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Sociodemographic determinates and risk factors related to the prevalence of gallstone disease associated with chronic salmonella carriers in Erbil City, Iraq

Amer Hameed Mustafa*, Alaa Zanzal Raad
Department of Medical Microbiology, College of Medicine, Tikrit University, Iraq

Abstract
Gallstones are a worldwide medical problem that requires surgical intervention and hospital stays. There are several predisposing factors for gallstones, including sedentary lifestyle, gender, pregnancy, food, gastric surgery, genetics, and chronic illness. Gallstones are caused by bacteria that are able to proliferate in inflamed gallbladders. *Salmonella typhi* induced typhoid fever is still a major health risk in low- and middle-income countries. The main organ where *Salmonella typhi* (*S. typhi*) infections persist is the gallbladder. The link between chronic illnesses, sociodemographic traits, and gallbladder disorders is the main focus of contemporary research. A cross-sectional study was conducted at the surgery department of Erbil and Rizgari Teaching Hospitals in Erbil City, Iraq, from October 2023 to March 2024, involving 125 patients aged 15 to 80 years old of both sexes diagnosed with gallbladder disease who underwent cholecystectomy. A questionnaire form was used to gather information from each participant, including their age, sex, place of residence, education level, and medical history. All gallbladder specimens (gallstone, bile, and gallbladder tissue samples) were collected and analyzed for bacterial growth. Out of 125 samples, only 8 (6.4%) of cases were positive for *S. typhi*, about 93 (74.4%) cases were positive for other types of bacteria, and 24 (19.2%) samples had no growth of bacteria. Gallstones had the highest proportion of *S. typhi* isolation 5 (4%). The most infected age group at 36–45 years were 41 (32.8%) cases, mostly female, 97 (77.6%), and 88 (70.4%) from urban areas. Out of the individuals who tested positive for *Salmonella typhi*, 3 (2.4%) resided in urban areas, while 5 (4%) were from rural areas. Hereditary factors were the most common comorbidities among the patients, with 58 cases, followed by typhoid fever with 36 cases. The study revealed that about 43 (34.4%) of cases were illiterate, and 39 (31.2%) had a primary level of education. We concluded that there is a need for further research to substantiate the connections we identified between certain sociodemographic and risk variables and gallbladder illness.

Keywords: Gallstone, sociodemographic determinates, risk factors, chronic *Salmonella* carrier

Introduction

Gallstones are hardened deposits of digestive fluid in the gallbladder that affect the gastrointestinal tract. They grow in various amounts, shapes, and sizes [1]. They are a common medical condition worldwide, causing hospital admissions and surgical treatment. Patients usually have no symptoms, yet they need surgery, which is the most frequent reason for hospital admission. Initially, most patients with gallstone disease are asymptomatic, but they may become symptomatic or asymptomatic when experiencing symptoms or complications [2].

Some predisposing factors for the formation of gallstones include sedentary lifestyle, gender, pregnancy, dietary factors, Crohn's disease, stomach surgery, and hereditary. Gallstones occur as a result of bacteria being able to proliferate in inflamed gallbladders [3].

Gallbladder inflammation leads to septic complications from stone development, regardless of peritoneal cavity contamination with infected bile. Both cholesterol and pigment (or bilirubinate)-based gallstones are possible. The development of cholesterol stones in the gallbladder is caused by changes in hepatic and gallbladder function [4]. Complications are greatly influenced by the chemical makeup of gallbladder stones, particularly when brown pigment stones are retained in the abdominal cavity [5].

Cholecystitis and mixed gallstones are often associated; 50% of gallstone disease patients have positive bile. Bacteria may cause both aerobic and anaerobic biliary infections by entering the gallbladder via the circulation. Biliary tract infections are caused by aerobics in 94% of cases and anaerobics in the other cases. Salmonella, Proteus, E. coli, Klebsiella, and Streptococcus are among the most prevalent organisms [6]. A number of reasons, including blood-borne infections, infections disseminated via portal-venous channels, and ascending infections from the duodenum, may result in biliary tract infections. Ascending infections are the main way that bacteria reach the bile [7]. Gallbladder stones have a low mortality rate but a high morbidity rate in developing countries because, due to obstruction, bile becomes infected [8].

The human host-restricted pathogen that causes typhoid fever is *Salmonella typhi* (*S. typhi*). Typhoid fever is a severe health problem for individuals living in many low- and middle-income countries that lack access to sanitary facilities and clean water. Traveling to typhoid-endemic regions is a common way for people in high-income countries to get typhoid fever, but long-term carriers who reside in these places may also transmit the disease to others. S. typhi shed in the urine and faeces of an individual with acute typhoid illness might contaminate food during handling or preparation by temporary or permanent carriers who do not follow adequate hygiene procedures, which can lead to short-cycle transmission to close contacts [9, 10]; "long cycle transmission" mostly occurs when crops are watered with raw sewage or when people drink water tainted with human waste [11].

