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Prevalence of Salmonella Typhi in Bile of the Patients Undergoing Cholecystectomy at a Tertiary Care Hospital Karachi

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Author`s Contribution

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ABSTRACT

Objective: To estimate the prevalence of salmonella typhi in bile specimens collected from patients undergoing cholecystectomy at a tertiary care Hospital Karachi.

Methodology: The descriptive cross-sectional study, was conducted at Department ofSurgical Unit 21, Jinnah Postgraduate Medical Center, Karachi, from January 2021 to June 2021. Patients with symptomatic Cholelithiasis like sudden pain in the upper right portion of your abdomen which radiate towards right shoulder, nausea, vomiting, undergo cholecystectomy of either gender male or female with age 14 to 60 years were included. After opencholecystectomy, bile was aspirated from the gallbladder at fundus in five ml syringe and long spinal needles was used in caseof laparoscopic cholecystectomy to collect bile under vision of telescope. Specimens were sent to laboratory according to protocol for culture sensitivity.

Results: A total of 171 patients who met the inclusion and exclusion criteriawere included. Mean age of the patients was 49.39±8.78 years. 83 (48.5%) were male and 88 (51.5%) were female. Prevalence of salmonella typhi in bile specimens collected from patients undergoing cholecystectomy, was found 17.54%. Furthermore, the frequency of salmonella isolate was statically insignificant according to the patient's gender, diabetes and obesity (p=>0.05), while it was statically significant according to age up to 40 years and residence in rural areas (p-<0.05.

Conclusion: A significant proportion of patients were found to have Salmonella in bile from patients undergoing cholecystectomy. Therefore, close monitoring of patients must bedone in all patients with regular follow-up.

Key words: Salmonella typhi, gall bladder, cholecystectomy, acute and chronic carrier state.

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Introduction

The gallbladder, positioned directly beneath the liver, is a small organ responsible for storing a digestive fluid called bile, which is subsequently released into the small intestine.[1] Gallstone disease represents a significant epidemiological and economic challenge globally, with cholesterol gallstone disease being the most prevalent form.[2] It is one of the most routine abdominal surgeries performed in worldwide.[1,2] About 95% of biliary tract diseases are due to gall stones.[3] Its incidence increases with age, about 20% of adult over 40 years of age and 30% over 70 years have biliary calculi. Diabetes mellitus, obesity, estrogen levels, pregnancy andcirrhosis are well known risk factors of gall stones.[4] increased gall stone size > 3cm become indication of cholecystectomy.[5] The prevalence of cholelithiasis varies with geographical and ethnicity factors. It shows lowest occurrence in Africans and highest in western countries.[6] In Asian countries about

17% of population with overall 11 to 36% prevalence exist.[7]

The occurrence of gallstones is often linked to gallbladder carcinoma, and the detection of Salmonella Typhi in the gallbladders of individuals with gallstone disease is suggested as a contributing factor to the development of cancer.[8] Normally bile is sterile but when cholecystitis occurs different kind of microbes can be cultured either from bile or wall of the gall bladder.[3,9] Occurrence of live bacteria in cores of gallstones is also potential threat to peritoneal cavity to leaving stones while performing cholecystectomy.[10] Previous studies revealed occurrence of aerobic and anaerobic bacteria from bile of inflamed gallbladder.[10,11,12] Among them enteric bacteria's are more frequent to present in bile and also causes carcinomas.[10]

Presence of salmonella typhi in bile culture varies with distribution of typhoid fever in country,as it is endemic in several cities of our country and If we compareon basis of gender, salmonella typhi is more dominant in bile sample of female than male.[9] Typhoid fever, resulting from the infection with Salmonella enterica subspecies enterica serotype Typhi, poses a significant public health concern in numerous low- and middle-income nations. It spreads through the consumption of water or food contaminated with feces or urine from individuals with acute or chronic S. Typhi infection.[13] Mostly patients survived from acute infection of typhoid but about 3 to 5% develop chronic infection of typhoid and they become more prone to develop Gallstones, in addition with or without gall stones chronic carrier have high risk to develop gall bladder carcinoma.[12] Previous literature has extensively investigated the frequency of infections and the isolation of organisms from bile. Conversely according to a study, the recent progress in the management of typhoid fever, there is still limited understanding of asymptomatic carriage of Salmonella Typhi in the gallbladder.[14]

