



## SALMONELLA SEPSIS IN CANCER PATIENTS

## Microbiology

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## ABSTRACT

**Background And Objective:** Bloodstream infections are a major hazard in cancer patients. Salmonella infections pose a big threat to the patients undergoing chemotherapy. The objectives of this study are to determine the prevalence of salmonella sepsis in cancer patients in a tertiary care hospital and to determine the susceptibility pattern of salmonella isolates from blood samples. **Methods:** A retrospective study was conducted spanning 3 years duration from January 2021 to December 2023. Blood samples were collected aseptically for culture. **Results:** During the three-year period the laboratory received 2,413 blood cultures that were positive for various organisms of which 58 salmonella species were isolated. The age group ranged from 1 year to 72 years with the mean age being 28 years  $\pm$  23.63 years. The prevalence of salmonella species was 2.4% (58/2413). *S. typhi* was the most commonly isolated species which accounted for 63.79% of the total number of cases followed by *S. paratyphi B* (32.8%) and *S. paratyphi A* (3.4%). These isolates were tested for antimicrobial susceptibility testing which included ciprofloxacin, ampicillin, chloramphenicol, ceftriaxone, cefotaxime, pefloxacin and cotrimoxazole. Ciprofloxacin showed a lower susceptibility pattern as compared to other drugs. **Interpretation And Conclusions:** The study showed that the initiation of chemotherapy is the most likely cause of salmonella sepsis amongst the cancer patients. The ever-increasing irrational use of antimicrobials has led to decreased susceptibility of the isolates to ciprofloxacin. More studies need to be undertaken as limited data is available about typhoid infections in cancer patients.

## KEYWORDS

*Salmonella typhi, Salmonella paratyphi A, Salmonella paratyphi B, susceptibility, ciprofloxacin, sepsis, resistance*

## INTRODUCTION

Bloodstream infection (BSI) remains the major cause of morbidity and mortality in patients undergoing treatment for cancer. Patients on chemotherapy in particular are at higher risk of developing bacterial and fungal infections.<sup>1</sup> A variety of factors such as neutropenia, altered gut flora, emerging advanced life-support facilities, damage of epithelial surfaces and disruption of skin increase their susceptibility to develop notorious infections.<sup>2</sup> The presence of bacterial BSIs and antimicrobial resistance many times result in failure of failure and prolonged infections in cancer patients.<sup>1</sup>

Salmonella is a gram-negative, rod-shaped, facultatively anaerobic bacterium, belonging to the Enterobacteriaceae family. It primarily lives in the digestive tracts of animals and humans.<sup>3</sup> Salmonella infection occurs globally and has diverse presentations including enteric fever, gastroenteritis, localized infection, chronic enteric or urinary carrier state and bacteraemias.<sup>4</sup> We had restricted our study to the salmonella species isolated from blood culture.

The aim of our study was to determine the prevalence and susceptibility pattern of salmonella species isolated in cancer patients and susceptibility pattern. Limited studies have been conducted determining susceptibility patterns of salmonella isolates in cancer patients. This study is one of its kind in which the susceptibility patterns of salmonella species has been studied.

## MATERIAL AND METHODS

## Study Design and period

This retrospective observational study was conducted in the Microbiology Department of Tata Memorial Hospital, Mumbai, India, a specialized hospital for cancer patients. The study spanned from January 2021 to December 2023

## Inclusion Criteria

Patients diagnosed with salmonella sepsis irrespective of age and gender were included in the study.

## Exclusion Criteria

All the blood cultures which were positive for organisms other than salmonella species.

## Microbiological Methods

Blood samples (upto 10 mL for adults, upto 4 mL for children) were collected aseptically and transferred into Bactec blood culture bottles.<sup>5</sup>

The samples were processed aerobically using the VIRTUO system for five days. The blood samples which flashed positive were processed using the standard techniques. For identification the VITEK system was used while antimicrobial susceptibility testing was performed using Kirby-Bauer's disc diffusion method. The antibiotics tested included ceftriaxone, ciprofloxacin, cotrimoxazole, ampicillin, pefloxacin, chloramphenicol, and cefotaxime. Serotyping was used to identify specific strains using BD diagnostics kit for speciation. Electronic medical records were utilized to extract demographic information, including age, sex, type of cancer, and clinical outcomes.