Salmonella typhi infections generally persist in the gall bladder and other parts of the human biliary system. The bacteria may proliferate and survive outside of the gall bladder lumen's cells, for example, in the form of biofilm on

gallstones or within the epithelium-containing cells [12]. Gallstones and other pre-existing biliary problems facilitate *Salmonella* survival in the biliary system [13, 14]. As of right now, the gall bladder seems to be the primary site of *S. typhi* carriage.

It is natural that the bulk of current research has focused on biliary carriers, the role of cholelithiasis, and the ability of *S. typhi* to build biofilms on gallstones, given that the gallbladder is the conventional physiological home for chronic *S. typhi* infection [12, 15]. Chronic gallbladder disease and cholelithiasis are equally common in endemic populations as chronic *S. typhi* carriers [16]. Therefore, chronic carriage is several times more likely in females than in males and in older persons (>40 years of age) compared to younger adults and teenagers [12].

Material and method

Data collection

A prospective cross-sectional study was conducted at the department of surgery at Erbil and Rizgari Teaching Hospitals in Erbil City, Iraq. From October 2023 to March 2024. This study included 125 patients aged 15 to 80 years old of both sexes with symptomatic cholelithiasis who underwent open or laparoscopic cholecystectomy. A detailed questionnaire was created to collect the participant's documented medical history, clinical parameters, and demographic and epidemiologic information, such as sex, age, place of residence, education, and employment.

Sample collection

The sample included all fresh gallbladder specimens (gallstone, bile, and gallbladder tissue) that were collected immediately following cholecystectomy. Once collected, the different types of gallbladder samples are carefully transferred to sterile containers and transported to a laboratory. Specimens were collected from each gallbladder sample site and subsequently cultured in accordance with established protocols outlined in previous research studies [17–19].

Isolation and identification of bacteria

Gallbladder samples were inoculated in tryptone soya broth for 24 hours at 37˚C for enrichment. Then enriched broth cultures were aseptically inoculated onto *Salmonella-Shigella* agar and incubated at 37˚C for 24 hours. After the incubation period, both the morphological and microscopic characteristics of the colonies were examined. To obtain pure cultures of the microorganisms, the colonies present on the Petri plates underwent multiple subcultures on selective solid media. Then standard biochemical tests were performed, including the triple sugar iron, catalase test, oxidase test, urease test, and Simmons's citrate test, to confirm the identity of the microorganisms using the VITEK-2 compact system.

Statistical analysis

Statistical analysis was conducted using IBM SPSS ver. 23. The determination of the statistical differences among different groups was performed using the chi-square test, and the probability of $P \leq 0.05$ was considered to be statistically significant.

Ethical Considerations

The study was conducted using ethical guidelines and obtained approval from the relevant institutional review board. Informed consent was obtained from all participants involved in the study. Confidentiality of participant information was ensured, and data were anonymized during analysis and reporting.

Limitations

Certain limitations should be considered when interpreting the results of this study. The sample size was small, and the study was conducted at specific hospitals in Erbil City, Iraq. Therefore, the findings may not be generalizable to the entire population. Additionally, the study focused on a particular characterization and did not examine other factors that could contribute to the developing gallstone disease.

Results

1. The present study showed that from a total of 125 samples of the gallbladder of cholelithiasis patients, only 8 (6.4%) cases were positive for *S. typhi* from total bacterial growth, about 93 (74.4%) cases were positive for other types of bacteria from total bacterial growth, and 24 (19.2%) samples had no growth of bacteria as shown in Figure 1.
2. The findings revealed that the growth distribution of *S. typhi* was categorized by the source of the gallbladder sample. For gallstone, out of 75 gallstone samples, 5 (4%) tested positive. For bile, out of 35 bile samples, 1 (0.8%) was positive. For gallbladder tissue, out of the 15 gallbladder tissue samples, 2 (1.6%) were positive. Using the chi-squared test result, we found that the chi-squared is 1.66 with a p-value of 0.043, indicating a statistically significant difference.
3. In the present study, the age group of 36–45 years (41 cases) was more commonly affected (32.8%), followed by 26–35 years (28%), 15–25 years (16%), and 46–55 years (15.2%) of the age group, and females were more commonly affected. Out of 125 patients, 97 (77.6%) were females, and males were 28 (22.4%), as shown in Figure 2.
4. The study shows the residence distribution of the patients, with 88 (70.4%) from urban areas and 37 (29.6%) from rural areas. Out of the individuals who tested positive for *Salmonella typhi*, 3 (2.4%) resided in urban areas, while 5 (4%) were from rural areas (Table 1). The chi-squared test result ($p = 0.025$) indicates that there is a statistically significant difference in the residential distribution of patients who tested positive for *S. typhi*.
5. Among the 125 cases reported, the most common comorbidities among the patients were hereditary factor (H.F.) in families with 58 cases, followed by typhoid fever (T.F.) with 36 cases, diabetes mellitus (D.M.) with 26 cases, and hypertension (H.T.) with 21 cases, as shown in Figure 3.
6. The current study presents the distribution of cholelithiasis patients according to their level of education. There were 43 (34.4%) categorized as ignorant, 39 (31.2%) categorized as primary, 24 (19.2%) categorized as secondary, and 19 (15.2%) categorized as university educated.

