

Original Research Article

<https://doi.org/10.20546/ijcmas.2020.910.158>

Study of Bacterial Agents Causing Febrile Illnesses in Children between 1 Month to 12 Years of Age in a Tertiary Care Hospital in Sikkim

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ABSTRACT

Febrile illnesses in children are a common cause of admission to hospital globally, with significant associated morbidity and mortality. The present study was mainly focussed to determine the bacterial agents causing febrile illnesses in children between 1 month to 12 years of age, and their antimicrobial susceptibility pattern and also to find out the distribution of different bacterial isolates among the study population. It is a hospital based descriptive study conducted on a sample size of total of 526 paediatric patients having febrile illnesses were taken as a study population. Different clinical samples blood, pus, urine, cerebrospinal fluid, stool, gastric aspirate, sputum, throat swab, ear swab and pleural fluid were collected constituted the material for this study and by using standard microbiological procedures to study morphological characteristics, cultural and biochemical characteristics the pathogens were identified in the samples. BacT/ALERT system was checked for any blood culture bottles. VITEK 2 system was used to identify the gram-negative bacilli using ID-GNB card. Majority of the samples from Gram-negative belonged to the age group of 1-3 years. In case of Gram- positive, more samples belonged to the age group 7-9 years (33%). Most of the isolates belonged to the age groups of 1year-3years and 4-6 years and 7-9 years. *E. coli* (56.3%) followed by *S. aureus* (21.9%) and *Salmonella typhi* (9.4%) were the most common isolates in the younger age group (1year-3 years) whereas *S. aureus* (53.8%) followed by *E. coli* (30.8%) predominated the older age group (7-9 years). *Staphylococcus aureus* showed high level resistance to Penicillin (63.6%) whereas they were sensitive to Vancomycin (45.45%) which are in accordance to the study of Rahbar *et al.*,⁽¹⁵⁾ found that *S. aureus* were resistant to penicillins (82.6%) but sensitive to Cotrimoxazole and Vancomycin. In this study, *E.coli* showed high resistance to Cotrimoxazole (46.4%), Ceftriaxone (39.3%) and showed sensitivity to Amikacin (78.57) whereas *Klebsiella pneumoniae* showed similar trends except that it was also resistant to Amoxicillin-Clavulanic acid (60%). *Salmonella typhi* showed high resistance to Amikacin (21.4%), while it showed sensitivity to Imipenem (78.57%). A regular epidemiological study of pathogenic culture isolates and determination of susceptibility to antibiotics is necessary in order to guide the clinicians to and choose the appropriate empirical therapy and switch over to the best regime based on the antibiotic susceptibility pattern to improve the overall outcome of the patient's health.

Keywords

Febrile illness,
Children,
Pathogenic
microorganisms,
Antibiotics,
Resistance,
Sensitivity

Article Info

Accepted:
12 September 2020
Available Online:
10 October 2020

Introduction

Febrile illnesses in children is a common cause of admission to hospital globally, with significant associated morbidity and mortality.⁽¹⁾ In developing countries, this is frequently compounded by low rates of immunisation, untreated co-morbidities, and late presentations.⁽²⁾ Febrile illnesses are caused by diverse pathogens, presenting with non-specific symptoms to healthcare facilities with limited diagnostic capacity.⁽³⁾ Clinical management guidelines for acute febrile illness are available, but rarely supported by knowledge of the locally prevalent causative agents.⁽⁴⁾ Fever is defined as a rectal temperature $\geq 38^{\circ}\text{C}$ and a value $>40^{\circ}\text{C}$ is called hyperpyrexia. Body temperature fluctuates in a defined normal range (36.6°C - 37.9°C rectally), so that the highest point is reached in early evening and the lowest point is reached in the morning. Any abnormal rise in body temperature should be considered a symptom of an underlying condition.⁽⁵⁾ Even with a thorough history and a complete physical examination, one in five acutely ill, non-toxic-appearing children have an unidentifiable source of fever. Although most of these children have a self-limited viral illness, studies from the 1980s and 1990s have shown that 7 to 13 percent of children younger than 36 months without evident sources of fever had occult bacteremia and serious bacterial infection (SBI) ⁽⁶⁾. The causes of febrile illnesses can be organized into 4 main categories: infectious, inflammatory, neoplastic, and miscellaneous. Bacterial infections are associated with a prompt resolution of fever after effective antimicrobial treatment is employed. Although administration of antimicrobial agents can result in a very rapid elimination of bacteria, if tissue injury has been extensive, the inflammatory response and fever can continue for days even after all microbes have been eradicated. The clinical features of