## RESULTS

In the study population, age group ranged from 1 year to 72 years with the mean age being 28 years  $\pm$  23.63 years. Adult population above the age of 14 years accounted for 56.9% (33/58) (Figure 1) while the paediatric population contributed to 43.1% (25/58) of the total number of cases. It showed a male predilection (Table 1) accounting to 74.1% (43/58) while 25.9% (15/58) were female patients. Furthermore, when a detailed analysis (Table 1) of the age, gender and salmonella species distribution was done it was observed that *S. typhi* was identified in almost 21 paediatric patients out of 25 (84%) followed by *S. paratyphi B* and *S. paratyphi A*. Demographic distribution of the study population showed that most of them were natives of Maharashtra 27.6% (16/58), followed by West Bengal 25.86% (15/58), Bihar 6.8% (4/58), Uttar Pradesh 5.1% (3/58).

## DISTRIBUTION AMONGST TARGET POPULATION

■ Adult ■ Paediatric

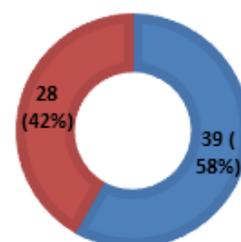


Figure 1: Distribution Of Patients Among Paediatric And Adults

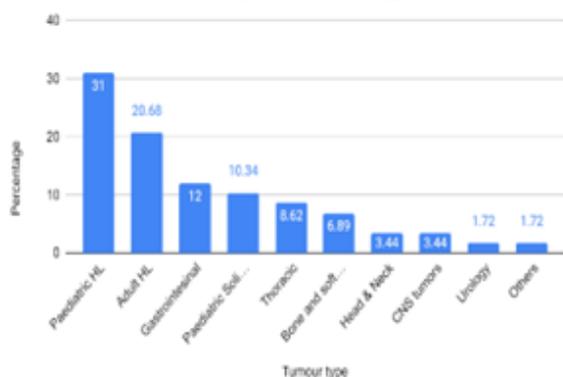
**Table 1: Age Wise Distribution Of Patients Enrolled In The Study Along With Salmonella Species Identified**

Age (yrs)	No. of patients	Male	Females	S. typhi	S. paratyphi A	S. paratyphi B
1- 14	25	18	7	21	1	3
15-30	8	7	1	5	1	1
31-45	8	5	3	6	0	5
46-60	10	7	3	3	0	5
> 60	7	6	1	2	0	5
Total	58	43 (74.13%)	15 (25.86%)	37 (63.8%)	2 (3.44%)	19 (32.8%)

Out of 2413 isolates from blood culture during the three-year period, 58 salmonella species were identified. Thus, the prevalence of salmonella species was 2.4% (58/2413). The salmonella isolates were categorized into *S. typhi*, *S. paratyphi B* and *S. paratyphi A* on the basis of serotyping (Table 1). *S. typhi* constituted 63.8% (37/58) amongst the strains which were studied. *S. paratyphi B* contributed to 32.8% (19/58) of the isolates while only two strains of *S. paratyphi A* were identified.

Majority of patients diagnosed with salmonella infections were known cases of hematolymphoid malignancies followed by gastrointestinal malignancies (Figure 2).

**Percentage vs. Tumour type**



Paediatric HL: Paediatric Hematolymphoid (HL) malignancies, Adult HL: Adult Hematolymphoid (HL) malignancies

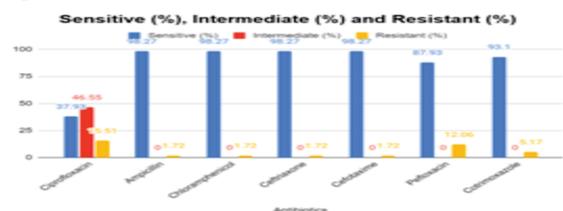
**Figure 2: Percentage Wise Distribution Of Malignancies In Salmonella Infected Patients**

Acute lymphoid leukemia (ALL) was the most common i.e. 66.6% (20/30) malignancy amongst these patients. A Chi-Squared test (Table 2) was performed to test the association between type of cancer and salmonella species. The test result was significant with a p value of 0.004. A statistically higher proportion of patients with blood cancer had *S. typhi* as compared to solid organ cancer who had a higher proportion of other species.

**Table 2: Contingency Table**

Chi-Squared Tests	Value	Df	p
X <sup>2</sup> continuity correction	8.108	1	0.004
N	57		

The antimicrobial susceptibility patterns of the salmonella isolates studies showed resistance to ciprofloxacin in 15.5% (9/58) of the strains. Pefloxacin showed resistance in 12% (7/58) of the total number of species.