Table 1: Distribution of patient positive with *S. typhi* according to residence

Residence	Patient group		Positive for *S. typhi*	
	NO.	%	NO.	%
Urban	88	70.4	3	2.4
Rural	37	29.6	5	4
Total	125	100	8	6.4
Chi squared test (p value)	5.76 (0.025 S)			

S: Significant difference between groups (p value < 0.05).

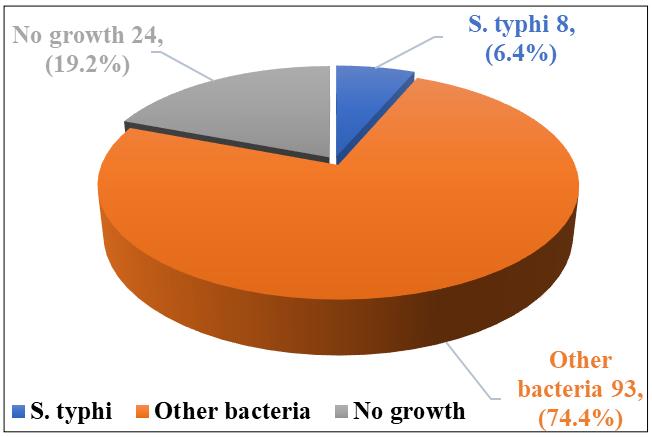

Fig 1: Distribution of bacterial growth from gallbladder specimen

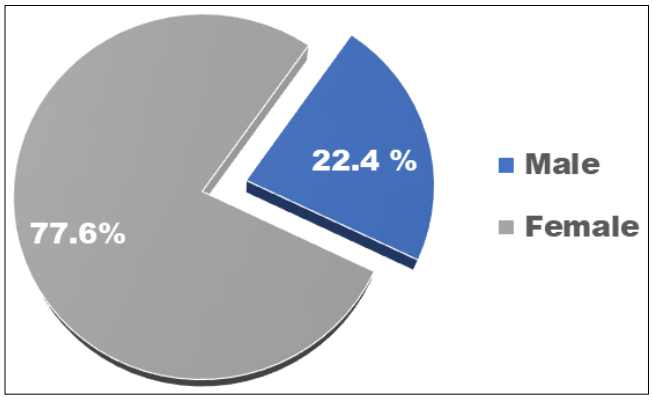

Fig 2: Frequency of cholelithiasis patient according to sex

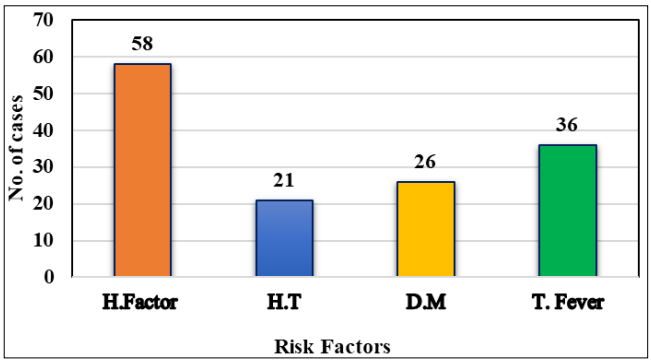

Fig 3: Distribution of risk factors and comorbidities in cholelithiasis patients

Discussion

Gallbladder diseases seriously affect the quality of life of patients. In this cross-sectional study, we investigated the annual prevalence of gallbladder diseases and related factors.