febrile illnesses can be associated with extreme malaise, feeling hot or cold, facial flushing, shivering, fatigue, irritability, decreased appetite, cough, sore throat, neck pain, watery stools, burning micturition and headache. Although the underlying etiologies can manifest in varied ways clinically, there are some predictable features. For instance, fever with petechiae in an ill-appearing patient indicates the high possibility of life-threatening conditions such as meningococemia, Rocky Mountain spotted fever, or acute bacterial endocarditis.⁶

If the cause of the fever is not apparent, history of presentation and abnormal physical examination findings can guide the evaluation. The child with respiratory symptoms and hypoxia would require a chest radiograph. The child with pharyngitis can benefit from rapid antigen detection testing for group A *Streptococcus* and a throat culture. Dysuria, back pain, or history of vesicoureteral reflux should prompt a urinalysis and urine culture, and bloody diarrhoea should prompt a stool culture. Diarrhoea in young children might be so severe that the child might need to be hospitalized.

A severe infection with high fever may also be associated with seizures in children less than 2 years old. *Shigella* spp still accounts for a significant proportion of bacillary dysentery in many tropical and subtropical countries. ^(7,8) It is the most prevalent etiological agent in childhood diarrhoea in most countries.⁽⁹⁾ A complete blood count and blood culture should be considered in the ill-appearing child, along with cerebrospinal fluid studies if the child has severe headache, vomiting and neck stiffness. In infants and young children worldwide, the most common causative organisms of meningitis are *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* type

b (Hib). Among children older than 5 years of age and adolescents, the predominant causative agents are *Streptococcus pneumoniae* and *Neisseria meningitides*.⁽¹⁰⁾

The present study was mainly focussed to determine the bacterial agents causing febrile illnesses in children between 1 month to 12 years of age, and their antimicrobial susceptibility pattern and also to find out the distribution of different bacterial isolates among the study population.

Materials and Methods

The present study was conducted in the Department of Microbiology, Sikkim Manipal Institute of Medical Sciences (SMIMS) and Central Referral Hospital (CRH) is the only referral hospital of the state Tadong, Gangtok, Sikkim. It is a hospital based descriptive study conducted during the period of October 2013 to September 2014. A total of 526 paediatric patients having febrile illnesses were taken as a study population.

The type of sampling was purposive sampling method. Study included patients aged 1 month to 12 years of age with febrile illnesses in Central Referral Hospital, Gangtok, Sikkim. Children between 1 month to 12 years of age presenting with fever at Central Referral Hospital and were not present either before admission or during disease prodrome and admitted in CRH were included in this study and parents of the children who did not give consent to be part of this study.

Statistical analysis

Data were analyzed using the SPSS software (Ver. 24; SPSS Inc., USA). Analysis of variance (ANOVA) tests were used to determine the significant differences between treatments at $p < 0.05$ using Tukey's HSD test.

Method of collection of data

After obtaining a written informed consent from patients satisfying the inclusion criteria, a detailed history was recorded, a thorough clinical examination was done and relevant investigations performed. The investigator also asked help of the staff nurses, junior residents and interns of the Paediatrics department for the conduct of the study. They were given adequate training regarding methods of collecting blood sample for investigation. The investigator visited the Emergency room, Paediatric ICU, Paediatric wards daily during the study periods and screened patients with Febrile illnesses. All the patients screened by the investigator during the study period who were eligible were taken as the denominator for the study. The criteria for selecting a patient was, any patient admitted under Paediatrics department at CRH who fulfill the criteria for febrile illnesses caused by infection or underlying etiology or at least clinical evidence of infection.