However, in the past five years, no studies have been conducted in this domain within our context. Therefore, the current study aims to fill this gap by specifically determining the frequency of Salmonella Typhi in bile obtained from patients undergoing cholecystectomy. This investigation holds significant potential as it may allow for the identification of asymptomatic typhoid carriers.

Methodology

The present descriptive cross-sectional study was conducted at Department of Surgical Unit 21, Jinnah Postgraduate Medical Center, Karachi. Duration of study was six months after approval of synopsis from January 2021 to June 2021. Sample size was estimated by using Open Epi software. The prevalence of 5.8**%** of salmonella typhi in bile,[15] the sample sizecalculated was 171.[15] Non-probability consecutive sampling was used. All patients with symptomatic cholelithiasis like sudden pain in the upper right portion of your abdomen which radiate towards right shoulder, nausea, vomiting, undergo cholecystectomy of either gender male or female with age 14 to 60 years were included. Participants who were denying to participate, Patients with acute cholecystitis (severe right upper quadrant pain, pyrexia and leukocytosis; 12000 to 15000 cells/uL), common bile duct stone,history of jaundice, dilated biliary duct and patients who were on anti-biotic previously due toany disease were excluded. Informed consent was sought from all participants after explaining the nature of procedure.

After opening abdomen in case of opencholecystectomy, bile was aspirated from the gallbladder at fundus in five ml syringe and long spinal needles was used in case of laparoscopic cholecystectomy to collect bile under vision of telescope. Bile sample was sent to laboratory in sterilize containerfor culture sensitivity. Post operatively patient was managed according to protocols. The participants were experienced any undue discomfort. The information such as age, gender, BMI, height, weight, duration of symptoms, co-morbidities and salmonella bile culture was noted on pre-designed proforma. Theethical approval of the proposed study was taken from institutional review committee of Jinnah Postgraduate Medical Center or Jinnah Sindh Medical University. SPSS version 20 software was used to analyze the data. Stratification was done according to age, gender, comorbid, sign and symptoms, salmonella typhi and post stratification analysis was done by using chi square test for categorical variables. P value <0.05 was considered significant.

Results

A total of 171 patients admitted at the Department of Surgical Unit 21, Jinnah Postgraduate Medical Center, Karachi. Mean age and duration of symptoms was 49.39±8.78 years and 4.26±3.54 days respectively. Out of 171 patients, 83 (48.5%) were male and 88 (51.5%) were female. Regarding residence status, 138 (80.7%) patients resided in urban areas, while 33 (19.3%) resided in rural areas. Among all patients, 61 (35.7%) had symptoms lasting ≤ 7 days, and 110 (64.3%) had symptoms lasting > 7 days. Additionally, 39 (22.8%) patients were diabetic, 43 (25.1%) were hypertensive, and 62 (36.3%) were obese. For abdominal pain, out of171 patients, 92 (53.8%), 35

(20.5%) and 44 (25.7%) patients had pain at right hypochondrium, left hypochondrium and epigastric regional pain respectively. he majority of cases (138, 80.7%) presented with vomiting, while nausea was reported in 63 (36.8%) patients, fever in 82 (48%), and dyspepsia in 30 (17.5%) patients. Table I

Table I: Bassline and clinical characteristics of the patients. (n=171)

