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Research Article

Study of multi drug resistant S.typhi and MIC in Ausa and Latur region in Maharashtra state of India

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ABSTRACT:

Enteric (typhoid) fever is a systemic disease characterized by fever and abdominal pain caused by dissemination of Salmonella Typhi or Salmonella Paratyphi type A, B, or C. Fever (38.8-40.5°C; 101.8-104.9°F) is documented at presentation in more than 75% of cases and is typically prolonged, continuing up to 4 weeks if untreated. Symptoms reported on initial medical evaluation include headache (80%), chills (35-45%), cough (30%), sweating (20-25%), myalgias (20%), malaise (10%), and arthralgia (2-4%). Gastrointestinal (GI) symptoms include anorexia (55%), abdominal pain (30-40%), nausea (18-24%), vomiting (18%), and diarrhea (22-28%) more commonly than constipation (13-16%). In a series in Delhi, India, only 527 isolates were obtained from 5,735 suspected cases (9.2%)(5).

This compares with 175 isolates in 243 cases (72%) in Rodesia(8) and 219 isolates from 298 clinical cases in a pediatric group in Natal(73%)(4).after removal of the serum and dissolution of the clot with streptokinase(6). Bile broth and Streptokinase broth were used. In the isolation both bill salt broth (broth culture) and streptokinase broth (clot culture) where used for the enrichment of blood samples.

Keywords: Clot Culture, Streptokinase, Bile broth, Entric fever, *Salmonella typhi.*

INTRODUCTION:

Enteric (typhoid) fever is a systemic disease characterized by fever and abdominal pain caused by dissemination of Salmonella Typhi or Salmonella Paratyphi type A, B, or C. Fever (38.8-40.5°C; 101.8-104.9°F) is documented at presentation in more than 75% of cases and is typically prolonged, continuing up to 4 weeks if untreated. Symptoms reported on initial medical evaluation include headache (80%), chills (35-45%), cough (30%), sweating (20-25%), myalgias (20%), malaise (10%), and arthralgia (2-4%).

Gastrointestinal (GI) symptoms include anorexia (55%), abdominal pain (30-40%), nausea (18-24%), vomiting (18%), and diarrhea (22-28%) more commonly than constipation (13-16%).

Travelers to southern Asia are at highest risk for infections that are nalidixic acid-resistant or multidrug-resistant (resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole). Nalidixic acid (a non-fluorinatede quinolone antibiotic) susceptibility is used as a marker for fluoroquinolone susceptibility. [1]

Emergence of multidrug resistant strains (MDRST) poses a risk to public health. In India, antibiotic resistance among s.typhi has been reported since 1960s and first outbreak of multidrug resistant s.typhi was reported in Calicut. Multidrug resistant s.typhi has appeared throught the world, especially in South America, Africa and south Asia.

Children have a higher incidence of positive stool cultures compared with adults (60 vs 27%), and stool cultures may become positive during the third week of illness in untreated patients.

Thus, the optimal diagnostic approach in both children and adults is to culture blood, bone marrow, gastric or duodenal secretions, and stool. Using this approach, the diagnosis can be established in more than 90% of patients.[1]

We had done the research to observe the sensitivity pattern according to the different regions.

Year of study	Year of publication	Author & Reference	No. of isolates	Study Design	Risk of Bias	
					QUIPS	JBI
2012	2017	Harichandran & Dinesh[17]	79	Retrospective	Low	No
2016	2016	Sharvani *et al*[33]	167	Retrospective	Low	No
2013-2014	2015	Misra *et al*[26]	50	Retrospective	Low	No
2015	2015	Narain & Gupta[29]	220	Prospective	Low	No
2012	2014	Srirangaraj *et al*[34]	16	Retrospective	Low	No
2014	2017	Dahiya *et al*[13]	380	Retrospective	Low	No
2010	2013	Choudhary *et al*[12]	322	Retrospective	Low	No
2012	2013	Venkatesh *et al*[35]	251	Retrospective	Low	No
2008-2010	2013	Gupta *et al*[16]	257	Retrospective	Low	No
2010-2012	2013	Jain & Chugh[18]	266	Retrospective	Low	No
2008	2011	Kumar *et al*[22]	128	Retrospective	Low	No
2011	2011	Adhikary *et al*[9]	2	Case Report	Low	Yes
2000-2006	2010	Verma *et al*[36]	159	Retrospective	Low	No
2008	2009	Kumar *et al*[21]	50	Retrospective	Low	No
1990	1992	Rodrigues *et al*[31]	74	Retrospective	Low	No
2004	2007	Joshi & Amarnath[19]	25	Retrospective	Low	No
2002	2007	Capoor *et al*[11]	178	Retrospective	Low	No
2003	2007	Banerjee *et al*[10]	60	Retrospective	Low	No
2004-2005	2006	Manchanda *et al*[25]	56	Retrospective	Low	No
2006	2006	Ray *et al*[30]	70	Cross-sectional	Low	No
1999-2004	2006	Mohanty *et al*[27]	629	Retrospective	Low	No
2001-2004	2006	Lakshmi *et al*[23]	60	Retrospective	Low	No
2003-2004	2005	Dutta *et al*[14]	379	Retrospective	Low	No
2004	2005	Senthilkumar *et al*[32]	6	Retrospective	Low	No
2002	2004	Madhulika *et al*[24]	157	Cross-sectional	Low	No
1997-2001	2002	Gautam *et al*[15]	436	Retrospective	Low	No
2001-2003	2005	Kadhiravan *et al*[20]	50	Retrospective	Low	No
2006-2007	2010	Nagshetty *et al*[28]	84	Retrospective	Low	No

QUIPS, Quality in Prognosis Studies tool[6]; JBI, Joanna Briggs Institute[7]

Table 2: Studies included in the systematic review in which phenotypic AMR trends of *S.* Typhi isolates were analysed

Thirty two studies [Table 2] [2-29] satisfied the inclusion criteria from which 49 yr-stratified summaries of *S.* Typhi antimicrobial-resistant isolates were obtained. For instance, Gautam *et al*[8]

MATERIALS AND METHODS:

The present study screened a total of 290 blood samples collected from the symptomatically suspected patients suffering from typhoid fever and attaining the various private and public hospitals of this region from May 2020 to 2021 may and isolated a total of 71 s.typhi isolates.

