

Antibiotic Susceptibility Pattern and Its Potential Correlates among Admitted Typhoid Patients in a Tertiary Care Hospital of Kolkata, India: A One Year Retrospective Evaluation

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Abstract

Introduction: Typhoid fever is a very common disease of the developing world, being a major public health concern in countries like India. The antibiotic susceptibility scenario varies significantly across regions. In India the pictures are conflicting. *Objective:* The objective of the study was to identify the antibiotic susceptibility pattern of *S. typhi* among registered patients in a tertiary care hospital in India. *Materials and Methods:* The study was done at Peerless Hospital and B. K. Roy Research Center which is a tertiary care Hospital in Kolkata. This was a record-based retrospective cross-sectional and descriptive analysis using SAS software version 9.3.2 during 2012 to 2013. The patients included in the study were admitted in the hospital with accessible medical records. *Results:* Among 86 recruited patients, the average age was 43.14 years and 59.30%, subjects were male. Overall, fever (91.86%) was the most common symptom followed by nausea (84.88%), diarrhea (83.72%), vomiting (63.95%) and body ache (51.16%). Of total 86 blood samples, 23 (26.74%) samples were blood culture positive. Of these 23 blood culture positive samples, 20 (23.26%) samples were positive for *Salmonella Ser.typhi* and 3 (3.49%) samples were positive for *Salmonella Ser. paratyphi*. Overall, among the 23 blood culture positive subjects, isolated bacterial strains were 100% sensitive to ampicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefoperazone/sulbactam, ceftriaxone, cefepime, ertapenem, imipenem, meropenem, tigecycline and colistin and 100% resistant to cefuroxime axetil, cefuroxime, amikacin and gentamycin. *Conclusion:* blood culture positivity and resistant pattern to commonly used antibiotics for *S. typhi* was substantially high among the patients admitted in a tertiary care hospital in eastern part of India and a standardized protocol for proper antibiotic treatment and management of the patients infected with *S. typhi* is warranted.

Keywords: Typhoid; Antibiotic; *Salmonella Ser. typhi*.

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Introduction

Typhoid fever is an infectious disease caused by the bacteria *Salmonella typhi*. The spread of the disease occurs mainly via faecal-oral route, through contaminated food and water supplies and also via direct spread from infected patients. Typhoid fever is a common disease & major public health concern in countries like India [1]. The etiologic agent of typhoid fever (*S.typhi*) is a gram negative, non-sporing facultative anaerobic bacilli that measure 2-3 by 0.4 to 0.6 μm . Humans are the only known hosts [1].

Antibiotic use is the mainstay of treatment and the success depends on the susceptibility pattern. The antibiotic susceptibility scenario varies significantly across regions. Antibiotic susceptibility pattern of any bacteria depends heavily on the local antibiotic use practice of the physicians and their rationality, socio-demographic and behavioral factors of the patients. The dearth of information and existing conflicting evidences regarding these factors in India and more so in eastern part of the country called for a detailed evaluation of these factors in relation to the susceptibility of *S. typhi* to regular antibiotics [1,2,3].

Objective

The objective of the study was to identify the antibiotic susceptibility pattern of *S. typhi* among registered patients in a tertiary care hospital in India

Materials and Methods

The study was done at Peerless Hospital and B. K. Roy Research Center which is a tertiary care Hospital in Kolkata. This was a record-based retrospective cross-sectional analysis in a tertiary care hospital in Kolkata, India during 2012 to 2013. Expected benefit of the study was that, the identified antibiotic susceptibility patterns and their correlates would help to identify and strategize policies to bridge gaps in the antibiotic management protocols in typhoid cases. The research proposal was conducted only after submission of the same to the ethical committee and subsequent approval of the same by the before said committee.

The patients who were included in the study were those whose who were only admitted in the hospital and medical records were accessible having complete records on demographic factors, presenting symptoms at the time of admission and had blood culture and antibiotic susceptibility pattern results. The patients who were not admitted were excluded from the study. Patients whose complete medical records were not accessible were also excluded. The patients' records of this hospital were used anonymously for the purpose of this study without mentioning any personal identifiers so that the data could not be linked with the participants. Information was collected on

socio-demographic characteristics, symptoms presented at the time of admission and blood culture reports for *S. typhi* and *S. paratyphi A* as well as antibiotic susceptibility pattern of the participating patients. Total 86 patients met the inclusion criteria.