The present study showed that out of 125 gallbladder samples from GD patients, only 6.4% were positive for *S. typhi*, while 74.4% were positive for other bacterial infections. The remaining 19.2% had no bacterial growth. Our findings agreed with those of Sadeq N. *et al.* [20], whose rate was 6%, and Shareef H. A. [21], whose rate was 6.6%.

The study indicates that the gallstone is the optimal location for bacterial development. *S. typhi* was found in around 5 cases in gallstones, 2 cases in gall bladder epithelial tissues, and 1 case in bile samples. These findings are consistent with a prior study conducted by Mansour *et al.* [19], which found approximately 28, 12, and 4 cases of *S. typhi* in gallstones, gall bladder epithelial tissues, and bile samples, respectively.

The study confirms that gallbladder inflammation affects all ages, with a 32.8% increase in the 36–45 age group, consistent with a previous study of 30% by Ali Rawaa Adday *et al.* [22]. Gallbladder diseases are rare in children under 10, but increase with age, with gallstones 4–10 times more common in older individuals due to bile composition changes and gallbladder function decline [23]. A plausible explanation for the outcome might be the notable ageing process of organ function, resulting in reduced disease resistance in the elderly. Additionally, it's possible that older adults have many chronic illnesses concurrently and that gallbladder ailments are exacerbated by other illnesses [24].

The study found that infection occurs in both sexes, with women experiencing a higher rate of infection (77.6%) than men (22.4%). The sex ratio is approximately 1:3.5. This ratio, which agrees with other studies [25, 26]. Possibly due to factors such as reproductive history, multiple births, and oral contraceptives. Some female hormones and special genes in the female body also contribute to this risk, making them more susceptible to gallbladder diseases than males [27].

According to this study, 88 patients (70.4%) with gallbladders were from cities, while 37 (29.6%) were from rural areas. In this investigation, we discovered that there was a higher association between people living in rural areas and gallbladder diseases compared to those living in city areas. This outcome might be explained by the fact that, in contrast to those who live in cities, residents in rural regions only eat one food, regardless of the standard of sanitation and medical care [4]. Urban diets, high in sugar, processed carbohydrates, and unhealthy fats, can cause gallstone formation due to changes in bile composition and cholesterol production, while rural diets, rich in fresh fruits, grains, and legumes, improve digestion [28]. Obesity in cities increases gallstone risk and may lead to a sluggish gallbladder due to less physical activity [29, 30].

These findings suggest that hereditary factors play a significant role in the occurrence of the condition in 58 cases. These results agreed with previous [31, 32]. Genetic predispositions, including cholesterol metabolism, bile composition, gallbladder function, and inflammatory response, significantly influence gallstone formation, increasing the risk, affecting gallbladder function, and contributing to inflammation [33].

Typhoid fever's high prevalence as a previous medical condition suggests a potential link or risk factor. *Salmonella typhi*, the bacterium responsible, is linked to increased gallstone formation through factors like biliary stasis, altered bile composition, gallbladder dysfunction, and biofilm formation [34, 35].

Diabetes and hypertension are linked to gallstone formation, but their relationship is not direct; obesity, insulin resistance, metabolic syndrome, hyperinsulinemia, and inflammation contribute to gallstone formation. The metabolic syndrome, which includes obesity, diabetes, hypertension, and dyslipidemia, raises the risk of gallstone development by lowering gallbladder mobility and producing more cholesterol [36].

The study revealed that about 43 (34.4%) of cases were illiterate, and 39 (31.2%) had a primary level of education. These finding were similar to those observed in a study conducted by Rajat Das *et al.* [37]. Lower education levels can indirectly influence the risk of developing cholelithiasis by limiting access to healthy eating habits and consuming diets high in fat and cholesterol, known risk factors for gallstone formation [38]. Also, lower education levels and socioeconomic status can lead to undiagnosed or untreated conditions like obesity, diabetes, or metabolic syndrome, which are risk factors for cholelithiasis [38]. Additionally, education level can influence lifestyle factors like physical activity, smoking, and alcohol consumption, with lower-educated individuals more likely to engage in sedentary and unhealthy habits [39]. Lastly, lower education levels may delay cholelithiasis diagnosis and treatment but indirectly influence the risk through diet, socioeconomic status, lifestyle, and healthcare utilization, despite not being a determining factor [40].

Conclusions

Our study's findings imply that eating habits, clinical background, and demographic traits are linked to gallbladder illness. Gallbladder disease is particularly associated with elderly adults and females. However, inherited variables are important in the development of the illness, and persistent typhoid fevers indicate that gallbladder disease may also be related to a possible risk factor. Furthermore, a lower level of education may indirectly affect the likelihood of gallstone development. Future studies are required to validate these results.

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