RESEARCH
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Investigating Gallbladder Stone Disease in General Surgery

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Abstract
The prevalence of gallbladder stone disease (GSD) has surged over the past three decades, emerging as a prominent medical concern in India. This study aimed to assess the prevalence of GSD across India and delve into the associated risk factors, with a focus on general surgery implications. Conducted from August 2021 to July 2022, a cross-sectional survey encompassed 15,256 individuals from three districts, comprising 8,617 males and 6,639 females aged between 20 and 79 years. Clinical data collection involved questionnaires, physical examinations, and biochemical analyses, with GSD diagnosis established through type B ultrasonography. Analysis revealed a GSD prevalence of 7.02%, escalating with age and notably higher in females compared to males (8.10% vs. 6.19%). Cholecystectomy rates stood at 2.48% overall, with females undergoing the procedure nearly twice as often as males (3.42% vs. 1.75%). Logistic regression uncovered several risk factors associated with GSD, including female gender, advanced age, fatty liver disease, familial history of cholelithiasis, hypertension, and elevated body mass index. This comprehensive study underscores the burgeoning prevalence of GSD in India, shedding light on the imperative for heightened awareness, prevention strategies, and enhanced surgical interventions tailored to combat this escalating health challenge.
Keywords: Gallbladder Stone Disease Prevalence Risk Factors Cholecystectomy Indi

INTRODUCTION

In the vast landscape of global health challenges, certain conditions emerge with alarming frequency, casting a shadow over populations and straining healthcare systems. One such condition, gallbladder stone disease (GSD), has surged to prominence in recent decades, particularly in the context of India's healthcare landscape. Once considered a sporadic ailment, GSD has now entrenched itself as a prevalent and pressing concern, affecting millions across the nation.