Data were analyzed using SAS software version 9.3.2 and descriptive analysis were performed to understand the distribution of demographic factors, symptoms presented at the time of admission and to estimate the percentage of blood culture results for *S. typhi* and *S. paratyphi A* as well as antibiotic susceptibility patterns among the participating patients. Analysis was also done to compare the distribution of these demographic factors, blood culture positivity and antibiotic susceptibility pattern across gender. Based on the number of symptoms present at the time admission, patients were categorized into three categories:

1. Less severe disease(symptoms ≤ 3)
2. Severe disease (symptoms ≤ 4)
3. Very severe disease(symptoms ≤ 5).

Overall antibiotic susceptibility was also additionally categorized into subjects infected by bacterial strain sensitive to less no. of antibiotics (if sensitive to <7 antibiotics) and those infected by bacterial strain sensitive to more no. of antibiotics (if sensitive to ≥ 7 antibiotics). Bi-variate logistic regression analyses were conducted to measure the associations of demographic factors, symptoms presented at the time of admission with blood culture positivity, overall severity of the disease, bacterial strains identified and lastly to determine the relationships between demographics, overall severity of the disease and higher antibiotic sensitivity pattern.

Results

Table 1: Age and gender distribution of the recruited patients

(N=86)

Continuous Variable		N	Mean	SE of the mean	95% Confidence Limits	
					Lower	Upper
Age		86	43.14	1.89	39.37	46.91
Categorical Variable	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits	
					Lower	Upper
Gender	Male	51	59.30	5.33	48.71	69.90
	Female	35	40.70	5.33	30.10	51.29

Table 2: Distribution of the symptoms among the participating patients

(N=86)

Symptoms	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits	
					Lower	Upper
Body Ache	Absent	42	48.84	5.42	38.06	59.62
	Present	44	51.16	5.42	40.38	61.94
Fever	Absent	7	8.14	2.97	2.24	14.04
	Present	79	91.86	2.97	85.96	97.76
Vomiting	Absent	31	36.05	5.21	25.69	46.40
	Present	55	63.95	5.21	53.60	74.31

Nausea	Absent	13	15.12	3.89	7.39	22.84
	Present	73	84.88	3.89	77.16	92.61
Diarrhea	Absent	14	16.28	4.00	8.32	24.24
	Present	72	83.72	4.00	75.76	91.68
Overall severity of the disease	Less severe disease (≤ 3 symptoms)	33	38.37	5.27	27.88	48.86
	Severe disease (4 symptoms)	37	43.02	5.37	32.35	53.70
	Very severe disease (All 5 symptoms)	16	18.60	4.22	10.21	27.00

Table 3: Distribution of the symptoms among the participating male patients (N=51)

Symptoms	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits Lower	Upper
Body Ache	Present	23	45.10	7.04	30.96	59.23
	Absent	28	54.90	7.04	40.77	69.04
Fever	Present	47	92.16	3.80	84.52	99.79
	Absent	4	7.84	3.80	0.21	15.48
Vomiting	Present	35	68.63	6.56	55.45	81.81
	Absent	16	31.37	6.56	18.19	44.55
Nausea	Present	47	92.16	3.80	84.52	99.79
	Absent	4	7.84	3.80	0.21	15.48
Diarrhea	Present	42	82.35	5.39	71.52	93.18
	Absent	9	17.65	5.39	6.82	28.48
Overall severity of the disease	Less severe disease (≤ 3 symptoms)	20	39.22	6.90	25.35	53.08
	Severe disease (4 symptoms)	19	37.25	6.84	23.52	50.99
	Very Severe disease (All 5 symptoms)	12	23.53	6.00	11.48	35.58

Table 4: Distribution of the symptoms among the participating female patients (N=35)

