Bacteriological and antibiotic profile of infection among infants in the post-neonatal period at a tertiary care hospital in South India

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Abstract

Purpose – Severe bacterial infection is a major cause of neonatal morbidity and mortality worldwide. Geographical-based demographic laboratory and clinical data are required to get a conclusion about the bacterial infection and their antibiotic susceptibility for the empiric antibiotic treatment in infants who presented with suspected infection. This study was aimed to find the most prevalent bacterial infection and antibiotic sensitivity among infants in the post-neonatal period presented at a tertiary care centre in South India.

Design/methodology/approach – A cross-sectional study was designed among infants (29 days to 1 year old) presented with suspected infection in the paediatric department. Infants with positive culture report were analysed for the bacteriological and antibiotic profile from the medical records. Antibiotic sensitivity was determined for the isolated bacteria according to standard procedure and data statically analysed.

Findings – Total of 218 samples (138 male and 80 female) were analysed. Most of the samples (171/218, 78.4%) were throat swab \( (p = 0.0247) \). Only one sample was cerebrospinal fluid from case of meningitis. Sample from upper RTI was major (162/218, 74.3%) with male dominance followed by stool samples from cases of diarrhoea (22/218, 10.0%). Staphylococcus aureus was the major organism identified in 46/171 (26.9 %) throat swabs. The most sensitive antibiotic against bacteria isolated from throat swab and CSF was gentamicin and cloxacillin. Netilmicin and piperacillin plus tazobactam were the sensitive antibiotics against bacteria isolated from stool, ear secretion and urine samples.

Research limitations/implications – Short duration and small sample size representing the population was the major limitations of this study. Furthermore, a multicentre population based study is warranted to develop a protocol/policy/rational use of antibiotics in the clinical setting for the empiric therapy.

Practical implications – Practicing good hygiene in child care is the best way to prevent infection. Community-based awareness and education should be given to parents in order to follow good hygiene in child care regularly. Furthermore, avoid delay in seeking treatment and provide the medicine prescribed at the right time and in the right dose to limit the morbidity and bacterial resistance.

Social implications – Despite the empirical antibiotic treatment in subjects presented with infection in the post-neonatal period, awareness about the exclusive breastfeeding, maternal and neonatal immunizations and antibiotic prophylaxis in case of suspected infection are warranted to reduce the incidence of infection. Furthermore, keeping the baby’s environment clean, keeping safe distance from people who are unwell or avoiding contact with infected people are major home-based activities to protect infants from common infectious diseases. Changing diaper at frequent intervals can reduce the UTI and washing child’s and caregiver’s hands frequently can prevent food bone and respiratory infections.

Originality/value – Upper RTI was the prevalent bacterial infection followed by diarrhoea in infants in the post-neonatal period. Klebsiella pneumoniae was the common organism identified in the overall report followed
by *E. coli* and *S. aureus*. Community-based awareness should be provided to follow good hygiene regularly in child care. Furthermore, avoid delay in seeking treatment and provide the medicine prescribed at the right time and in the right dose to limit the morbidity and bacterial resistance.

**Keywords** Antibiotic susceptibility, Bacteremia, Neonates, Neonatal sepsis, Urinary tract infection, India

**Paper type** Research paper

### Introduction

A serious bacterial infection is one of the major causes of neonatal mortality worldwide. Despite high-resource settings, diagnosis is challenging due to nonspecific signs and symptoms in neonates. Incidence of serious bacterial infections in infants during the post-neonatal period, identification of the organism and appropriate antibiotic selection remains a major challenge to clinicians. Bacterial strains’ resistance to antibiotics is the common cause of serious bacterial infections in febrile post-neonatal infants. In most cases, the initial antibiotic therapy will be changed after the identification of the organism in culture. Therefore, antibiotic susceptibility patterns of bacteria are necessary to know the local surveillance of pathogens and also very critical to determine appropriate antibiotic therapy. A recent systematic review reported that urinary tract infection (UTI) was the most common bacterial infection in young infants [1, 2]. Wang *et al.* reported a wide local variation in bacterial infections [3]. Studies reported that febrile illnesses such as pneumonia, UTI, blood-stream infections, and meningitis were the most severe bacterial infections in Indian infants [4–7].