Enterobacteriaceae inhabit a wide variety of niches that include the human gastrointestinal tract and various environmental niches. When blood samples from a patient with suspected enteric fever is submitted for the widal test, it is useful as a routine to culture the clot after separation of serum (30). Peptone serves as a source of nitrogen,

carbon, long chain amio acids and other essential amino acids. Sodium taurocholate would inhibit majority of Gram-positive species. Sodium chloride maintains the isotonicity of the medium. Whereas addition of streptokinase solution causes rapid clot lysis with release of bacteria trapped in the clot (31).

In the isolation both bill salt broth (broth culture) and streptokinase broth (clot culture) where used for the enrichment of blood samples .the enriched samples were incubated till visible turbidity. A medium destined to inoculate onto other less selective media Streaked on the mac-conkey and Wilson Blair bismuth sulfite agar. The isolates producing the characteristic colonies were identified by standard biochemical tests and confirmed sereotypically by agglutination with salmonella O9,Vi specific and Hd antisera for s.typhi and paraA for the S.paratyphi A (kings institute of preventive medicine Guindy)

Antimicrobial susceptibility testing:

The antibiotic susceptibility testing of the isolates was done bye Kirby-Bauer disk diffusion method according to CLSI guidelines as. Ampicillin (10µg/disk), chloramphenicol (30µg/disk), co-trimaxazole (25 µg/disk) ciprofloxacin (5µg/disk), tetracycline (30µg/disk) cefatriaxone (5 µg/disk) nalidixic acid (30µg/disk), cefataxime (30µg/disk) Impenem (10µg/disk).Escherichia.coli ATCC..Was used as a negative control and s.typhi with MTCC.was used as a positive control commercially available six mm disks (Himedia laborites Mumbai) were used.(1999,2004).

MICs of isolates resistant to Ciprofloxin, nalidixic acid, Ampicillin and co-trimaxazole were done by using Hicomb strips (Hi media laboratories, Mumbai) MICs of ciprofloxacin were determined for both ciprofloxacin resistant and selected nalidixic acid resistant isolates. Isolates resistant to Ampicillin, chloramphenicol and co-trimaxazole were termed as MDR.

RESULTS & DISCUSSION:

A total of 71 s.typhi isolates were isolated from 290 samples showing the incidence of Antibiogram of these isolates revealed that all the isolates are sensitive to the Impenem.(Table-2)highest resistance was observed equally in Ampicillin (89%) and nalidixic acid (89%)followed by chloramphenicol(76.12%).the s.typhi isolates showed low level resistance against the majority of remaining antibiotics .

MICs of the isolates, among the 61 Ampicillin resistant s.typhi isolates, 11 isolates showed an MIC of 64µg/ml while 30 isolates showed MIC of 128 µg/ml. and remaining 20 isolates showed, the MIC of 256 µg/ml. among the 60 chloramphenicol resistant s.typhi isolates, 20 have shown MIC of 32 µg/ml while the remaining 40 isolates

have shown the MIC of 256 µg/ml.among the 41 co-trimaxazole resistant isolates, 5 isolates have shown the MIC of 10 µg/ml and 11 isolates have shown the MIC of 30 µg/ml and remaining 25 isolates have shown the MIC of 240 µg/ml .out of 11 ciprofloxacin resistant isolates 5 have shown the MIC 0.25 µg/ml and remaining 6 isolates have shown (Table-3) the MIC of 0.5 µg/ml. Among the 61 nalidixic acid resistant isolates chosen for the ciprofloxacin.

Table 1: Percentages of antibiotics are resistance to different antibiotics:

Antibiotics screened	No of isolates	Percentage
Ampicillin	61	89.00%
chloramphenicol	60	76.12%
Co-trimaxazole	41	67.60%
Nalidixic acid	61	89.00%
Ciprofloxacin	11	22.00%
Ceftriaxone	2	2.5%
Cefatzidime	6	17.35%
Azithromycin	45	85.52%
Gatifloxacin	41	61.36%
Sparofloxacin	05	69.00%
cefotaxime	27	11.50%
MDR	37	76.25%

MDR resistant to Ampicillin, chloramphenicol and co-trimaxazole

Table 2. MIC value of resistant S.typhi to various antibiotics.

Antibiotic	No. of isolates	Range (µg/ml)
Ampicillin N = 61	11 30 20	64µg/ml 128 µg/ml 256 µg/ml
Chloramphenicol N=60	20 40	32 µg/ml 256 µg/ml
Cotrimoxzole N=41	5 11 25	10 µg/ml 30 µg/ml 240 µg/ml .
ciprofloxacin N=11	5 6	0.25 µg/ml 0.50 µg/ml

CONCLUSION:

Despite public health efforts, typhoid fever is still a significant cause of morbidity and mortality worldwide. Sanitation management, public healthcare awareness, and nutritional programs boost both the control and prevention of disease should be maintained. We highlights that typhoid fever remains a major problem in most resource. Different seasons we collected samples and this disease is more occurs especially as per our studies in the month of july-Sept peoples suffering from this infection.

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