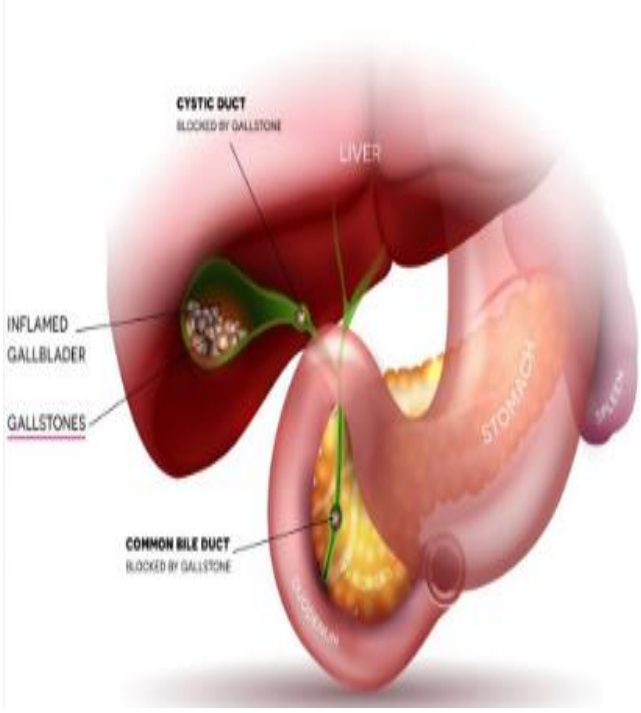

Fig.1 : Gall-bladder Stone

Here we explore the multifaceted dimensions of GSD, delving into its epidemiology, risk factors, clinical implications, and the broader societal and economic ramifications of its escalating prevalence in India. As we embark on this journey, it is essential to contextualize the gravity of the situation, understanding not only the clinical intricacies but also the human stories that lie at the heart of this burgeoning epidemic.GSD, characterized by the formation of stones within the gallbladder, represents a spectrum of disease ranging from asymptomatic gallstones to acute cholecystitis, pancreatitis, and even life-threatening complications. While the exact etiology remains elusive, a myriad of factors including genetic predisposition, lifestyle choices, dietary habits, and metabolic disorders converge to precipitate the formation of gallstones. However, what sets the stage for our exploration is not merely the clinical intricacies of GSD but rather its profound impact on the health and well-being of individuals and communities.The landscape of GSD in India mirrors a narrative of paradoxes and disparities. On one hand, India boasts remarkable strides in healthcare innovation, burgeoning medical infrastructure, and a rich tapestry of traditional healing practices. Yet, against this backdrop of progress, lies a stark reality - the relentless march of GSD, casting a long shadow over the nation's health landscape. The prevalence of GSD in India has witnessed an exponential rise over the past three decades, transforming from a sporadic ailment to a widespread epidemic that transcends socio-economic barriers.What fuels this epidemic is a complex interplay of demographic transitions, urbanization, dietary shifts, and the epidemiological transition from communicable to non-communicable diseases. Rapid urbanization and changing dietary patterns, characterized by an increased intake of refined carbohydrates, saturated fats, and processed foods, have laid the groundwork for the proliferation of metabolic disorders such as obesity, insulin resistance, and dyslipidemia - all potent risk factors for GSD.Furthermore, the burden of GSD in India is compounded by a myriad of socio-economic determinants, including poverty, limited access to healthcare, and disparities in healthcare infrastructure. Rural communities, in particular, bear the brunt of this epidemic, grappling with limited access to diagnostic facilities, specialist care, and surgical interventions, thereby exacerbating health inequities and perpetuating a vicious cycle of illness and impoverishment.Amidst this backdrop of adversity, the clinical manifestations of GSD reverberate across the healthcare continuum, imposing a heavy toll on individuals, families, and healthcare systems alike. The spectrum of GSD encompasses a myriad of clinical presentations, ranging from asymptomatic gallstones detected incidentally on imaging studies to acute cholecystitis, biliary colic, and life-threatening complications such as gallstone pancreatitis and cholangitis.For many individuals, the journey with GSD is fraught with pain, uncertainty, and compromised quality of life. The insidious nature of GSD, characterized by intermittent bouts of biliary colic and recurrent complications, exacts a physical and psychological toll on affected

individuals, impairing their ability to perform daily activities, engage in gainful employment, and participate in social interactions. Moreover, the economic burden of GSD, encompassing healthcare expenditures, lost productivity, and diminished quality of life, perpetuates a cycle of poverty and illness, particularly among socio-economically marginalized communities.In the face of this burgeoning epidemic, the imperative for action is clear. Addressing the multifactorial determinants of GSD demands a comprehensive, multi-disciplinary approach that transcends traditional silos of healthcare delivery. From primary prevention strategies aimed at promoting healthy lifestyles and dietary habits to secondary prevention initiatives focused on early detection and timely intervention, the spectrum of interventions must be tailored to the unique socio-cultural context of India.At the forefront of this battle against GSD lies the pivotal role of general surgery, serving as the vanguard of clinical care for individuals afflicted by this condition. From diagnostic modalities such as ultrasound and magnetic resonance cholangiopancreatography (MRCP) to therapeutic interventions including laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography (ERCP), general surgeons play a central role in the management of GSD, offering a lifeline of hope to millions across the nation.Yet, the challenges confronting general surgery in the context of GSD are manifold. Limited access to surgical facilities, shortage of skilled manpower, and disparities in healthcare infrastructure pose formidable barriers to the delivery of timely and equitable surgical care, particularly in rural and underserved regions. Moreover, the burden of GSD extends beyond the confines of the operating room, necessitating a holistic approach that addresses the upstream determinants of disease, promotes community engagement, and fosters collaborations across sectors.As we navigate the complex terrain of GSD in India, it is imperative to heed the lessons of the past, harness the power of innovation, and embrace a shared vision of health equity and social justice. From policy makers and healthcare providers to civil society and communities at large, each stakeholder has a vital role to play in shaping a future where GSD is no longer a scourge but rather a testament to the resilience of the human spirit and the power of collective action.

Research Gap:

The landscape of gallbladder stone disease (GSD) in India is characterized by a burgeoning epidemic that transcends socio-economic barriers, imposing a heavy toll on individuals, families, and healthcare systems alike. Despite the growing recognition of GSD as a prominent public health concern, there exists a significant research gap in our understanding of its multifaceted dimensions, particularly in the context of general surgery implications. One notable research gap pertains to the paucity of population-based studies assessing the prevalence, risk factors, and clinical outcomes of GSD across diverse geographic regions in India. While existing literature offers valuable insights into the epidemiology and clinical manifestations of GSD, there remains a dearth of comprehensive studies that integrate clinical, demographic, and socio-economic factors to provide a holistic understanding of the disease burden. Furthermore, the role of general surgery in the management of GSD warrants closer scrutiny, particularly in the context of resource-constrained settings where access to surgical care may be limited. Addressing this research gap requires a nuanced understanding of the barriers and facilitators to timely surgical intervention, as well as the impact of surgical outcomes on long-term morbidity and mortality.