Different clinical samples blood, pus, urine, cerebrospinal fluid, stool, gastric aspirate, sputum, throat swab, ear swab and pleural fluid were collected constituted the material for this study. Gram's staining was performed initially to study the morphological characteristics of the clinical isolates. The specimens were inoculated on to 5% sheep Blood agar, Chocolate agar, Mac- Conkey agar and Cysteine Lactose Electrolyte Deficient (CLED) agar. With exception of Chocolate agar that was incubated in increased carbon dioxide, all other inoculated agar plates were incubated aerobically at 35–37 °C for 24 hr. After 24 hours of incubation, the BacT/ALERT system was checked for any blood culture bottles showing growth. Growth in any bottle was indicated on the system screen. The bottles that showed growth were subcultured. The blood culture

bottles were examined daily to look for growth which was observed as turbidity, hemolysis of red blood cells, gas bubbles in the medium, small aggregates of growth in the broth or occasionally along the walls of the bottles.

Identification of isolates was done using combination of colonial characteristics, Gram staining characteristics and conventional standard biochemical tests. The culture of pathogens enables colonies of pure growth to be isolated for identification and antimicrobial susceptibility testing. The specimen is streaked on the culture plates (Blood agar, Chocolate agar and Mac-Conkey agar) and incubated at 37°C for 24 hours. Urine samples were inoculated into CLED agar.

Following culture methods, biochemical tests are often required to identify pathogens by using substrates and sugars to detect their enzymatic and fermentation reactions. The tests include carbohydrate fermentation tests with glucose, lactose, sucrose, xylose, mannitol and maltose etc. The organisms were also tested for Indole production, Methyl red test, Voges-proskauer test, Citrate utilization, Urease test, Oxidase test, Catalase test, Nitrate reduction test, Triple sugar iron agar test etc.

ID-GNB card and VITEK 2 system

A bacterial suspension was adjusted to a McFarland standard of 0.5 in 2.5 ml of a 0.45% sodium chloride solution with an ATB 1550 densitometer (bioMérieux). The identification card for gram-negative bacilli (ID-GNB card) for the VITEK 2 system is a 64-well plastic card containing 41 fluorescent biochemical tests, including 18 enzymatic tests for aminopeptidases and oxidases. The card was automatically filled by a vacuum device and automatically sealed. It was manually inserted in the VITEK 2 reader-

incubator module (incubation temperature, 35.5°C), and every card was automatically subjected to a kinetic fluorescence measurement every 15 min. The results were interpreted by the ID-GNB database after the incubation period of 3 h. All used cards were automatically discarded in a waste container. The ID-GNB database contained 101 different taxa of gram-negative rods. The card was automatically filled by a vacuum device, sealed and inserted into the VITEK 2 reader-incubator module (incubation temperature, 35.5°C), and subjected to a kinetic fluorescence measurement every 15 min. The results were interpreted by the ID-GPC database, and final results were obtained automatically. All cards used were automatically discarded into a waste container. The results were interpreted by the ID-GPC database, and final results were obtained automatically.

Antibiotic susceptibility testing

Disc diffusion method: Antibiotic susceptibility was checked by Kirby-Bauer's disc diffusion method. The procedure was performed according to CLSI guidelines. Selected antibiotic discs were placed aseptically on the surface of the inoculated media after 5 minutes using sterile pair of forceps. The MHA plates were incubated at 37°C for 16-18h hrs.

The antibiotic discs used in this study were Piperacillin (100µg), Amikacin (30µg), Gentamicin (10µg), Ceftazidime (30µg), Ciprofloxacin (5µg), Imipenem (10µg), Ampicillin/Sulbactam (10/10µg), Colistin E strips, Ampicillin (10 µg), Amoxycylav (20/10 µg), Co-trimoxazole (25 µg), Cefepime (30 µg), Cefuroxime (30 µg), Ceftazidime/Clavulanic acid (30/10 µg), Nitrofurantoin (300 µg), Tetracycline (30 µg). The inhibition zone was measured according to CLSI guidelines (CLSI Catalogue, 2016).

