the disease is multifactorial [15].

Sonography has become a widely accessible and cost-effective method of investigation within the field of abdominal diseases. The prevalence of asymptomatic gallstones is believed to be up to eighty percent [16], indicating a continuous increase in the number of patients being identified with these stones. Given that conventional surgery is not a viable

means of treating this specific subset of patients, the surgical community is confronted with a challenging predicament. Currently, surgical interventions for asymptomatic gallstone removal are indicated for patients with biliary cancer, choledocholithiasis, sickle cell disease, gallstones larger than three cm, and significant immunosuppression [17].

Only a small fraction, ranging from 10 to twenty-five percent, of patients who are unintentionally or asymptotically diagnosed with gallstones may eventually have symptoms of gallstones throughout their lives [16]. As a consequence, roughly seventy-five percent of these individuals will undergo a non-essential operation. Furthermore, this not only exposes the patient to avoidable risks of illness and death, but also results in an exorbitant cost of healthcare, which is particularly burdensome for a country such as Pakistan and even for a highly developed nation like the United States. Although the aforementioned indicators do help identify the patients who are most likely to benefit from surgery, it remains challenging to ascertain which individuals are most prone to developing symptomatic disease in the future.

Evaluation of metabolic syndrome is a straightforward and easily measurable metric that can be conducted in an outpatient setting. Empirical evidence has confirmed that metabolic syndrome is a risk factor that exists independently of the occurrence of gallstones [4,18]. The objective of this study was to examine the correlation between it and more complex gallstones. The results of this study suggest that patients with complex gallstone disease had a higher prevalence of metabolic syndrome compared to those with uncomplicated gallstone pathology. Nevertheless, the disparity did not reach the threshold of statistical significance in our study. Although the results of this study align with those of similar studies, such as Ata et al. [8], which similarly observed the same trend in their patient group, the present study reveals a greater occurrence of metabolic syndrome in patients with complex gallstones. Considering the inability to attain the necessary level of statistical power for the study and the use of a smaller sample size, it is crucial to carefully evaluate our results. In the present investigation, the group deemed more challenging exhibited a greater overall incidence of metabolic syndrome.

5. Conclusion

Undoubtedly, the paramount element of modern medical practice is the provision of patient education and their active involvement in decision-making procedures. The provision of a precise assessment of the probability of future symptom occurrence is of paramount significance. Administration of 'prophylactic' surgery may be justified in cases when a patient with incidental gallstones exhibits metabolic syndrome. The reason for this is that individuals with metabolic syndrome are at an increased susceptibility to developing gallstone disease, which presents greater challenges. Implementing this approach will mitigate the potential for surgical complications among patients, while also reducing the burden on the healthcare system and the expenses associated with delivering medical treatment. Furthermore, it will help to decrease the frequency of unnecessary surgeries

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

IEC clearance sought.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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