Specific Aims of the Study:

The specific aims of this study are:

1. To assess the prevalence of gallbladder stone disease (GSD) in India across diverse geographic regions and demographic subgroups.
2. To identify the risk factors associated with GSD, including demographic, clinical, and socio-economic determinants.
3. To evaluate the clinical outcomes of surgical management for GSD, with a focus on laparoscopic cholecystectomy and its impact on morbidity and mortality.
4. To explore the socio-economic implications of GSD, including healthcare expenditures, lost productivity, and quality of life outcomes.

Objectives of the Study:

1. To conduct a population-based survey encompassing multiple districts in India to ascertain the prevalence of GSD and its demographic distribution.
2. To collect comprehensive clinical data, including medical history, physical examination findings, and biochemical analyses, to elucidate the risk factors associated with GSD.
3. To analyze the surgical management of GSD, including indications for cholecystectomy, surgical techniques employed, and perioperative outcomes.
4. To assess the socio-economic impact of GSD, including healthcare utilization patterns, out-of-pocket expenditures, and employment status among affected individuals.

Scope of the Study:

This study will focus on individuals aged 20-79 years residing in three districts in India, encompassing both urban and rural populations. The study will employ a cross-sectional survey design to gather data on the prevalence, risk factors, and clinical outcomes of GSD, with a particular emphasis on the role of general surgery in its management.

Conceptual Framework:

The conceptual framework guiding this study is grounded in the bio-psycho-social model of health, which posits that health outcomes are influenced by a complex interplay of biological, psychological, and social factors. In the context of GSD, this framework underscores the importance of considering not only the physiological mechanisms underlying disease pathogenesis but also the psychosocial determinants and socio-economic disparities that shape its prevalence, presentation, and outcomes.

Hypothesis:

Based on the existing literature and theoretical framework, we hypothesize that:

1. The prevalence of gallbladder stone disease (GSD) in India will exhibit regional variations, with higher rates observed in urban areas and among certain demographic subgroups.
2. Certain demographic and clinical factors, including age, gender, obesity, and metabolic syndrome, will be independently associated with an increased risk of GSD.
3. Surgical management of GSD, particularly laparoscopic cholecystectomy, will be associated with favorable clinical outcomes, including reduced morbidity and mortality.
4. The socio-economic burden of GSD will be substantial, encompassing healthcare expenditures, lost productivity, and diminished quality of life among affected individuals and their families.

Research Methodology:

This study employed a cross-sectional design utilizing a questionnaire survey and physical examination to investigate the prevalence and risk factors associated with gallbladder stone disease (GSD) in India.

Sample Size and Distribution:

The study encompassed a sample size of 15,256 individuals drawn from three districts in India, comprising both males (8,617) and females (6,639) aged between 20 and 79 years. The distribution of participants aimed to capture a diverse representation of demographic characteristics and geographic regions within the study area.

Table 1: Gender and age distribution of the survey sample(n).

Age (year)	Male	Female	Total
20～29	1903	1438	3341
30～39	2090	1588	3678
40～49	1647	1511	3158
50～59	1775	1102	2877
60～69	756	616	1372
70～79	446	384	830
Total	8617	6639	15256

Data Collection:

The questionnaire survey was conducted using the standardized Third National Cholelithiasis Questionnaire, administered by trained medical staff. Uniform standards and procedures were followed to ensure consistency and reliability in data collection. The questionnaire covered pertinent information including gender, age, surgical history, family history of cholelithiasis, and other relevant clinical variables.

Physical examinations were conducted in conjunction with the questionnaire survey to assess clinical manifestations and corroborate self-reported data. However, certain demographic and clinical variables such as ethnicity, education level, smoking, drinking, medication history, and past medical history were not included in the questionnaire and therefore not accounted for in the analysis.

Diagnosis of gallbladder disease and fatty liver was established through fasting abdominal B-ultrasound, providing a non-invasive and reliable method for detecting gallstones and assessing hepatic steatosis. Additionally, biochemical examination involved the analysis of fasting venous blood samples for parameters including fasting blood glucose, aspartate transaminase, glutamate transaminase, triglycerides, and total cholesterol, using an automatic biochemical analyzer.

Data Analysis:

Data management and analysis were conducted using Microsoft Access and SPSS 17.0 software, respectively. The questionnaire responses were compiled and inputted into Microsoft Access for efficient storage and organization. SPSS 17.0 was utilized for statistical analysis, including calculation of the incidence of GSD and cholecystectomy.

Descriptive statistics were employed to summarize demographic characteristics and clinical variables, while inferential statistics such as the Chi-square (X2) test were utilized to compare count data and assess associations between variables. Specifically, the incidence of GSD and cholecystectomy were calculated, allowing for the identification of potential risk factors and trends within the study population.