Results and Discussion

During the period of one year study (October 2013- September 2014), an attempt was made to study the bacterial agents causing febrile illnesses in children between 1 month to 12 years of age and antibiotic susceptibility of the isolates in Central Referral Hospital, Tadong, East Sikkim. 526 clinical samples of blood, urine, stool, pus, cerebrospinal fluid, throat swabs and other respiratory secretions were collected from children suffering from fever from Paediatric ward, Paediatric outpatient department (OPD), paediatric intensive care unit (PICU) and Emergency department (ER). Out of the total 526 samples received, 264 (50.2%) were from male children and 262 (49.8%) were from female children.

Maximum number (63.1%) of the sample belonged to the age group 1-3 years. This trend was found to be almost similar in both male and female children as shown in Table 1. Out of the total 526 samples studied, majority (47.0%) of them were from the Paediatric Ward. 31.7% of the samples were from the Paediatric OPD, 19.6% were from the PICU and only 1.7% were from the Emergency department. The results were insignificant 'p' value 0.1. Out of the total 526 samples obtained, blood (47%) was the most common sample received followed by urine sample (29%) (Figure 1).

Out of 526 samples received, bacterial growth was seen in 79 samples. The culture positivity rate was observed to be 15.0%. 447 (85.0%) samples were sterile whereas out of 79 samples received with positive growth, on gram staining, 27 samples (34.2%) were found to be gram-positive and 52 samples (65.8%) were found to be gram-negative.

The maximum number of the isolates was found within in the age group of 1-3 years

which accounted for 41% of the total 79 culture positive cases and the results were significant p- value is 0.000 (Figure 2).

Male children contributed 38% of the total culture positive cases while female children accounted for 62% of the total of 79 culture positive samples and the values were significant p-value is 0.018. Majority of the samples from gram-negative belonged to the age group 1- 3 years (48%) followed by 1-12 months and 4-6 years (17%). In case of gram-positive, more samples belonged to the age group 7-9 years (33%) followed by 1-3 years (26%) respectively as shown below in Figure 3. The p-value is 0.031. A 51.9% of the samples from gram-positive isolates were from male children and 48.1% were from female children while 30.8% of the samples from gram-negative were from male children and 69.2% were from female children as shown in Figure 4. The p-value is 0.067.

Majority of the culture positives were found in urine samples (39%) followed by pus samples (37%) shown in Figure 5.

Total of eight bacterial species were isolated. *Escherichia coli* (49.4%) followed by *Staphylococcus aureus* (31.6%) were the two most common isolates. Among the gram-positive isolates, the most common organism isolated was *Staphylococcus aureus* (31.6%) followed by *Streptococcus pyogenes* (2.5%). Among gram-negative bacilli, the most common organism isolated was *Escherichia coli* (49.4%) (Table 2).

Most of the isolates belonged to the age groups of 1-3 years and *E.coli* (56.3%) followed by *S.aureus* (21.9%) were the most common organisms isolated in the age group 1-3 years. The most common organism isolated in the age group 4-6 years was *E.coli* (46.7%) followed by *S.aureus* (40%) whereas in the age group 7-9 years *S.aureus* (53.8%)

followed by *E.coli* (30.8%) were the common ones as given in Table 3. The p-value is 0.238.

S.aureus (40%) followed by *E.coli* (36.7%), were the common isolates in males whereas the common organisms isolated in females were *E.coli* (57.1%) depicted in Table 4. The p-value is 0.045.

Maximum number of isolates were from the Paediatric ward (49.37%) followed by OPD (44.3%) and the predominant isolate in the Paediatric ward is *E.coli* (33.3%), whereas in OPD was predominated by *E.coli* (74.3%). The most common organism isolated from PICU was *S.aureus* (40.0%) illustrated in Table 5.

