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Short Communication

Prevalence of *Salmonella enterica* Serovar Typhi in Bile and Stool of Patients with Biliary Diseases and Those Requiring Biliary Drainage for Other Purposes

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SUMMARY: Acute suppurative cholangitis is a serious complication of biliary obstructions due to infection. *Salmonella enterica* serovar Typhi is an important biliary pathogen. Bile samples from 445 patients with biliary diseases as well as those requiring biliary drainage for other miscellaneous gastrointestinal diseases were investigated bacteriologically with special emphasis on *Salmonella*. Fecal samples or rectal swabs were also obtained from 402 of these patients. Bactericholia was detected in 68.8% patients and *Salmonella* in 5.8% of all bile samples. Other strains of salmonellae were also present in a fair number of the samples. Some of the patients had the same type of bacterial isolates from their stool samples as those from their bile samples. Colonization of the biliary system may not be clinically apparent, but is associated with an increased risk of infection.

Cholangitis is a frequent and potentially serious complication in patients with bile duct obstruction (1) and it is a major cause of morbidity and mortality. Bile, which is bacteriologically sterile in healthy persons, becomes a medium of growth for many microorganisms in cases of biliary obstruction and results in acute suppurative cholangitis. Before a health policy regarding the management of such cases can be formulated, the extent of infection and the type of bacteria commonly present in a given sample should be investigated. However most hospitals located in tropical regions cannot perform cultures due to the specific lack of facilities for biliary drainage, as well as a general lack of materials, equipment, expertise, and financing.

Salmonella enterica serovar Typhi is among the major known biliary pathogens. In India, typhoid fever is common, serious, and increasingly difficult to treat due to multidrug resistance. The gallbladder is a frequent and an important site of lodgment of typhoid bacilli, which are generally more numerous in the bile than in feces. This bacterium may persist there for many years after convalescence and it can increase the risk of hepatobiliary cancer. The present study was conducted in order to determine the prevalence of positive aerobic bacterial culture in bile, with special emphasis on *S.* Typhi in patients with biliary diseases as well as those requiring biliary drainage for other miscellaneous gastrointestinal diseases. A comparison of bile isolates with those from parallel stool cultures was carried out, with consideration of *Salmonella* sp. in particular.

Bile samples were collected from 445 consecutive patients with various biliary diseases or with diseases requiring biliary drainage for other miscellaneous gastrointestinal ailments. These patients visited the Gastroenterology and General Surgery clinics of the Postgraduate Institute of Medical Education and Research in Chandigarh, India between June 1999 to January 2003. The age range of the patients was 18 to 90 years. The male-to-female gender ratio was 1:1.1.

For the analysis, the bile samples were divided into the following 4 groups, depending upon the nature of the disease of the patients from whom they were collected: Group A consisted of 231 patients with gallbladder/common bile duct stones; Group B consisted of 26 patients with carcinoma of gallbladder; Group C consisted of 36 patients with cholangiocarcinoma, obstructive jaundice, or carcinoma of the pancreas/ampulla; and Group D consisted of 152 patients with miscellaneous gastrointestinal ailments such as inflammatory bowel disease, chronic pancreatitis, anorexia, reflux disease, abdominal pain, liver diseases, etc., and of patients requiring biliary drainage.

Fecal samples were also obtained from 402 of the above-mentioned patients; the samples were either collected in sterile stool containers (Hi Media, Mumbai India) or were obtained as rectal swabs. All specimens collected were inoculated into various bacteriological media which contained selective media for *Salmonella* sp. The colonies that grew in these cultures were identified by various routine biochemical tests and the results were verified serologically by antisera obtained from Denka Seiken (Tokyo, Japan).

