

Original Research Article

Study on the Incidence of Salmonella Infection in Patients with Carcinoma Gall Bladder

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Abstract

Objectives- This study was conducted to study the association of salmonella infection with carcinoma gall bladder.

Materials and Method- A total of 36 radiologically or histologically proven cases of Carcinoma Gall Bladder were included in the study and their thorough clinical history was taken and WIDAL titres were recorded using the 'Stained Salmonella' Antigen set.

Results- The ratio of male to females among salmonella positive and salmonella negative patient were 1:3 & 1:2.2 respectively.

Keywords - Carcinoma gall bladder, Salmonella.

Introduction

Carcinoma of the gallbladder (CaGB) is the fifth most common cancer of the gastrointestinal tract and is one of the commonest biliary tract (BT) malignancies^[1]. It is seen that for the majority of patients, late diagnosis and lack of effective treatment is a typical feature of the disease even today^[2-4]. Carcinoma of the gallbladder is an aggressive disease with poor prognosis and it's incidence has marked ethnic and geographical variations. Ca GB is more common in females than in males, except in countries like Japan and China. The highest rates of incidence were documented in women from Delhi, India (21.5/100 000)^[5]. In India, carcinoma of gall bladder is much more common among women in the northern and central part. In Kashmir, it is the third most common cancer in females after cancer cervix and

breast cancer. In Delhi, gall bladder carcinoma is the fourth commonest malignancy, and the most frequent gastrointestinal cancer in women^[6]. A number of factors, such as genetics, infections, and life style have been reported to be associated with Ca GB.^[7]

Understanding bacteria-induced carcinogenesis might enable us to prevent and cure some forms of cancers^[8]. The involvement of bacteria in carcinogenesis is still not without controversy because no clear agreement has been achieved on the molecular mechanism/s by which they might promote carcinogenesis. In the 21st century, scientists started hypothesizing that: (1) Chronic inflammation caused by persistent bacterial infections might lead to carcinogenesis^[9-11]; and (2) Bacterial toxins and secondary metabolites produced by the chronic bacterial infection might induce carcinogenesis^[10].

Objectives- To study the association of salmonella infection with carcinoma gall bladder.

Materials and Method

This study was conducted at Shri Guru Ram Rai Institute of Medical and Health sciences and Shri Mahant Indresh Hospital (SMIH), Dehradun Uttarakhand over

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a period of 24 months. Patients attending the in-patient or out-patient department in Shri Guru Ram Rai Institute of Medical and Health sciences and Shri Mahant Indresh Hospital (SMIH), Dehradun who were a radiologically or histologically proven case of Carcinoma Gall Bladder were included in the study. A total of 36 patients were included in the study and their thorough clinical history was taken and WIDAL titres were recorded using the ‘Stained Salmonella’ Antigen set by ARKRAY Healthcare Pvt. Ltd.

Results and Observation

The male to female ratio among the patients suffering from carcinoma gall bladder in our study was 1 : 2.6.

Table 1: Baseline characteristics of study group according to age in %

Age group	No.	%
<40yrs	6	16.7
41 – 50yrs	10	27.8
51 – 60yrs	7	19.4
61 – 70yrs	8	22.2
>70yrs	5	13.9

TABLE 1 shows the distribution of carcinoma gall bladder in accordance with the age group. There were 6 patients below the age of 40 years which presented with aggressive disease, and 5 cases were above the age of 70years. Maximum number of cases i.e. 10 cases were found in 5th decade followed by 8 patients in the age group of 60-70years and 7 patients among 50-60 years of age.