Among 79 culture positive isolates, *E.coli* (49.4%) was found to be the most common organism isolated followed by *S.aureus* (31.6%). *P.aeruginosa*, *S.typhi* and *Klebsiella spp* (3.8%) had equal distribution as shown in Figure 6. Among 31 positive urine samples, the most common organism isolated was *E.coli* (96.8%) and the least common organism isolated was *Pseudomonas aeruginosa* (3.2%). Among 10 positive blood samples, the most common organisms isolated was *S.aureus* (40%) and the least common organism isolated was *E.coli* (10%). Among 29 positive pus samples, the most common organism isolated was *S.aureus*

(69%) and the least common organism isolated was *Pseudomonas aeruginosa* (3.4%). Out of 7 stool samples, only 4 samples were culture positive. The only organism isolated was *E.coli* (100%) and they were seen in children less than 1 year of age. The most common organism isolated in respiratory tract infections was *Streptococcus pyogenes* (40%). No organisms were isolated in cerebrospinal fluid and pleural fluids.

Staphylococcus aureus showed high level resistance to Penicillin (63.6%) whereas they were sensitive to Vancomycin (45.45%), Linezolid (42.4%) and Gentamycin (30.3%) (Table 6). *E.coli* showed high resistance to Cotrimoxazole (46.4%). It showed highest sensitivity to Imipenem (96.4%). *K. pneumonia* showed highest resistance to Amoxyclav (60.0%), while it is highly sensitive to Imipenem (70%). *Enterobacter cloacae* showed resistance to Amoxyclav but was sensitive to Ceftriaxone as shown in Table 7. *Salmonella typhi* showed high resistance to Ciprofloxacin (100%), while it showed high sensitivity to Imipenem (100%). *Pseudomonas spp* showed resistance (100%) to Amikacin, while it showed sensitivity (66.6%) to Piperacillin and Cefuroxime. *Proteus mirabilis* showed high resistance (100%) to Cotrimoxazole and Amikacin while it showed high sensitivity (100%) to Imipenem and Cefoperazone as shown below in Table 8.

Table.1 Age-sex wise distribution of children with febrile illnesses

Age Group	Male	Female	Total
1 - 12 Months	22 (8.3%)	19 (7.3%)	41 (7.8%)
1 - 3 Years	171 (64.8%)	161 (61.5%)	332 (63.1%)
4 - 6 Years	32 (12.1%)	36 (13.7%)	68 (12.9%)
7 - 9 Years	21 (8.0%)	24 (9.2%)	45 (8.6%)
10 - 12 Years	18 (6.8%)	22 (8.4%)	40 (7.6%)
Total (p-value is 0.853)	264 (50.2%)	262 (49.8%)	526 (100%)

Table.2 Pattern of the organisms isolated

Organism	Frequency	Percent
GRAM POSITIVE COCCI		
<i>Staphylococcus aureus</i>	25	31.6%
<i>Streptococcus pyogenes</i>	2	2.5%
Total	27	33.7%
GRAM NEGATIVE BACILLI		
<i>Escherichia coli</i>	39	49.4%
<i>Enterobacter cloacae</i>	2	2.5%
<i>Klebsiella spp</i>	3	3.8%
<i>Proteus mirabilis</i>	2	2.5%
<i>Pseudomonas aeruginosa</i>	3	3.8%
<i>Salmonella typhi</i>	3	3.8%
Total	52	10.1%
Total	79	100.0%

Table.3 Age-wise distribution of the culture isolates

Culture Isolates	1 - 12 Months	1 - 3 Years	4 - 6 Years	7 - 9 Years	10 - 12 Years
<i>Escherichia coli</i>	6 (54.5%)	18 (56.3%)	7 (46.7%)	4 (30.8%)	4 (50.0%)
<i>Enterobacter cloacae</i>	0 (0.0%)	2 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<i>Klebsiella spp</i>	2 (18.2%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<i>Proteus mirabilis</i>	1 (9.1%)	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)
<i>Pseudomonas aeruginosa</i>	0 (0.0%)	1 (3.1%)	1 (6.7%)	0 (0.0%)	1 (12.5%)
<i>Salmonella typhi</i>	0 (0.0%)	3 (9.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<i>Staphylococcus aureus</i>	2 (18.2%)	7 (21.9%)	6 (40.0%)	7 (53.8%)	3 (37.5%)
<i>Streptococcus pyogenes</i>	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (15.4%)	0 (0.0%)
Total	11 (100%)	32 (100%)	15 (100%)	13 (100%)	8 (100%)