From a total of 445 bile samples, bacteria were found to grow in 306 (68.8%). The most common organisms isolated were *Escherichia coli* in 78 (17.5%), *Klebsiella* sp. in 70 (15.7%) and *Pseudomonas aeruginosa* in 65 (14.6%) samples. Other isolated organisms were *Enterobacter* sp. in 35 (7.8%), *Salmonella* in 26 (5.8%), *Acinetobacter* sp. and *Proteus* sp. in 16 (3.6%) each, *Citrobacter* sp. in 13 (2.9%), *Staphylococcus* sp. in 10 (2.2%), and *Serratia marcescens* in 9 (2.0%) samples. Table 1 shows the distribution of various microorganisms in the 4 groups. Monomicrobial infection was found in 256/445 (57.5%) samples, bimicrobial infection was observed in 48/445 (10.8%) samples, and polymicrobial infection was found in 2/445 (0.5%) samples.

One or more of the samples grew *Streptococcus* sp.,

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Providencia sp., *Shigella boydii*, *Morganella morgani*, *Lactobacillus* sp. and/or *Candida*. Bacteria were isolated from 144/231 (62.3%) samples in Group A, 18/26 (69.2%) samples in Group B, 25/36 (69.4%) samples in Group C, and 119/152 (78.2%) samples in Group D. There were 9 *S*. Typhi in Group A, 2 in Group B, 1 in Group C, and 2 in Group D. Moreover, as regards other *Salmonella* sp. strains identified in this study, 7 were identified in Group A, 0 in Group B, 3 in Group C, and 4 in Group D. Table 2 shows the distribution of various *Salmonellae* spp. among the different groups.

Of 402 fecal samples cultured, 94 (23.4%) grew some type of microorganisms, either as a pure isolate or as various different types of isolate from a single sample. Among the isolates were pathogens such as *Salmonella* and *Shigella*. Here, *S*. Typhi grew in 7 cases; *S*. Enteritidis in 5 cases, and *S*. Choleraesuis, *S*. Typhimurium, and *Shigella boydii* in 1 case each. It was of note that in many cases, the same type of bacterial isolation was observed in the stool and bile samples from the same patient.

Acute suppurative cholangitis and cholangiohepatitis may occur due to the presence of bacteria, which originates in the gut and ascends to the liver via the bile duct due to predisposing condition such as biliary stasis, cholelithiasis, chronic pancreatitis, inflammatory bowel disease, or some anatomic abnormality. As patients with cholelithiasis are admitted to the hospital only after a severe attack or after recurrent episodes, superadded infection is a common complication. Many of the organisms that can colonize the T tube are introduced into a germ-free biliary tract during surgery, either from the gallbladder wall during surgical manipulation or during dilatation of the obstructed bile duct, when bacteria are introduced from the duodenum. In our study, a range of 62 to 78% bactericholia was observed in different groups exhibiting predominant monomicrobial growth. Interestingly, *S. boydii* was recovered both from the bile and the stool samples of a 19-year-old male patient with acute pancreatitis. To the best of our knowledge, this is the first report on the isolation of *S. boydii* from a bile sample.

Table 1. The distribution of various microorganisms among the different groups

Microorganisms	Group A	Group B	Group C	Group D	Total
Sterile	87	8	11	33	139
Klebsiella sp.	35	3	2	30	70
E. coli	33	5	9	31	78
P. aeruginosa	29	2	5	29	65
Salmonellae	16	2	2	6	26
Enterobacter	13	2	4	16	35
Acinetobacter	9	1	3	3	16
Proteus	8	0	3	5	16
Citrobacter	6	2	2	3	13
Staphylococcus	5	1	0	4	10
Serratia marcescens	3	1	0	5	9
Streptococcus	1	0	0	2	3
Providencia	1	0	0	1	2
Shigella boydii	0	0	0	1	1
M. morganii	1	0	0	0	1
Lactobacillus	0	1	0	0	1
Candida	1	1	0	1	3

Accumulation of purulent bile may lead to continued elevation of intrabiliary pressure, which can eventually overwhelm the integrity of the biliary epithelium and lead to reflux of bacteria into the systemic circulation (2), resulting in infections of other regions such as the urinary tract system. Vaishnavi et al. (3) have reported bacteriuria in 12.6% of patients with gallbladder and biliary tract diseases. In patients not responding to antibiotic therapy, urgent biliary drainage is required to reverse development of fatal septicemia.

