# MICROBIOLOGICAL AND CLINICAL FEATURES OF BLOOD SALMONELLA INFECTIONS AT A TERTIARY PAEDIATRIC CARE HOSPITAL IN SOUTH INDIA

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**Background and Introduction:** Enteric fever is a global health problem with a huge disease burden in the developing world with poor sanitation, food and water safety. There is a paucity of studies bringing out the clinical features, epidemiology and the mammoth problem of antimicrobial resistance seen in Salmonella species. This work reviews the clinical and laboratory profile, treatment and emerging trends of antimicrobial resistance of pediatric Salmonella infections as seen in a tertiary care pediatric hospital in South India.

Table 1: Demographic characteristics of the 352 patients with bloodstream *Salmonella* infection (n=352)

| Variable | Category | No. of Cases (%) |
|---|---|---|
| Sex | Male | 187 (53) |
| | Female | 165 (47) |
| Age | 0-2 yrs | 61 (17.33) |
| | 2-5 yrs | 83 (23.58) |
| | 5-10 yrs | 129 (36.65) |
| | 10-14 yrs | 43 (12.21) |
| | >14 yrs | 36 (10.23) |
| | Mean Age | 6.73 y |
| | Median Age | 6.25 y |
| | Least Age | 23 days |
| | Maximum Age | 17 y |

Table 2: Clinical features at admission (n=352)

| Symptoms | No. of cases (%) |
|---|---|
| Fever | 352 (100) |
| Vomiting | 104 (29.55) |
| Diarrhea | 58 (16.48) |
| Abdominal pain | 53 (15.06) |
| Anorexia | 28 (7.95) |
| Dry cough/throat congestion | 23 (6.53) |
| Neurological manifestations (irritability, altered sensorium, convulsions) | 6 (1.7) |
| Headache | (1.14) |
| Rash (erythematous) | 4 (1.14) |
| Jaundice | 3 (0.85) |
| Decreased urine output | 2 (0.57) |
| Constipation2 (0.57) | 2 (0.57) |
| Signs | |
| Fever | 180 (51.13) |
| 99-100°C | 22 (6.25) |
| 101-103°C | 150 (42.61) |
| >103°C | 8 (2.27) |
| Hepatomegaly | 54 (15.34) |
| Throat congestion | 18 (5.11) |
| Abdominal tenderness | 16 (4.55) |
| Splenomegaly | 16 (4.55) |
| Tachycardia | 14 (3.98) |
| Hepatosplenomegaly | 8 (2.27) |
| Coated tongue | 8 (2.27) |
| Neurological signs (low Glasgow coma score, altered sensorium, tonic posturing, hyperreflexia) | 5 (1.42) |
| Respiratory signs (decreased air entry, wheeze, crepitations) | 4 (2.27) |
| Bradycardia | 3 (0.85) |
| Icterus | 3 (0.85) |

## Methods :

- Eight year retrospective study at a tertiary care pediatric hospital in South India ( January 2007 – December 2014)
- Total of 352 patients with blood culture proven Salmonella species included in the study \
- Blood cultures were performed (Two sets in each case_) loaded onto the BD BACTEC 9120/ 9050 / FX200 Systems ( BD Sparks MD USA) Peds Plus and Aerobic F Bactec bottles were used.
- Blood cultures were collected using strict aseptic precautions & volume of the blood depended on the age and weight of the child.
- Aerobic incubation at 37oC for 7 days protocol.
- Loopfuls of the Blood broth mixture from Positive bottles were explanted onto Blood agar ( 5-6% sheep blood), MacConkey agar, Chocolate agar, CLED agar and Brain Heart Infusion agar and Gram smears were seen
- Conventional identification biochemical reactions performed and serotyping of isolates done using anti- sera from BIORAD France . (slide agglutination )
- Antimicrobial susceptibility testing performed using disc diffusion technique and MIC's were performed using E test methodology :

**Antimicrobial agents tested**

Ampicillin
Trimethoprim sulphamethoxazole
Chloramphenicol
Nalidixic acid Ceftriaxone

**MIC's performed for**

Ciprofloxacin *
Ceftriaxone **
Azithromycin***

Interpretation done using the BSAC (British Society for Antimicrobial Chemotherapy) guidelines