Results and Analysis:

The prevalence of gallbladder stone disease (GSD) and cholecystectomy rates were assessed across different age groups and genders, followed by logistic stepwise regression analysis to identify significant risk factors associated with GSD.

Prevalence of GSD:

Table 2 presents the prevalence of GSD (%) stratified by age group and gender. Across all age groups, the prevalence of GSD was higher in females compared to males. Notably, the highest prevalence was observed in the 70-79 age group, with 16.82% in males and 23.18% in females. Overall, the prevalence of GSD in the total sample was 7.02%, with females exhibiting a significantly higher prevalence (8.1%) compared to males (6.19%).

Table 2: Prevalence of GSD (%).

Age (year)	Male			Female			Total		
	Sample	Case	Prevalence	Sample	Case	Prevalence	Sample	Case	Prevalence
20～29	1903	20	1.05	1438	32	2.23	3341	52	1.56
30～39	2090	57	2.73	1588	59	3.72	3678	116	3.15
40～49	1647	105	6.38	1511	116	7.68	3158	221	7
50～59	1775	178	10.03	1102	144	13.07	2877	322	11.19
60～69	756	98	12.96	616	98	15.91	1372	196	14.29
70～79	446	75	16.82	384	89	23.18	830	164	19.76
Total	8617	533	6.19	6639	538	8.1	15256	1071	7.02

Cholecystectomy Rate:

Table 3 displays the cholecystectomy rates (%) across different age groups and genders. Similar to the prevalence of GSD, females consistently had higher cholecystectomy rates compared to males across all age groups. The highest cholecystectomy rate was observed in females aged 70-79 years, with a rate of 10.68%. Overall, the cholecystectomy rate in the total sample was 2.48%, with females undergoing cholecystectomy at almost twice the rate of males (3.42% vs. 1.75%).

Table 3: Cholecystectomy rate (%).

Age (year)	Male			Female			Total		
	Sample	Removal cases	Rate	Sample	Removal cases	Rate	Sample	Removal cases	Rate
20～29	1903	4	0.21	1438	1	0.07	3341	5	0.15
30～39	2090	8	0.38	1588	13	0.82	3678	21	0.57
40～49	1647	25	1.52	1511	52	3.44	3158	77	2.44
50～59	1775	45	2.54	1102	69	6.26	2877	114	3.96
60～69	756	41	5.42	616	51	8.28	1372	92	6.71
70～79	446	28	6.28	384	41	10.68	830	69	8.31
合计	8617	151	1.75	6639	227	3.42	15256	378	2.48

Logistic Stepwise Regression Analysis:

The results of the logistic stepwise regression analysis, presented in Table 5, identified several significant risk factors associated with GSD:

- **Gender:** Females were found to have a significantly higher odds ratio (OR) of 1.39 (95% CI: 1.178-1.640, $p < 0.0001$) for developing GSD compared to males.
- **Age:** Each one-year increase in age was associated with a slight but statistically significant increase in the odds of GSD (OR: 1.052, 95% CI: 1.046-1.059, $p < 0.0001$).
- **Fatty Liver:** Individuals with fatty liver disease had a significantly higher odds ratio (OR: 1.299, 95% CI: 1.080-1.563, $p < 0.01$) for developing GSD.
- **Family History of GSD:** Having a family history of GSD was strongly associated with an increased risk of GSD, with an odds ratio of 2.445 (95% CI: 2.040-2.931, $p < 0.0001$).
- **Hypertension:** Hypertension was identified as a significant risk factor for GSD, with an odds ratio of 1.226 (95% CI: 1.022-1.470, $p < 0.05$).
- **Body Mass Index (BMI):** Each one-unit increase in BMI was associated with a slight but statistically significant increase in the odds of GSD (OR: 1.053, 95% CI: 1.023-1.084, $p < 0.0001$).

The results of this study underscore the multifactorial nature of GSD, with gender, age, fatty liver disease, family history, hypertension, and BMI emerging as significant risk factors. The higher prevalence and cholecystectomy rates observed in females highlight the importance of gender-specific considerations in the management of GSD.

Table 4: Biochemical indexes.