S. Typhi can be isolated from the gallbladder in most fatal cases of typhoid. This microorganism may persist in the gallbladder for many years after convalescence, and it is occasionally found in gallstones in the absence of a history of typhoid fever. Kuba et al. (4) reported a patient with gallbladder carcinoma who was found to be an incidental biliary typhoid carrier. In the present study, *S*. Typhi was present in 9 bile and 5 stool samples from patients in Group A, with other types of salmonellae also present in moderate number. Contrary to our expectations, *S*. Typhi was found in only two of the samples in Group B of the present study. However, the sample size of Group B ($n = 26$) was mush smaller than that of Group A ($n = 231$), and therefore these groups could not be reliably compared. When the two groups with gallbladder disease (Groups A and B) were considered together, and were compared to the two groups with other ailments (Groups C and D) considered together, *S*. Typhi was found to be present in 4.3% of the cases in the former category, and in 1.6% of those in the latter category. In an earlier study, Vaishnavi et al. (5) reported a highly significant increase in the presence of Vi agglutinins in patients with biliary, gastrointestinal, and other related diseases. Fecal carriage does not give a true figure of carrier incidence due to the intermittent shedding of typhoid bacilli and the need to carry out several examinations before carriage can be excluded.

In the interest of formulating a health policy regarding the management of such infections, it will remain important to quantify the infection in patients with biliary disease. Empiric antibiotic selection is primarily based on data pertaining to bile cultures obtained at surgery. Polymicrobial infection is more likely to be present in patients with an occluded stent, and therefore the selection of appropriate antibiotics remains challenging. Most fecal carriers of typhoid and paratyphoid bacilli are permanently cured by cholecystectomy,

Table 2. The distribution of various *Salmonellae* spp. among the different groups

	Group A		Group B		Group C		Group D		Total	
	Bile	Stool	Bile	Stool	Bile	Stool	Bile	Stool	Bile	Stool
S. Typhi	9	5	2	0	1	0	2	2	14	7
S. Enteritidis	3	3	0	0	1	1	1	1	5	5
S. Typhimurium	3	1	0	0	0	0	0	0	3	1
Salmonella O1	0	0	0	0	1	0	2	0	3	0
S. Paratyphi A	0	0	0	0	1	0	1	0	2	0
S. Choleraesuis	1	0	0	1	0	0	0	0	1	1

which is recommended after all other chemotherapeutic possibilities have been exhausted.

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REFERENCES

1. Rerknimitr, R., Fogel, E., Kalayci, C., Esber, E., Lehman, G. A. and Sherman, S. (2002): Microbiology of bile in patients with cholangitis or cholestasis with and without plastic biliary endoprosthesis. Gastrointest. Endoscopy, 56, 885-887.
2. Lee, J. G. (1998): Role of endoscopic therapy in cholangitis. Am. J. Gastroenterol., 93, 2016-2018.
3. Vaishnavi, C., Singh, S., Kochhar, R., Singh, G. and Singh, K. (2004): Bacteriuria in patients with biliary tract diseases. Ind. J. Pathol. Microbiol., 47, 556-558.
4. Kuba, K., Yamaguchi, K., Nishiyama, K., Noshiro, H., Shimizu, S., Chijiiwa, K. and Tanaka, M. (1978): Gallbladder carcinoma in an asymptomatic biliary typhoid carrier: report of a case. Am. J. Gastroenterol., 93, 656-657.
5. Vaishnavi, C., Kochhar, R., Singh, G., Kumar, S., Singh, S. and Singh, K. (2005): Epidemiology of typhoid carriers among blood donors and patients with biliary, gastrointestinal and other related diseases. Microbiol. Immunol., 49, 107-112.