Symptoms	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits Lower	Upper
Body Ache	Present	21	60.00	8.40	42.93	77.07
	Absent	14	40.00	8.40	22.93	57.07
Fever	Present	32	91.43	4.80	81.67	100.00
	Absent	3	8.57	4.80	0.00	18.33
Vomiting	Present	20	57.14	8.49	39.90	74.39
	Absent	15	42.86	8.49	25.61	60.10
Nausea	Present	26	74.29	7.50	59.05	89.52
	Absent	9	25.71	7.50	10.48	40.95
Diarrhea	Present	30	85.71	6.00	73.52	97.91
	Absent	5	14.29	6.00	2.09	26.48
Overall severity of the disease	Less severe disease (≤ 3 symptoms)	13	37.14	8.29	20.30	53.98
	Severe disease (4 symptoms)	18	51.43	8.57	34.01	68.85
	Very severe disease (All 5 symptoms)	4	11.43	5.46	0.34	22.52

Table 5: Distribution of the laboratory results among the participating patients (N=86)

Laboratory results	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits Lower	Upper
Blood culture results	Negative	63	73.26	4.80	63.71	82.80
	Positive	23	26.74	4.80	17.20	36.29
Bacterial strain identified	None	63	73.26	4.80	63.71	82.80
	<i>Salmonella Ser. typhi</i>	20	23.26	4.58	14.15	32.37
	<i>Salmonella Ser. paratyphi A</i>	3	3.49	1.99	0.00	7.45

Table 6: Distribution of the laboratory results among the participating male patients (N=51)

Laboratory results	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits Lower	Upper
Blood culture results	Positive	14	27.45	6.31	14.77	40.13
	Negative	37	72.55	6.31	59.87	85.23
Bacterial strain identified	None	37	72.55	6.31	59.87	85.23
	<i>Salmonella Ser. typhi</i>	13	25.49	6.16	13.11	37.87
	<i>Salmonella Ser. paratyphi A</i>	1	1.96	1.96	0.00	5.90

Table 7: Distribution of the laboratory results among the participating female patients

(N=35)

Laboratory results	Categories	N	Proportion (%)	SE of the Proportion	95% Confidence Limits Lower	Upper
Blood culture results	Positive	9	25.71	7.50	10.48	40.95
	Negative	26	74.29	7.50	59.05	89.52
Bacterial strain identified	None	26	74.29	7.50	59.05	89.52
	<i>Salmonella Ser. typhi</i>	7	20.00	6.86	6.06	33.94
	<i>Salmonella Ser. paratyphi A</i>	2	5.71	3.98	0.00	13.80

Table 8: Antibiotic susceptibility pattern among the participating patients

(N=86)

Antibiotic	Categories	N	Proportion (%)	Male (N=51)		Female(N=35)	
				N	Proportion (%)	N	Proportion (%)
Ampicillin	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Amoxicillin/Clavulanic acid	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Piperacillin/Tazobactam	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Cefoperazone/Sulbactam	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Cefuroxime Axetil	Sensitive	0	0.00	0	0.00	0	0.00
	Resistant	23	100.00	14	100.00	9	100.00
Cefuroxime	Sensitive	0	0.00	0	0.00	0	0.00
	Resistant	23	100.00	14	100.00	9	100.00
Ceftriaxone	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Cefepime	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Ertapenem	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Imipenem	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Meropenem	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Amikacin	Sensitive	0	0.00	0	0.00	0	0.00
	Resistant	23	100.00	14	100.00	9	100.00
Gentamicin	Sensitive	0	0.00	0	0.00	0	0.00
	Resistant	23	100.00	14	100.00	9	100.00
Nalidixic Acid	Sensitive	3	13.04	2	14.29	1	11.11
	Resistant	20	86.96	12	85.71	8	88.89
Ciprofloxacin	Sensitive	3	13.04	2	14.29	1	11.11
	Resistant	20	86.96	12	85.71	8	88.89
Nitrofurantoin	Sensitive	2	8.70	1	7.14	1	11.11
	Resistant	21	91.30	13	92.86	8	88.89
Trimethoprim/Sulfamethoxazole	Sensitive	20	86.96	12	85.71	8	88.89
	Resistant	3	13.04	2	14.29	1	11.11
Tigecycline	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Colistin	Sensitive	23	100.00	14	100.00	9	100.00
	Resistant	0	0.00	0	0.00	0	0.00
Overall antibiotic susceptibility pattern	Sensitive to less no. of antibiotics (<7)	5	21.74	3	21.43	2	22.22
	Sensitive to more no. of antibiotics (≥7)	18	78.26	11	78.57	7	77.78