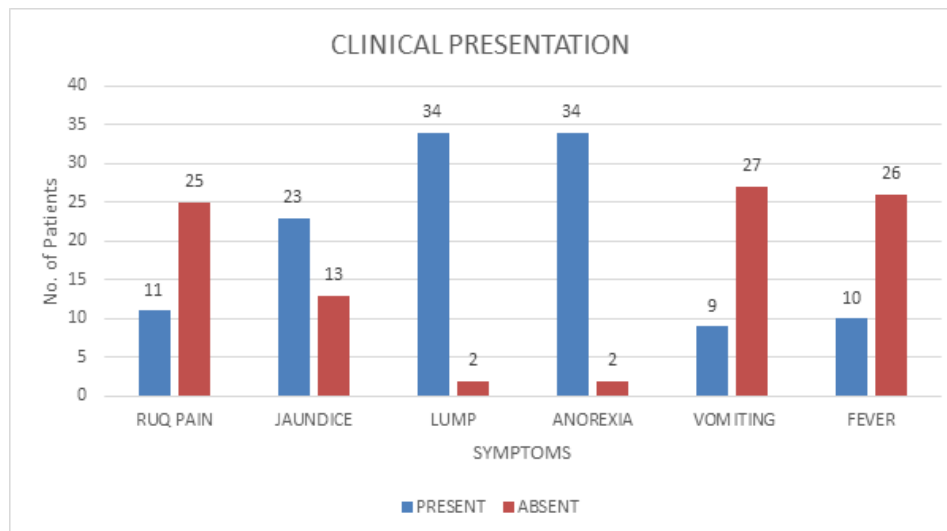


Chart 1: Graphical representation of distribution of study subjects according to symptoms

TABLE 2: Total number of salmonella positive subjects in study group in %

Salmonella	No.	%
Positive	4	11.11
Negative	32	88.89
Total	36	100.0

TABLE 2 shows salmonella infection detected by significant widal titres (the agglutinin titre greater than 1:80 for anti “O” antibodies and titre 1:160 for anti “H” antibody) which was positive in only 4(11%) patients

out of the total 36 patients of carcinoma gall bladder.

TABLE 3: Association of chronic salmonella infection with carcinoma gall bladder

Observed Proportion	11.11%
Point prevalence of Salmonella in Dehradun district	1.78%
Z statistic	4.23
95 % CI	3.11% - 26.06%
p Value	0.0001*

TABLE 3 It shows association using Z score of salmonella infection with carcinoma gall bladder based on point prevalence in Dehradun district i.e 1.78% which was derived from data given by a survey report “Burden of diseases on hospitals in selected districts of Uttarakhand” by Directorate of Economics and

Statistics Uttarakhand for CENTRE FOR RESEARCH, PLANNING AND ACTION, NEW DELHI 110001 in May – 2017. According to 95% CI (confidence interval) the association of chronic salmonella infection was found to be highly significant with p value <0.05(p value of 0.0001*)