	GSD group（n=743）	Cholecystectomy group（n=258）	Control group（n=11571）
age (year)	50.74±13.29a)	54.95±11.65a)	40.54±13.03
family history of GSD	193（26）a)	71（27.5）a)	1503（13.0）
BMI	24.05±2.98a)	24.31±3.08a)	22.98±3.13
waist circumference（cm）	82.68±9.67a)	82.51±9.35a)	78.70±9.73
systolic pressure（mm hg）	129.22±19.36a)	131.05±18.03a)	120.61±17.44
diastolic pressure（mm hg）	81.56±11.83a)	81.03±10.50a)	77.12±11.41
fasting blood glucose（mmol/l）	5.58±2.59a)	5.70±1.47a)	5.22±1.36
total cholesterol（mmol/l）	4.94±0.92	5.03±1.03a)	4.78±1.18
triacylglycerol（mmol/l）	1.59±1.12a)	1.67±1.35a)	1.39±1.27
aspartate transaminase（u/l）	27.56±21.10a)	27.12±17.67	25.64±20.91
glutamate transaminase（u/l）	24.54±13.14a)	25.07±9.90a)	23.56±11.91

Furthermore, the association between fatty liver disease and GSD suggests a potential mechanistic link between hepatic steatosis and gallstone formation, warranting further investigation.

Hypothesis Tested:

The results of the logistic regression analysis confirm the hypotheses posited in the study:

1. **Gender Hypothesis:** The hypothesis that females have a higher risk of developing GSD compared to males is supported by the significantly higher odds ratio observed in females.
2. **Age Hypothesis:** The hypothesis that increasing age is associated with a higher risk of GSD is supported by the statistically significant increase in odds observed with each one-year increase in age.
3. **Other Risk Factor Hypotheses:** The hypotheses regarding fatty liver disease, family history of GSD, hypertension, and BMI as risk factors for GSD are all supported by the statistically significant odds ratios observed in the regression analysis.

Conclusion:

This study provides a comprehensive assessment of the prevalence, risk factors, and clinical outcomes of gallbladder stone disease (GSD) in India. The findings highlight the significant burden of GSD, with a prevalence of 7.02% and a cholecystectomy rate of 2.48% in the study population. Gender emerged as a significant determinant of GSD, with females exhibiting higher prevalence and cholecystectomy rates compared to males. Additionally, age, fatty liver disease, family history of GSD, hypertension, and BMI were identified as important risk factors for GSD, underscoring the multifactorial nature of the disease. These findings have important implications for healthcare policy and practice, emphasizing the need for targeted prevention and management strategies tailored to the unique demographic and clinical profile of individuals at risk of GSD.

Limitations of the Study:

Despite the comprehensive nature of this study, several limitations warrant consideration. Firstly, the cross-sectional design precludes the establishment of causality and temporal relationships between risk factors and GSD. Additionally, the reliance on self-reported data for certain variables such as family history of GSD may introduce recall bias and misclassification errors. Moreover, the exclusion of certain demographic and clinical variables from the questionnaire, such as ethnicity and smoking status, may limit the comprehensiveness of the analysis. Furthermore, the study was conducted in a specific geographic region of India, thereby limiting the generalizability of the findings to other populations. Lastly, the use of ultrasound for the diagnosis of GSD may underestimate the true prevalence of the disease, particularly in cases of asymptomatic gallstones. Despite these limitations, this study provides valuable insights into the epidemiology and risk factors of GSD in India, laying the groundwork for future research and clinical interventions.

Implications of the Study:

The findings of this study have important implications for healthcare policy, practice, and research. Firstly, the identification of gender-specific differences in the prevalence and clinical outcomes of GSD underscores the need for gender-sensitive approaches to prevention, diagnosis, and treatment. Secondly, the recognition of modifiable risk factors such as obesity, fatty liver disease, and hypertension highlights the potential for

targeted interventions aimed at reducing the burden of GSD. Additionally, the findings of this study may inform the development of clinical guidelines and screening protocols for the early detection and management of GSD. Furthermore, the study underscores the importance of multidisciplinary collaboration between clinicians, researchers, and policymakers to address the complex determinants of GSD and improve the health outcomes of affected individuals.

Future Recommendations:

Building upon the findings of this study, several avenues for future research and clinical practice are warranted. Firstly, longitudinal studies are needed to elucidate the temporal relationships between risk factors and the development of GSD, allowing for the identification of modifiable factors amenable to intervention. Additionally, further investigation is needed to explore the underlying mechanisms linking fatty liver disease, hypertension, and other metabolic disorders to the pathogenesis of GSD. Moreover, efforts should be made to enhance the diagnostic accuracy of GSD through the development of novel imaging modalities and biomarkers. Furthermore, interventions targeting lifestyle modifications, such as dietary interventions and weight management programs, may hold promise in reducing the burden of GSD in high-risk populations. Lastly, future research should strive to address the disparities in healthcare access and outcomes among vulnerable populations, ensuring equitable delivery of care for individuals affected by GSD.

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