Table.4 Sex-wise distribution of the culture isolates

Culture Isolates	Male	Female	Total
<i>Escherichia coli</i>	11 (36.7%)	28 (57.1%)	39 (49.4%)
<i>Enterobacter cloacae</i>	0 (0.0%)	2 (4.1%)	2 (2.5%)
<i>Klebsiella spp</i>	1 (3.3%)	2 (4.1%)	3 (3.8%)
<i>Proteus mirabilis</i>	2 (6.7%)	0 (0.0%)	2 (2.5%)
<i>Pseudomonas aeruginosa</i>	0 (0.0%)	3 (6.1%)	3 (3.8%)
<i>Salmonella typhi</i>	2 (6.7%)	1 (2.0%)	3 (3.8%)
<i>Staphylococcus aureus</i>	12 (40.0%)	13 (26.5%)	25 (31.6%)
<i>Streptococcus pyogenes</i>	2 (6.7%)	0 (0.0%)	2 (2.5%)
Total	30 (100%)	49 (100%)	79 (100%)

Table.5 Ward-wise distribution of the culture isolates

Culture Isolates	PICU	OPD	Ward	Total
<i>Escherichia coli</i>	0 (0.0%)	26 (74.3%)	13 (33.3%)	39 (49.4%)
<i>Enterobacter cloacae</i>	1 (20.0%)	0 (0.0%)	1 (2.6%)	2 (2.5%)
<i>Klebsiella spp</i>	1 (20.0%)	0 (0.0%)	2 (5.1%)	3 (3.8%)
<i>Proteus mirabilis</i>	0 (0.0%)	0 (0.0%)	2 (5.1%)	2 (2.5%)
<i>Pseudomonas aeruginosa</i>	0 (0.0%)	0 (0.0%)	3 (7.7%)	3 (3.8%)
<i>Salmonella typhi</i>	1 (20.0%)	0 (0.0%)	2 (5.1%)	3 (3.8%)
<i>Staphylococcus aureus</i>	2 (40.0%)	8 (22.9%)	15 (38.5%)	25 (31.6%)
<i>Streptococcus pyogenes</i>	0 (0.0%)	1 (2.9%)	1 (2.6%)	2 (2.5%)
Total	5 (100%)	35 (100%)	39 (100%)	79 (100%)

Fig.1 Distribution of different samples obtained from children with febrile illnesses