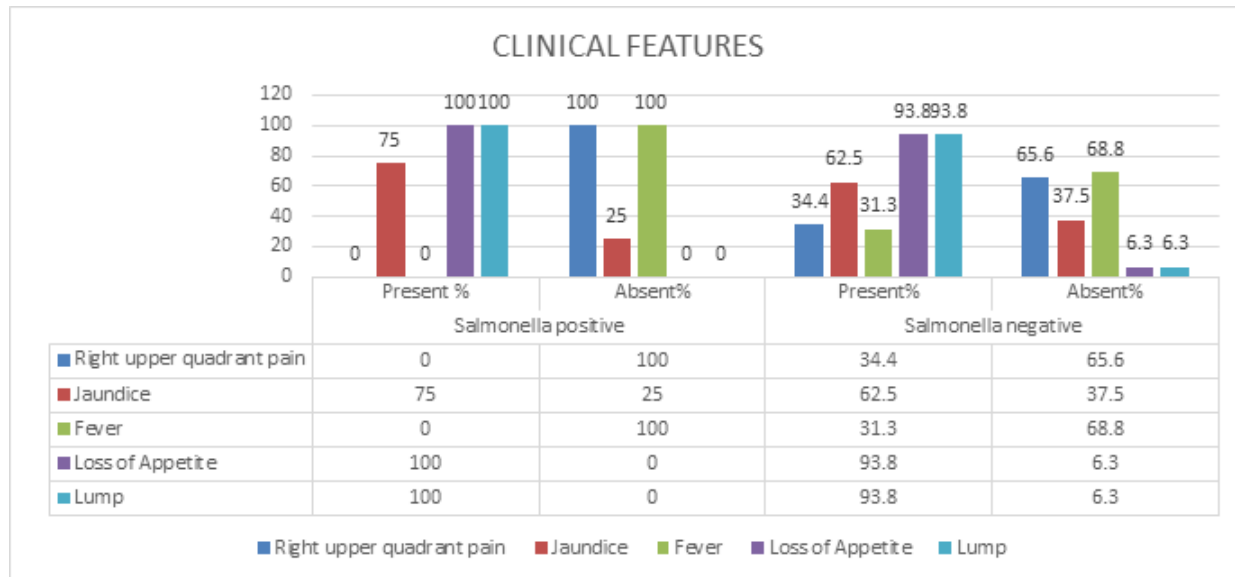


CHART 2: Compares clinical features among salmonella positive and negative cases

TABLE 4: Correlation of Liver Function Tests with salmonella positive and negative cases of carcinoma gall bladder

Variable	Salmonella				p Value
	Positive		Negative		
	Mean	SD	Mean	SD	
Total bilirubin	13.70	9.92	6.87	6.33	0.06
Conjugated bilirubin	10.30	8.71	4.63	4.47	0.04*
unconjugated bilirubin	2.00	1.44	1.26	0.96	0.18
SGOT	164.5	131.0	78.0	58.98	0.02*
SGPT	179.0	157.65	72.98	71.28	0.02*
ALP	592.75	516.63	288.50	319.67	0.10
Serum Total Protein	6.47	0.54	6.56	1.51	0.90
Serum Albumin	3.27	0.26	3.44	0.96	0.72
Serum Globulin	3.27	0.65	3.08	0.66	0.59

SGOT-serum glutamic oxaloacetic transaminase, SGPT- serum glutamic pyruvate transaminase, ALP- alkaline phosphate

TABLE 4 shows correlation of liver function tests among salmonella positive and salmonella negative cases among the study group. Independent sample t test was applied to calculate the p value . Conjugated bilirubin, SGOT & SGPT had p values <0.05 which were

(0.04,0.02 & 0.02 respectively) statistically significant .

Discussion

In a period of two years, a total of 36 cases of confirmed CAGB were studied ,out of which 72.22%

were females and 27.78% were males. . There were 6 patients below the age of 40 years which presented with aggressive disease, and 5 cases were above the age of 70years while the peak incidence of GBC in the present study was observed in the age group of 41-50 years (27.8%). Similar results were seen in other studies from India (Shukla et al., [12]; Pandey et al., [13]; Kapoor et al., [14]; Nissar Hussain et al., [15]; Imran et al., [16]). In stark contrast, studies from west reported the mean age of 67 years (Beltz et al., [17]) and the peak age of incidence in the seventh decade of life (Perpetuo et al., [3]). In our study, the female to male ratio was 2.6, with the mean age for females (mean 55.36 years) being higher than in males(mean 53.63636 years) . Females usually present at a younger age at diagnosis compared to their male counterparts. The above findings were in contrast with that of other studies (Beltz et al., [17]; Shukla et al., [12]; Pandey et al., [13]) where the female to male ratio was reported to be 3, 3 and 2.5 respectively. Based on the review of literature of the worldwide incidence of GBC, the average female to male ratio was reported between 2 and 3 [18] while it was more decisively skewed toward the female sex in our study. This pattern of distribution of GBC in females is more strikingly observed in countries and regions with the highest incidence rates of GBC, such as northern India [19]. This marked gender bias for GBC—which to some extent reflects a gender bias for cholelithiasis and the distinct geographic and genetic factors involved in pathogenesis—warrants the need for a more detailed evaluation of the role of hormonal (estrogen/progesterone) receptors in the pathogenesis of GBC.