Variables		N	%
Gender	Male	83	(48.54%)
	Female	88	(51.46%)
Residential status	Rural	33	(19.30%)
	Urban	138	(80.70%)
Diabetes	Yes	39	(22.81%)
	No	132	(77.19%)
Hypertension	Yes	43	(25.15%)
	No	128	(74.85%)
Obesity	Yes	62	(36.26%)
	No	109	(63.74%)
Sign/ symptoms	Right hypochondrium	92	(53.80%)
	Left hypochondrium	35	(2047%)
	Epigastrium	44	(25.37%)
	Nausea	63	(36.84%)
	Vomiting	139	(80.70%)
	Fever	82	(47.95%)
	Dyspepsia	30	(17.54%)
Mean age of the patients		49.39±8.78 years	
Duration of symptoms		4.26±3.54 days	

Overall prevalence of salmonella typhi in bile specimens collected from patients undergoing cholecystectomy, was found 17.54%. Figure 1

In terms to the stratification, the frequency of salmonella isolate was statically insignificant according to the patient's gender, diabetes and obesity (p=>0.05), while it was statically significant according to age up to 40 years and residence in rural areas (p-<0.05). Table II

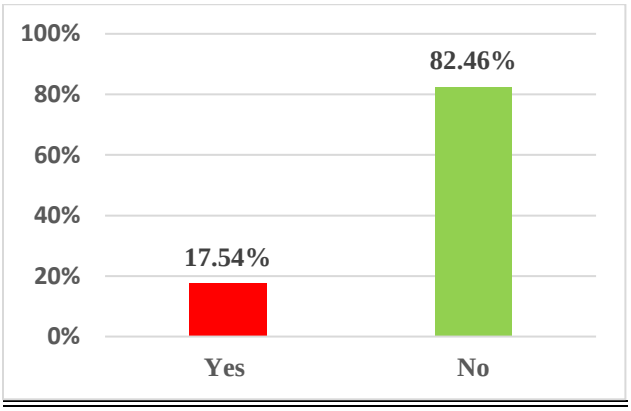

Figure 1. Frequency of salmonella typhi. (n=171)

Discussion

Gallstones are formed from solidified digestive fluid, typically in the form of small pellets. These stones may manifest with symptoms or remain without symptoms. In this study, 171 patients with symptomatic cholelithiasis were included, with an average age of 49.39±8.78 years. Female patients slightly predominated at 51.5%, while males accounted for 48.5%. The majority of individuals resided in urban areas (138, 80.7%). In comparison, Naeem M et al,[16] reported a mean patient age of 43.8 ± 9.59 years, with approximately 85.4% being female. They noted that around 61% of patients had no formal education, and all participants were from a low socioeconomic status background. Conversely, Ali A et al,[17] found a higher proportion of female patients with cholelithiasis (81%). However, they reported a lower mean patient age of 25 ± 3 years. This discrepancy could be attributed to their study's inclusion criteria, which focused on patients below the age of 30. Consistently, KHAN AN et al,[18] also observed that the average age of the patients was 42.44±16.58 years, with a male to female ratio of

Table II: Stratification of Salmonella Isolate Frequency by Patient Characteristics.

Variables		SALMONELLA TYPHI		Total	P-value
		Yes	No		
Age groups	14-40 years	18 (32.1%)	38 (67.9%)	56(100%)	
	41-60 years	12 (10.4%)	103 89.6%)	115(100%)	0.001
Gender	Male	16 (19.3%)	67 (80.7%)	83 (100%)	
	Female	14 (15.9%)	74 (84.1%)	88(100%)	0.563
Residence	Urban	19 (13.8%)	119 (86.2%)	138(100%)	
	Riral	11 (33.3%)	22 (66.7%)	33(100%)	0.014
Diabetes	Yes	10 (25.6%)	29 (74.4%)	39(100%)	
	No	20 (15.2%)	112 (84.8%)	132(100%)	0.13
Obesity	Yes	11 (17.7%)	51 (82.3%)	62(100%)	
	No	19 (17.4%)	90 (82.6%)	109(100%)	0.95

1:1.8. Female predominance with cholelithiasis may due to hormonal, physiological, lifestyle, and genetic factors that collectively contribute to a higher risk of gallstone formation in women compared to males.