Neonatal sepsis was associated with broad ranges of bacteria that showed variation in the antibiotic susceptibility pattern [8]. Widespread use of antibiotics has resulted in *Streptococcus pneumoniae*, one of the bacteria that causes life-threatening infections in infants in South India, but is non-susceptible to some commonly used antibiotics [9]. This warrants the necessary modification of existing empirical therapy regimens and implementation of effective preventive strategies to combat the emergence of antibiotic resistance in treating infants. In order to achieve a significant reduction of infants’ morbidity and mortality in India, documentation of the demographic and geographical details of changes in cause-specific neonatal infection is required [10]. Hence, the geographical-based demographic, laboratory and clinical data are required to get a conclusion about the bacteria and their antibiotic susceptibility to start the empiric treatment in infants who presented with suspected invasive bacterial infection [11]. At present, data on neonatal infections, mainly the types of bacterial infections, are scant or incomplete among the post-neonatal infants in the Indian community setting. This study aimed to describe the bacterial infection, type of bacteria, and their antimicrobial profile in post-neonatal infants presented with infection at a tertiary care hospital.

### Methods

**Study design and population**

A cross-sectional study was designed among the infants (29 days to 1 year old) presented with a suspected bacterial infection in the Paediatric Department of a tertiary care children’s hospital in central Kerala, India between October 2019 and March 2020. All infants in the post-neonatal period with positive pathogenic bacteria identified in the biological sample culture were included in the study. Cases with incomplete medical records or cases with samples positive in oral secretion or gastrointestinal aspirations of unknown infection were excluded from the study. Informed consent was taken from the parent/guardian of infants. The study was performed in accordance with the procedures of the institutional research committee.

**Sample size calculation**

Based on the prevalence ($p$) of respiratory tract infection, 65% (in the preliminary study conducted in this lab), the relative precision $d$, 10% of $p$ and $Z_{1-\alpha/2} = 1.96$ at 5% significant
level, the minimum sample size was calculated as 216 using the equation \( n = \left(\frac{Z_{1-\alpha/2}}{C_0}\right)^2 \frac{p(1-p)}{d^2} \)

**Study procedure**

Results of only positive bacterial culture of urine, stool, CSF, ear secretion and throat swab and the corresponding antimicrobial susceptibilities were collected from the microbiology lab database. The bacterial identification was done as per the standard procedure [12]. The antibiotic susceptibility testing was done by the standardized disc diffusion method (Kirby-Bauer Method) described by Bauer et al. [13].

Antibiotic discs used for throat swab with gram-negative bacilli isolated were amoxicillin, gentamicin, cephealexin, cefuroxime, cefotaxime, (instead of cefotaxime ceftazidime used for *Pseudomonas aeruginosa*), co-trimoxazole, chloramphenicol, tigecyclin, ciprofloxacin, imipenem, piperacillin + tazobactum, and polymixin B. For throat swab specimens, isolated gram-positive cocci, the antibiotic discs used were penicillin, amoxicillin, cloxacillin, gentamicin, netilmicin, cephealexin, ceforoxime, cefotaxime, erythromycin, azithromycin, vancomycin and linezolid. For gram-positive cocci isolated from urine/stool/blood/CSF/ear swab, penicillin, amoxicillin, cloxacillin, gentamicin, netilmicin, cephealexin, cefuroxime, ciprofloxacin, erythromycin, azithromycin, vancomycin and linezolid were used. Nitrofurantoin was used in a bacterial isolate from urine only. For gram-negative bacilli isolated from urine/stool/blood/CSF/ear swab, the antibiotic discs used were amoxicillin, gentamicin, amikacin, netilmicin, cephealexin, cefuroxime, cefotaxime, cotrimoxazole, chloramphenicol, ciprofloxacin, tigecyclin, imipenem, (nitrofurantoin only in urine), piperacillin + tazobactum and polymixin B. These antibiotic discs were used as 12 discs in 2 plates. The cut-point for the susceptibility for each antibiotic was selected as per the CLSI guideline [14]. The case-specific clinically apparent infection was also collected from the medical record. The data were analysed for statistical significance.

**Statistical analysis**

All categorical data were analysed using SPSS (v.16, IBM, CA) software. Data expressed as frequency and percent incidence. A Chi-square test was used to find the statistical significance between the types of infection. \( p < 0.05 \) was considered as significant.

**Ethical issue**

The study was conducted according to the Helsinki declaration, 1975 as revised in 2000 and approved by the Institutional Ethics Committee (NH/HRD/EC/04/2020).