* *Ciprofloxacin MIC's from 2007- 2010 of (0.125-1µg/ml) considered as reduced susceptibility >1 µg/ml considered to be resistant Ciprofloxacin MIC's from 2011-2014 of > 0.06µg/ml were considered to denote failure of monotherapy*

** *Ceftriaxone MIC's performed from January 2012 <1µg/ml considered as susceptible*

*** *Azithromycin MIC's performed from January 2012 <16µg/ml considered as susceptible*

**Demographic details, clinical and laboratory findings and outcome of patients were noted from the in patient case records**

Table 3: Antimicrobial resistance pattern (%) of *Salmonella typhi* (n=285)

| Year | AMP | CO | CH | NA | CIP | CRO | AZI | MDR |
|---|---|---|---|---|---|---|---|---|
| 2007 (n=7) | 3 | 0 | 0 | 2 | R - 2, RS - 1 | 0 | - | 0 |
| 2008 (n=16) | 4 | 2 | 1 | 4 | R - 1, RS - 11 | 0 | 0 | 1 |
| 2009 (n=47) | 12 (25.5) | 0 | 0 | 16 | R - 2 (4.3) RS - 28 (59.6) | 0 | 0 | 0 |
| 2010 (n=36) | 3 (8.3) | 1 (2.8) | 1 (2.8) | 20 (55.6) | R - 4 (11.1) RS - 21 (58.3 | 0 | 0 | 0 |
| 2011 (n=51) | 1 (1.9) | 1 (1.9) | 1 (1.9) | 48 (94.1) | 49 (96.1) | 0 | 0 | 1 (1.9) |
| 2012 (n=50) | 4 (8) | 3 (6) | 2 (4) | 50 (100) | 50 (100) | 0 | 0 | 2 (4) |
| 2013 (n=36) | 2 (5.5) | 2 (5.5) | 1 (2.8) | 34 (94.4) | 34 (94.4) | 0 | 0 | 0 |
| 2014 (n=36) | 1 (2.4) | 1 (2.4) | 0 | 39 (75.1) | 39 (92.8) | 0 | 0 | 0 |
| Total (n=285) | 30 (10.5) | 10 (3.5) | 6 (2.1) | 214 (75.1) | 181 (63.5) | 0 | 0 | 4 (1.4) |

(AMP- Ampicillin, CO-Cotrimoxazole, CH-Chloramphenicol, NA-Nalidixic acid, CIP-Ciprofloxacin, CRO-Ceftriaxone, AZI-Azithromycin, MDR-Multidrug resistant, R-Resistant, RS-Reduced susceptibility to ciprofloxacin, NAS-FQ RS – Nalidixic acid susceptible and fluoroquinolone reduced suceptibility.

Table 4: Antimicrobial resistance pattern of *Salmonella Paratyphi* (n=62)

| Year | AMP | CO | CH | NA | CIP | CRO | AZI | MDR |
|---|---|---|---|---|---|---|---|---|
| 2007 (n=2) | 1 | 0 | 0 | 2 | R - 1, RS - 1 | 0 | - | 0 |
| 2008 (n=6) | 0 | 0 | 0 | 3 | R - 1, RS - 3 | 0 | 0 | 0 |
| 2009 (n=23) | 10 | 0 | 0 | 18 | R - 1 RS - 20 | 0 | 0 | 0 |
| 2010 (n=7) | 1 | 0 | 0 | 4 | R - 0 RS - 6 | 0 | 0 | 0 |
| 2011 (n=5) | 1 | 0 | 0 | 4 | 5 | 0 | 0 | 0 |
| 2012 (n=9) | 0 | 1 | 0 | 9 | 9 | 0 | 0 | 0 |
| 2013 (n=6) | 0 | 0 | 0 | 6 | 6 | 0 | 0 | 0 |
| 2014 (n=4) | 0 | 0 | 0 | 4 | 4 | 0 | 0 | 0 |
| Total (n=285) | 13 (21) | 1 (1.6) | 0 | 50 (80.6) | 27 (43.5) | 0 | 0 | 0 |

(AMP- Ampicillin, CO-Cotrimoxazole, CH-Chloramphenicol, NA-Nalidixic acid, CIP-Ciprofloxacin, CRO-Ceftriaxone, AZI-Azithromycin, MDR-Multidrug resistant, R-Resistant, RS-Reduced susceptibility to ciprofloxacin)