Table 9: Association of age, gender and symptoms with blood culture positivity (N=86)

Variables	Categories	OR	95%Confidence limits		p value
			Lower	Upper	
Age		0.99	0.96	1.02	0.3800
Gender	Male	1.09	0.41	2.90	0.8582
	Female			Reference	
Body ache	Yes	1.34	0.51	3.51	0.5486
	No			Reference	
Fever	Yes	0.91	0.16	5.03	0.9093
	No			Reference	
Vomiting	Yes	3.56	1.09	11.69	0.0361
	No			Reference	
Nausea	Yes	5.18	0.63	42.29	0.1250
	No			Reference	
Diarrhea	Yes	1.41	0.36	5.59	0.6247
	No			Reference	
Overall severity of the disease	Less severe disease (≤ 3 symptoms)			Reference	
	Severe disease (4 symptoms)	2.07	0.63	6.86	0.2321
	Very severe disease (All 5 symptoms)	5.60	1.43	21.95	0.0134

Table 10: Association of age and gender with overall severity of the disease (N=86)

Over all severity of the disease (reference= Less Severe (≤ 3 symptoms))	Age and gender	Categories	OR	95%Confidence limits		p value
				Lower	Upper	
Severe disease (4 symptoms)	Age		1.01	0.98	1.04	0.4184
	Gender	Male	0.69	0.27	1.78	0.4372
		Female			Reference	
Very severe disease (All 5 symptoms)	Age		0.99	0.96	1.03	0.5969
	Gender	Male	1.95	0.52	7.37	0.3249
		Female			Reference	

Table 11: Association of age, gender and overall severity of the disease with bacterial strain identified (N=86)

Bacterial strain identified [reference=none]	Age, gender, symptoms and severity	Categories	OR	95%Confidence limits		p value
				Lower	Upper	
<i>Salmonella Ser. Typhi</i>	Age		0.98	0.96	1.02	0.3078
	Gender	Male	1.31	0.46	3.72	0.2484
		Female			Reference	
	Body ache	Present	0.97	0.35	2.65	0.9507
		Absent			Reference	
	Fever	Present	1.29	0.23	7.22	0.7728
		Absent			Reference	
	Vomiting	Present	0.33	0.10	1.11	0.0737
		Absent			Reference	
	Nausea	Present	0.22	0.03	1.84	0.1636
		Absent			Reference	
	Diarrhea	Present	0.83	0.21	3.35	0.7981
		Absent			Reference	
	Overall severity of the disease	Less severe disease (≤ 3 symptoms)			Reference	
		Severe disease (4 symptoms)	2.07	0.63	6.86	0.2321
Very severe disease (All 5 symptoms)		3.50	0.81	15.19	0.0943	
<i>Salmonella Ser. Paratyphi A</i>	Age		1.01	0.94	1.07	0.8582
	Gender	Male	0.35	0.03	4.08	0.6989
		Female			Reference	

Table 12: Association of age, gender and overall severity of the disease with higher antibiotic sensitivity (N=23)

Age, gender and severity	Categories	OR	95% Confidence limits		p value
			Lower	Upper	
Gender	Age	1.03	0.96	1.11	0.3827
	Male	1.05	0.14	7.93	0.9640
Overall severity of the disease	Female			Reference	
	Less severe disease (≤3 symptoms)			Reference	
	Severe disease (4 symptoms)	1.56	0.17	14.65	0.6994