**Results**

A total of 218 positive culture reports were included in the study whilst 12 reports with incomplete data on clinical presentation were excluded from the study. No mortality from the infection was found during the period of this study. Among the total reports, 171 reports were from a throat swab, reports on urine sample were only 19, stool samples were 22 and the CSF sample was only 1. Among the total cases, 138 cases were males and the remaining were females. The male-to-female ratio was found to be 1.7:1. Over 90% of infants were febrile at the time of presentation. The major bacterial infection was respiratory tract infection (RTI) which was found in 171/218 (78.4%) cases (Tables 1 and 2). A statistically significant difference was found between males and females with RTI from other infections \( (p = 0.0247) \). Among the RTI cases, 162/171 (94.7%) were due to upper RTI with male dominance (Table 1). Lower RTI was only 9/171 (5.2%) (Table 2). However, no statistically significant difference \( (p = 0.2388) \) could be found between the males and females with RTI. *Staphylococcus aureus*
| Type of sample | Type of bacterial infection | Gender | Bacterial isolate identified | Sensitive antibiotics | Resistant antibiotics |
|----------------|-----------------------------|--------|-----------------------------|-----------------------|----------------------|
| Throat swab    | URTI \( n = 162/218 \) (74.3%) | M = 109/162 (67.2%) F = 53/162 (10.5%) | *K. pneumoniae* (44/162, 27.1%) | Gentamicin, Piperacillin + Tazobactem, Imipenem, Polymixin B | Ciprofloxacin, Cephalexin, Cefuroxime, Ceftazidim, Ceftazidime, Amoxicillin, Clindamycin, Ceftriaxone, Tetracycline, Erythromycin |
|                |                             |        | *E. coli* (18/162, 11.1%)   | Gentamicin, Chloramphenicol, Ciprofloxacin, Tigecycline, Imipenem, Piperacillin + Tazobactem, Polymixin B | Amoxicillin, Ceftriaxone, Cefotaxime, Cotrimoxazole, Cephalaxin, Cefotaxime |
|                |                             |        | *S. aureus* (46/162, 28.3%) | Gentamicin, Cloxacillin, Azithromycin, Cefuroxime, Cephalexin, Cefotaxime, Vancomycin, Linezolid, Netilmicin | Penicillin, Amoxicillin, Erythromycin |
|                |                             |        | *P. aeruginosa* (20/162, 9.1%) | Gentamicin, Ciprofloxacin, Imipenem, Piperacillin + Tazobactem, Polymixin B | Amoxicillin, Ceftazidim, Cotrimoxazole, Cephalaxin, Cefotaxime, Cotrimoxazole |
|                |                             |        | *S. pyogenes* (14/162, 6.4%) | Gentamicin, Amoxicillin, Azithromycin, Cloxacillin, Netilmicin, Cephalexin, Cefotaxime, Cefuroxime, Vancomycin, Linezolid | Penicillin, Erythromycin |
|                |                             |        | *Coagulase-negative staphylococci* (16/162, 7.3%) | Gentamicin, Cloxacillin, Azithromycin, Cefuroxime, Cephalexin, Cefotaxime, Vancomycin, Linezolid, Netilmicin | Penicillin, Amoxicillin, Erythromycin |
|                |                             |        | *S. pneumoniae* (4/162, 1.8%) | Gentamicin, Amoxicillin, Azithromycin, Cloxacillin, Netilmicin, Cephalexin, Cefotaxime, Cefuroxime, Vancomycin, Linezolid, Erythromycin | Penicillin |

**Note(s):** M: Male; F: Female; URTI: Upper urinary tract infection; LRTI: Lower respiratory tract infection. \( p = 0.2388 \) (Chi-square test), non-significant between the males and females or between LRTI and URTI.
**Bacteriological and antibiotic profile**

| Type of sample | Type of bacterial infection | Gender | Bacterial isolate identified | Sensitive antibiotics | Resistant antibiotics |
|----------------|----------------------------|--------|------------------------------|-----------------------|-----------------------|
| Throat swab    | LRTI                       | M = 5/218 (55.5%) | **Coagulase-negative staphylococci** (2/9, 22.2%) | Netilmicin, Vancomycin, Linezolid | Amoxicillin, Erythromycin, Gentamicin, Cloxacillin, Penicillin, Cephalaxin, Cefuroxime, Cefotaxime, Azithromycin |
|                | n = 9/218 (4.1%)           | F = 4/9 (44.4%) | **Coagulase-negative staphylococci** (2/9, 22.2%) | Netilmicin, Vancomycin, Linezolid | Amoxicillin, Erythromycin, Gentamicin, Cloxacillin, Penicillin, Cephalaxin, Cefuroxime, Cefotaxime, Azithromycin |
|                |                            |        | **Acinetobacter** (2/9, 22.9%) | Co-trimaxazole; Polymyxin B; Tigecycline, Imipenem, pipracilin + tazobactem | Ciprofloxacin, Netilmicin, Amoxicillin, Gentamicin, Cefuroxime, Co-trimoxazole, Tigecycline |
|                |                            |        | **P. aeruginosa** (4/9, 44.4%) | Gentamicin, Imipenem, Polymixin B, Pipracilin + tazobactem, Netilmicin | Ciprofloxacin, Amoxicillin, Gentamicin, Cefuroxime, Co-trimoxazole, Tigecycline |
|                |                            |        | **K. pneumoniae** (1/9, 11.1%) | Tigecycline, Imipenem, polymixin B, Pipracilin + tazobactem | Ciprofloxacin, Netilmicin, Amoxicillin, Gentamicin, Cefuroxime, Cefotaxime, Co-trimoxazole |