Table 5: MICs of antimicrobial agents

| Drug | MIC Range (µg/ml) | Mean MIC (µg/ml) | Median MIC (µg/ml) |
|---|---|---|---|
| Ciprofloxacin | 0.006 - >32 | 1.2 | 0.25 |
| Ceftriaxone | 0.023 - 1 | 0.12 | 0.08 |
| Azithromycin | 0.47 - 16 | 2.0 | 8 |

Table 6: Laboratory findings of cases at admission (n=352)

| Parameter | No. of cases (%) |
|---|---|
| **WSC count** | |
| Normal | 256 (72.7) |
| Leucocytosis | 64 (18.1) |
| Leucopenia | 32 (9.1) |
| **Platelet Count** | |
| Normal | 302 (85.5) |
| Thrombocytopenia | 50 (14.2) |
| **Elevated CRP** | 345 (98) |
| **Elevated ESR** | 352 (100) |
| **Widal Test** Significant titre | 295 (83.8) |

CRP: C - Reactive protein, ESR: Erythrocyte sedimentation rate, LFT: Liver Function tests

Figure 1

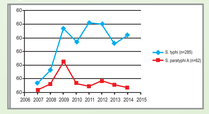
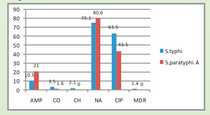



Figure 2




## Results:

Table 1: Demographic characteristics of the 352 patients with Salmonella infections
Table 2: Clinical Features of patients at admission for Salmonella infections
Figure 1: Year wise distribution of Salmonella typhi and Samonella paratyphi A isolates
Table 3 & Table 4 and Figure 2: Antimicrobial Resistance of Salmonella typhi and Salmonella paratyphiA
Table 6: Laboratory findings at admission for 352 patients

**Salient Features**

- **Five (1.42%) and two ( 0.57%) of the patients were coinfected with dengue and Hepatitis A respectively**
- **Relative bradycardia and constipation were seen less frequently in our patients.**

**Common species**

- Salmonella typhi – 285 ( 80.97%)
- Salmonella paratyphi A – 62( 17.61%)
- Salmonella typhimurium – 3 ( 0.85%0
- Salmonella enteric serovar paratyphi B – 1 (0.28%)
- Salmonella enteric serovar paratyphi C – 1 (0.28%)
- Salmonella infections were most common in monsoons -128 (36.36%) followed by winter -120 (34.1%) and summer – 104 (29.54%).

**Common Reasons for admission** – 170 in patients (48.29%)

- Unresponsiveness to outpatient treatment – 153(90%)
- Neurological manifestations – 4 (2.35%)
- Dehydration – 4 (2.35%)
- Relapsed enteric fever – 3 (1.76%)
- Anorexia – 3 (1.76%)
- Septic shock – 1 (0.59%)

**Underlying comorbid conditions** - 2 (1.18%)

- Thalassemia major
- Acute myeloid leukaemia

**Treatment Characteristics:**

- Monotherapy with 3rd gen cepphalosporins (ceftriaxone) - 54 (15.34%)
- Combination therapy – 298 (84.66%)

**Frequently used regimens:**

- 3rd generation cephalosporin & a fluoroquinolone – 153 (43.47%)
- 3rd generation cephalosporin & cotrimoxazole – 89 (25.28%)
- 3rd generation cephalosporin & azithromycin – 8 (2.27%)

**Complications : Fatal outcome – 3 (0.85%)**

- Dehydration – 4 (1.14%)
- Hepatitis – 3 (0.85%)
- Encephalitis – 3 (0.85%)
- Relapse – 3 (0.85%)
- SIRS – 2 (0.57%)
- Pancreatitis – 1 (0.28%)
- Pneumonia – 1 (0.28%)
- Meningitis – 1 (0.28%)
- Septic shock – 1 (0.28%)

* 2 pts with AML & Thalassmia major
* One patient due to sepsis and MODS

**Conclusions :**

- Suspect enteric fever in infants, children and adolscents even with non specific manifestations
- High fluoroquinolone resistance as seen in this study makes them an unsuitable choice for empiric or combination therapy
- 100% susceptibility to 3rd generation cephalosporins and azithromycin makes them suitable alternatives for treating enteric fever
- MDR isolates were minimal & improved susceptibility to chloramphenicol observed
- Early recognition of causative agents and ABST patterns helps prevent complications