In this study pain was almost in all of the cases as 92 (53.8%), 35 (20.5%) and 44 (25.7%) patients had pain at right hypochondrium, left hypochondrium and epigastric regionalpain respectively, majority of cases (138, 80.7%) presented with vomiting, while nausea was reported in 63 (36.8%) patients, fever in 82 (48%), and dyspepsia in 30 (17.5%) patients. These findings were supported by Memon, J. et al[19], who discovered that the most common clinical presentation noted in 93.95% of cases, was epigastrium pain. In 73.82% of instances, there was right hypochondrial pain, and in 50.33% of cases, there was pain radiating to the scapula. Furthermore, nausea was reported in 44 individuals, and dyspepsia in 49.66% of patients, while the least prevalent symptom was vomiting, which occurred in 21.47% of cases.[19] Consistently Lodha M et al[20] reported that the predominant symptoms upon presentation included abdominal pain (96.1%), accompanied by dyspepsia (60.5%) and vomiting (55.3%). Additionally, a subset of patients reported loss of appetite (47.4%) and back pain (32.9%). Fever (23.7%) and yellowish discoloration of the skin (9.2%) were less frequently reported symptoms.[20] In terms to the comorbidities 39 (22.8%) patients were diabetic, 43 (25.1%) were hypertensive, and 62 (36.3%) were obese, these findings were close to the studies by Ali A et al,[17], Lodha M et al[20] and Memon, J. et al[19].

In accordance to the outcome findings of the study the overall prevalence of salmonella typhi in bile specimens collected from patients undergoing cholecystectomy, was found 17.54%, which statically insignificant according to the patient's gender, diabetes and obesity (p=>0.05), while statically significant according to age up to 40 years and residence in rural areas (p-<0.05). Consistently a previous study by Walawalkar YD et al[8] reported that the 7 (17.5%), all of which tested negative for culture, yielded positive PCR results for Salmonella Typhi. Among these cases, 4 (10%) were from tissue samples, 2 (5%) from bile samples, and 1 (2.5%) from a gallstone sample. In aligns to this study Shukla R et al[21] demonstrated that the serum antibodies against Salmonella were found to be more commonly positive in patients with gallbladder cancer (GBC) at a rate of 22% and in those with xanthogranulomatous cholecystitis (XGC) at a rate of 29%, especially among males aged 50 years and older.

However, study by Sadeq Noomi B et al[22] revealed that among the 50 patients diagnosed with gallstones, three were found to harbor the bacteria responsible for typhoid fever, resulting in a prevalence rate of 6%. In the comparison of this series Farhana N et al[13], stated that among the 246 bile samples examined, microorganisms were detected in 69.51% of cases and among these, they identified Salmonella enterica serovar Typhi in 8 cases (3.45%). According to a study it has been observed and recommend ed that the chronic carrier state of Salmonella typhi presents a significant risk factor in patients diagnosed with gallbladder carcinoma. Given the increased risk associated with this carrier condition, treatment plans ought to include either preventative monitoring or surgical cholecystectomy.[24] The study encountered many limitations, including a restricted sample size, a lack of sensitive drug analysis, which could have provided valuable insights into treatment efficacy. To address these shortcomings and enhance our understanding of the adverse issue under investigation, it is imperative to conduct further comprehensive studies. Because there is a need to explore local data to better understand the specific challenges and factors contributing to adverse outcomes in this context.

Conclusion

Study revealed a significant proportion of patients undergoing cholecystectomy were observed to have Salmonella present in their bile. This adds to the growing body of evidence suggesting that S. Typhi can endure in the gallbladder of carriers, particularly those with gallstones. Ongoing research aims to better understand the factors contributing to biofilm formation on gallstones and the interaction between S. enterica and the gallbladder epithelium, yet numerous questions persist. Consequently, it is imperative to establish close monitoring protocols, along with appropriate diagnostic and management strategies, for all patients. These measures are essential for mitigating morbidity and mortality associated with this condition.

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