**Note(s):** M: Male; F: Female; URTI: Upper urinary tract infection; LRTI: Lower respiratory tract infection; p = 0.2388 (Chi-square test), non-significant between the males and females or between LRTI and URTI; p = 0.0491 (Chi-square test), significant difference found between *S. aureus* and *K. pneumonia* associated RTI; p = 0.0247 (Chi-Square test), significant difference was found between males and females with RTI from other infections

(46/171) was the major bacterium that causes 26.9% of RTI followed by *Klebsiella pneumoniae* (45/171, 26.3%). There was a significant difference found between *S. aureus* and *K. pneumonia* associated RTI from others (p = 0.0491). *Coagulase negative staphylococcus* was isolated only in 16/171 (10.5%) throat samples from infants presented with RTI (16 cases of upper RTI and 2 cases of lower RTI). Lower RTI was found only in 9/171 (5.2%) cases with *P. aeruginosa* as the major bacteria (4/171, 2.3%). *E. coli* was the major organism found in the urine and stool samples of infants with UTI (Table 3) and diarrhoea (Table 4). Stool samples from infants presented with diarrhoea showed *E. coli* in 19/22 samples (86.3%) while its presence in urine was 11/19 (57.8%). Only 1 CSF sample with *Staphylococcus aureus* isolate was obtained during the period of the study which was from an infant presenting with meningitis (Table 5). Details of various bacteria isolated from 218 samples are depicted in Figure 1. *K. pneumoniae* was the common organism identified in overall culture (49/218, 22.4%), followed by *E. coli* and *S. aureus* (48/218, 22.0%). The most sensitive antibiotic
against bacteria isolated in a throat swab and CSF samples were gentamicin and cloxacillin. Netilmicin and piperacillin plus tazobactam were the sensitive antibiotics against bacteria isolated from urine, stool, and ear secretion samples. Bacteria isolated from blood samples were sensitive to netilmicin. Ciprofloxacin was found resistant to most of the bacteria isolated from urine and stool while penicillin was resistant against bacteria isolated from a throat swab.

**Discussion**

Upper RTI is the major morbidity in infants in the post-neonatal period with *S. aureus* and *K. pneumonia* being the prevalent bacteria. Male infants were dominant. While *K. pneumoniae* was the major pathogen causing overall infection followed by *E. coli* and
S. aureus. Diarrhoea was the second most prevalent morbidity with E. coli as the associated organism. The results of this study are consistent with a community-based cross-sectional study which showed that the prevalence of acute RTI was about 22–27% among children below five years of age in Eastern and Southern parts of India [15, 16]. Pneumonia and diarrhoea were the two causes accounting for 50% of infant deaths in India. Among these, pneumonia caused five-times higher mortality rates in girls in central India than boys, while diarrhoea in South Indian boys had a four-times higher mortality rate than girls in West India [17]. But a recent study conducted in Ujjain, India demonstrated that UTIs were the most common bacterial infection in infants with equal distribution of sex [7]. This concluded the geographic variation of the type of bacterial infection among infants. The bacterial infection in the respiratory tract may be probably associated with viral infections of the lower respiratory tract [18].