Among 86 recruited patients, the average age was 43.14 years and 59.30%, subjects were male. Overall, fever (91.86%) was the most common symptom followed by nausea (84.88%), diarrhea (83.72%), vomiting (63.95%) and body ache (51.16%). Among all the symptoms, fever (92.16%) and nausea (92.16%) were the most complains among male patients followed by diarrhea (82.35%), vomiting (68.63%) and body ache (45.10%). Alike male patients, fever (91.43%) was most frequent symptom among female patients followed by diarrhea (85.71%), nausea (74.29%), body ache (60%) and vomiting (57.14%). Of total 86 blood samples, 23 (26.74%) samples were blood culture positive. Of these 23 blood culture positive samples, 20 (23.26%) samples were positive for Salmonella Ser.typhi and 3 (3.49%) samples were positive for Salmonella Ser. paratyphi. Of total 51 blood samples among male subjects, 14 (27.45%) samples were blood culture positive. Of these 14 blood culture positive samples, 13 (25.49%) samples were positive for Salmonella Ser.typhi and 1 (1.96%) sample was positive for Salmonella Ser. paratyphi. Of total 35 blood samples among female patients, 9 (25.71%) samples were blood culture positive. Of these 9 blood culture positive samples, 7 (20%) samples were positive for Salmonella Ser.typhi and 2 (5.71%) samples were positive for Salmonella Ser. paratyphi.

Overall, among the 23 blood culture positive subjects, isolated bacterial strains were 100% sensitive to ampicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefoperazone/sulbactam, ceftriaxone, cefepime, ertapenem, imipenem, meropenem, tigecycline and colistin and 100% resistant to cefuroxime axetil, cefuroxime, amikacin and gentamycin.

Although in bi-variate regression analyses, there were some associations between socio-demographic factors, symptoms presented with at the time of admission with odds of having blood culture positivity and overall severity of disease as well as associations of age, gender and overall severity of the disease with bacterial strain identified and higher antibiotic sensitivity though the results were not

statistically significant except vomiting was positively associated with blood culture positivity (OR=3.56, 95% CI: 1.09, 11.69) and the result was statistically significant and compared to those having less severe disease, subjects suffering from very severe disease were more likely to have blood culture positivity (OR=5.60, 95% CI: 1.43, 21.95) and result was statistically significant.

Discussions

A hospital based cross-sectional analyses was conducted among 86 patients who were admitted in a tertiary care hospital in the past year (2012-2013) and were tested for S. typhi and S. paratyphi A as well as antibiotic susceptibility pattern. Overall, more than 90% participating patients had fever followed by nausea, diarrhea, vomiting and body ache. When we categorized patients based on the presenting symptoms at the time of hospital admission, it was observed that majority had four symptoms or had severe disease, slightly above one-third had three or less symptoms or less severe disease and less than one-fifth had all five symptoms or very severe disease. Thus, it seemed that patients who were admitted at this tertiary care hospital were more likely to be symptomatic.

Of total 86 blood samples, 23 (26.74%) samples were blood culture positive. Of these 23 blood culture positive samples, 20 (23.26%) samples were positive for Salmonella Ser. typhi and 3 (3.49%) samples were positive for Salmonella Ser. paratyphi. Thus, more Salmonella typhi cases were detected among participating patients during our study period.

Overall, among the 23 blood culture positive subjects, isolated bacterial strains were 100% sensitive to ampicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefoperazone/sulbactam, ceftriaxone, cefepime, ertapenem, imipenem, meropenem, tigecycline and colistin and 100% resistant to cefuroxime axetil, cefuroxime, amikacin and gentamycin. Among other drugs, isolated

bacterial strains were 13.04% susceptible to nalidixic acid, 13.04% susceptible to ciprofloxacin, 8.70% susceptible to nitrofurantoin, and 86.96% susceptible to trimethoprim/sulfamethoxazole. Overall, 21.74% isolated bacterial strains were susceptible to less than seven antibiotics and 78.26% were susceptible to seven or more antibiotics. These findings were consistent with previous studies like in Kathmandu, Medical College, Nepal, during 2010-11[6], In the Buea health district, Cameroon, researchers isolated 21 (21%) culture positive Salmonella species out of 100 cases. 12 (57.1%) were S paratyphi A, 8 (38.1%) were S typhi and 1 (4.8%) was S paratyphi C among these samples.

Conclusion

Thus, findings from the current study revealed that the blood culture positivity and resistant pattern to commonly used antibiotics for S. typhi was substantially high among the patients admitted in a tertiary care hospital in eastern part of India and thus it seemed a standardized protocol for proper antibiotic treatment and management of the patients infected with S. typhi is a critical public health issue in endemic areas like India.

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