Clinical predilection

Pain is a presenting feature in nearly all the cases (97 %) followed by weight loss (77 %), hepatomegaly (65 %) and nausea and vomiting (64 %) [20]. Shukla reviewed 315 patients and reported pain to be the commonest symptom (85 %) followed by icterus (60.3 %), lump(40 %) and loss of appetite(40 %) [12]. They noted hepatomegaly in 85.7 % and a palpable gall bladder in 47 %. Al-Hadeedi reported Pain abdomen, anorexia, jaundice, weight loss, right upper quadrant mass in 47.3 %, 39.4 %, 36.4 %, 39.4 % and 34.2 % respectively out of 38 patients of gall bladder carcinoma from Queen Mary Hospital, Hong Kong [21]. In our study, lump and anorexia were the commonest complaints (94.44 %), followed by jaundice, right upper quadrant

pain, fever and nausea & vomiting in 63.88 %, 30.55 %, 27.77%, 25 % patients, respectively.

Laboratory Findings

The baseline liver parameters of the study group were as follows. Total bilirubin 7.62±6.98 mg/dl with conjugated bilirubin and unconjugated 5.26±5.24 mg/dl and 1.34±1.02 mg/dl respectively. Transaminases levels in the study ,SGOT and SGPT were found to be 87.61±72.89U/L and 84.76±88.16 U/L respectively. Serum alkaline phosphatase level were 322.3±350.42 U/L. Total serum protein were 6.55±1.43 gm/dl of which serum albumin and serum globulin were 3.42±0.91 gm/dl and 3.10±0.66 gm/dl respectively .Independent sample t test was applied to calculate the p value . Conjugated bilirubin, SGOT & SGPT had p values < 0.05 which were (0.04,0.02 & 0.02 respectively) statistically significant .

Baseline renal function test among the study group showed that serum urea was 38.59±36.76mg/dl , serum creatinine 1.03±1.18mg/dl, serum sodium 134.64±4.36 mmol/L , serum potassium 3.96±0.72mmol/L and serum calcium was 8.48±0.84mg/dl.

Salmonella typhi has been frequently associated with gall bladder carcinoma. The relationship of typhoid carrier state and gall bladder carcinoma was first reported by Axelord in 1978 [22]. It was also reported by Mellemggaard that a six times higher risk for hepatobiliary cancer exists among typhoid carriers [23]. In our study, WIDAL test was performed to assess the carrier status of *Salmonella typhi* using ‘Stained Salmonella’ Antigen set for Widal Test by ARKRAY Healthcare Pvt. Ltd which was positive in 4 patients out of the 36 patients of gall bladder carcinoma(11.11%) ,in accordance to the findings of the study carried out by Nath et.al. at Banaras Hindu University,Varanasi [24]

Of the 4 patients positive for *Salmonella*, 75% were females and 25% male.(a difference in male to female ratio among salmonella positive and salmonella negative patient being 1:3 & 1:2.2 respectively)Thus showing a greater percentage of female preponderance among salmonella positive patients of carcinoma gall bladder. Right upper quadrant pain was a presenting feature of all salmonella negative patients whereas all 4 salmonella positive patients of carcinoma gallbladder were inconsistent with pain as a symptom. While jaundice was present in 75% of salmonella positive patients compared

to 62.5% patients in salmonella negative group. Fever was absent in all of salmonella positive patients whereas 10 patients presented with fever of salmonella negative group. Among all patients of the study group, loss of appetite was a consistent clinical feature with no significant difference in either of the two groups. Lump was also a consistent finding among both the groups, with all four salmonella positive patient presenting with abdominal lump. Vomiting was not a consistent clinical feature among both the groups, only 28.1% patients presented with vomiting, all of which belonged to the salmonella negative group

Conclusion

Our study draws a strong association between chronic salmonella infection and carcinoma gall bladder, thus favoring a strategy of advocacy of prophylactic cholecystectomy for all individuals with silent gall stones in this geographical area. This is because Salmonella is an endemic infection, and itself represents a significant risk factor for gall bladder cancer, besides the additional risk from gall stones.

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