**Figure 3: Susceptibility patterns of the antibiotics tested**

(Figure 3) Cotrimoxazole showed 5% (3/58) resistance while ampicillin, chloramphenicol, ceftriaxone and cefotaxime showed 1.72% (1/58) resistance each. Maximum resistance to ciprofloxacin was noted in *S. typhi* (8.62%) followed by *S. paratyphi B* (5.17%) and *S. paratyphi A* (1.72%).

Organism			
Type of cancer	Other salmonella species	S. typhi	Total
Blood	Count	5	24
	% within row	17.24%	82.76%
	% within column	23.81%	66.67%
Solid organ	Count	16	19
	% within row	57.14%	42.86%
	% within column	76.19%	33.33%
Total	Count	21	36
	% within row	36.84%	63.16%
	% within column	100%	100%

**DISCUSSION**

Cancer can affect any body part and is a disabling, challenging, and frightening disease.<sup>6</sup> Typhoid fever is an infectious disease which is widely spread and tends to affect millions all over world.<sup>7</sup> Every year an estimated 11–21 million cases of enteric fever and 5 million cases of paratyphoid fever occur globally, causing approximately 135,000–230,000 deaths.<sup>13</sup> Non-typhoidal salmonellae are known to cause severe infections in immunocompromised individuals.<sup>14</sup> There are limited studies with regards to typhoidal infections in cancer patients.<sup>7</sup> Thus, we evaluated retrospectively the trends of salmonella infection in cancer patients along with the susceptibility patterns of salmonella isolates.

The study showed male predominance, with the male: female ratio of 2.8:1. However, in a study conducted by Aslam et al<sup>7</sup>, female preponderance was observed. It was seen that adult age groups were more affected than the paediatric population in solid organ tumors. Vice versa trend was seen in case of hematological malignancies. This finding was consistent with the study conducted by Sinkovics et al<sup>8</sup>. In another study by Noriega et al<sup>16</sup>, similar findings were reported. Salmonella infections are many times associated with lower socioeconomic status.<sup>18</sup> Poor hand hygiene and improper food handling are major risk factors in the spread of typhoid infections.<sup>18</sup> As the patients visiting Tata Memorial Hospital belong to lower socioeconomic class and tend to eat street food with lack of hygiene are at greater risk of catching the infection. Immunity is suppressed due to the chemotherapy and thus becomes a predisposing factor.

The most commonly isolated species in the present study was *S. typhi* (63.8%). This finding was found to be in concordance with the study conducted Aslam et al,<sup>7</sup> in cancer patients. However, the work of Mori et al.<sup>9</sup> Chia-Wen Li et al<sup>10</sup> identified non-typhoidal salmonellae in cancer patients. *S. typhimurium* was most commonly identified amongst them. Few other studies led by Wolfe et al,<sup>15</sup> Noriega et al<sup>16</sup> also documented infection caused by non-typhoidal salmonellae.

In this study (figure 3), the susceptibility patterns of salmonella species were analyzed. Resistance was mainly noted against ciprofloxacin followed by pefloxacin. All of the patients survived after appropriate treatment. Although nine deaths were noted, they were unrelated to the infection caused by salmonella species. The patients died much later after getting recovered. The data for salmonella infections caused by typhoidal salmonellae in cancer patients is limited. Thus, the sensitivity patterns of the typhoidal and paratyphoidal isolates were compared to the typhoidal salmonellae recovered from blood samples of non-cancer patients. A study by Islam et al,<sup>11</sup> showed findings similar to our study wherein decreased susceptibility to ciprofloxacin in *S. typhi* isolates was reported in non-cancer patients.

Study headed by Zehra et al<sup>12</sup> documented similar findings. Madhulika et al<sup>17</sup> also reported increased resistance to ciprofloxacin amongst the *S. typhi* and *S. paratyphi A* strains. In North India, in a study led by Behl et al<sup>18</sup> similar findings were seen. Gaind et al<sup>19</sup> also reported resistance to ciprofloxacin in *S. typhi* and *S. paratyphi A*.

**CONCLUSION**

The patients with cancer should be careful while having food. As patients are immunosuppressed, they are at a higher risk of catching salmonella infections due to improper food handling. More studies are needed to assess the susceptibility pattern of salmonella isolates from cancer patients.

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