This study revealed that infections in male infants were more prevalent than amongst females. The exact reason for this remains elusive. This finding is also similar to studies conducted at Ahmedabad district in Gujarat, India, and Kancheepuram district in South India [16, 19]. Among the total cases analysed during the study period, more than 90% of cases were with the acute febrile syndrome. Mendez Espinola and Herrera Labarca reported that children less than 3 months were hospitalized due to acute febrile syndrome [20]. Fever was the most frequently reported sign among neonates in India [21]. For the empiric treatment of infants below 60 days of age, presented with a suspected invasive bacterial infection, the narrowest spectrum antimicrobial therapy was recommended. Furthermore, there should be

### Table 4. Distribution of bacterial infection among infants presented with diarrhoea

| Type of sample | Type of bacterial infection | Gender | Bacterial isolate identified | Sensitive antibiotics | Resistant antibiotics |
|---------------|-----------------------------|--------|-------------------------------|-----------------------|----------------------|
| Stool         | Diarrhoea n = 22/218 (10.0%) | M = 10/22 (45.4%) | P. aeruginosa (2/22, 9.0%) | Imipenem, Piperacilin + tazobactem | Ciprofloxacin, Amoxicillin, Netilmicin, Gentamicin, Amikacin, Ceftazidime, Cephalexin, Cefuroxime, Co-trimaxazole, Tigecycline |
|               |                             | F = 12/22 (54.5%) | E. coli (19/22, 86.3%) | Chloramphenicol, Amikacin, piperacilin + tazobactem Netilmicin, Tigecycline, Imipenem | Gentamicin, Amoxicillin, Ciprofloxacin, Cephalexin, Cefotaxim, Co-trimaxazole |
|               |                             |        | S. aureus (1/22, 4.5%) (MRSA) | Netilmicin, Vancomycin, Linezolid | Ciprofloxacin, Amoxicillin, Azithromycin |

Note(s): M: Male; F: Female; MRSA: Methicillin resistant Staphylococcus aureus
a more tolerable side effect profile. Results of the recent study demonstrated that co-trimoxazole and amoxicillin were the two antibiotics that were commonly recommended against *Acinetobacter* [22]. According to a recent study, the combination of ampicillin plus either gentamicin or a third-generation cephalosporin was an appropriate empiric antimicrobial treatment regimen [11]. However, de Man *et al.* reported that the use of third-generation cephalosporin caused the development of resistant bacteria [23]. Greenhow and Cantey also concluded that for empiric use in most infants with suspected bacteremia,
ampicillin plus gentamicin was an effective combination while awaiting results of bacterial culture. This combination has a lower risk of toxicity with once-daily dosing [24]. Pokhrel et al. recommend a combination of piperacillin-tazobactam and ofloxacin as the first-line therapy and a combination of vancomycin and meropenem as the second-line empirical therapy in infants admitted with sepsis in a neonatal intensive care unit [25]. The most sensitive antibiotic against bacteria isolated from a throat swab and CSF samples was gentamicin and cloxacillin. Netilmicin and piperacillin plus tazobactam were the sensitive antibiotics against bacteria isolated from urine, stool, and ear secretion samples. Empirical therapy using piperacillin + tazobactam and netilmicin was found to be effective with good tolerance in infants and even in neutropenic children with fever [26, 27]. However, in vitro susceptibilities do not necessarily correlate with in vivo effectiveness [2]. Hence, an empirical antibiotic regimen as per the updated antibiotic policy should be developed based on an individualized community established antimicrobial sensitivity pattern of microorganisms to prevent morbidity and mortality in infants [3, 28]. Short duration and small sample size representing the population were the major limitations of this study. Further, a multicentre population-based study is warranted to develop a protocol/policy/ rational use of antibiotics in the clinical setting for empiric therapy.

Despite the empirical antibiotic treatment in subjects presented with infection in the post-neonatal period, awareness about exclusive breastfeeding, maternal and neonatal immunizations, and antibiotic prophylaxis in case of suspected infection are warranted to reduce the incidence of infection. Furthermore, keeping the baby’s environment clean, keeping a safe distance from people who are unwell, or avoiding contact with infected people are major home-based activities to protect infants from common infectious diseases. Changing diapers at frequent intervals can reduce occurrence of a UTI and washing the child’s and caregiver’s hands frequently can prevent food and respiratory infections. Therefore, practicing good hygiene in child care is the best way to prevent infection. Community-based awareness and education should be given to parents in order to follow regular good hygiene in childcare. Furthermore, avoiding delay in seeking treatment and providing the medicine prescribed at the right time and in the right dose limits morbidity and bacterial resistance.

Conclusion
Upper RTI is the major bacterial infection and Klebsiella is the major organism causing infection in infants in their post-neonatal period. The common antibiotic found sensitive against bacteria isolated from throat swab was gentamicin and cloxacillin. Netilmicin and piperacillin plus tazobactam were the sensitive antibiotics against bacteria isolated from other sources. Community-based awareness should be provided to follow good hygiene in child care.

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