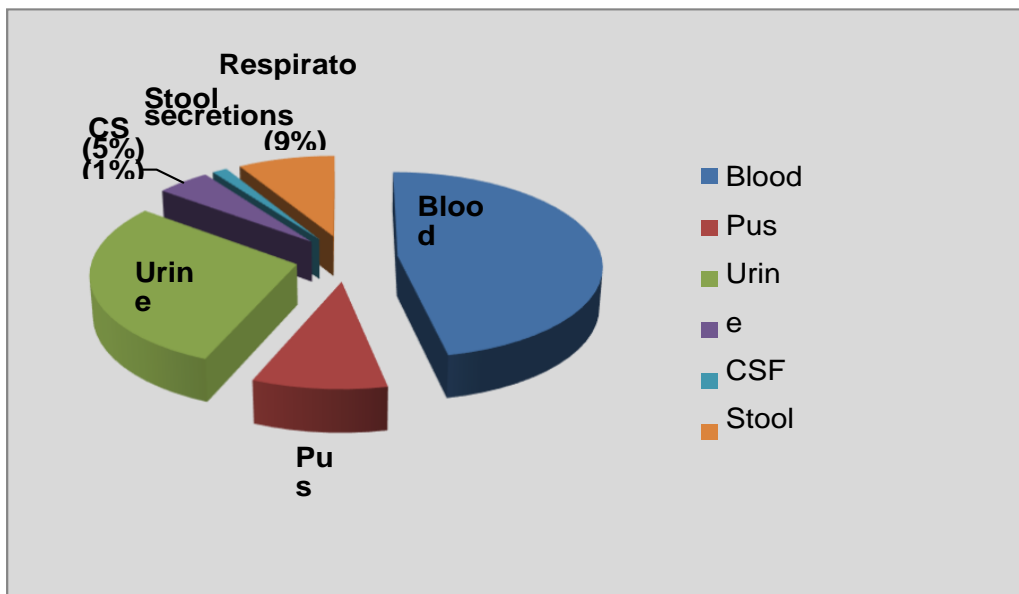


Table.6 Antibiotic susceptibility pattern of the Gram-positive cocci

Antibiotics	<i>Staphylococcus aureus</i>	
	Sensitive (S)	Resistant (R)
Amikacin	4	0
Ampicillin	0	0
Cefepime	0	0
Ceftriaxone	1	1
Ciprofloxacin	6	5
Clindamycin	17	6
Cotrimoxazole	7	12
Erythromycin	11	12
Gentamycin	10	1
Imipenem	2	0
Linezolid	14	0
Meropenem	0	0
Nitrofurantoin	11	2
Penicillin	1	21
Teicoplanin	5	0
Tigecycline	9	0
Vancomycin	15	0
Piperacillin	0	0
Cefoperazone	0	0
Cefuroxime	0	0
Amoxyclav	4	5

Fig.2 Age-wise distribution of febrile cases based on culture results

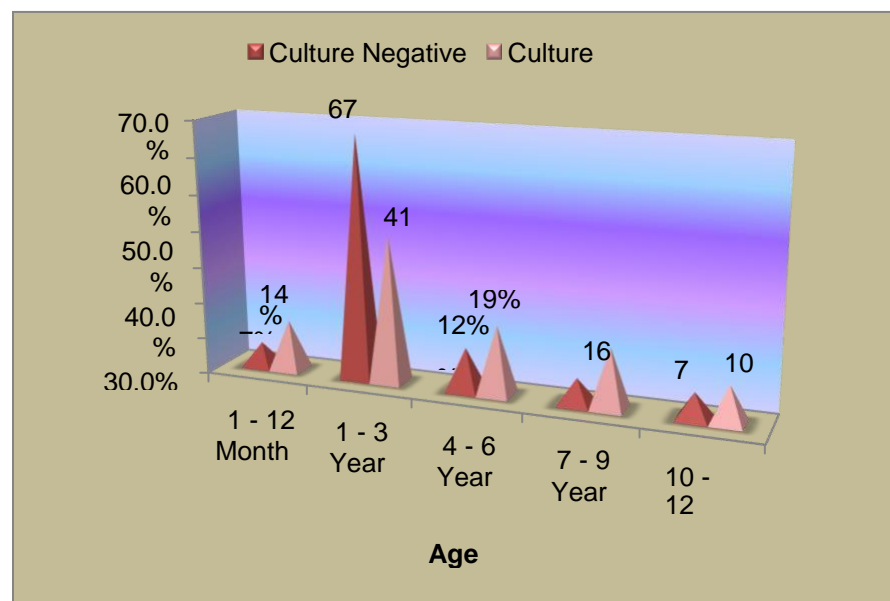


Table.7 Antibiotic susceptibility pattern of the Gram-negative bacilli

Antibiotics	<i>Escherichia coli</i>		<i>Klebsiella pneumoniae</i>		<i>Enterobacter cloacae</i>	
	S	R	S	R	S	R
Amikacin	22	0	6	1	0	0
Ampicillin	6	10	0	5	0	0
Cefepime	11	9	3	5	1	0
Ceftriaxone	9	11	2	4	1	0
Ciprofloxacin	14	9	5	2	1	0
Cotrimoxazole	5	13	2	3	1	0
Erythromycin	5	0	0	1	0	0
Gentamycin	19	5	5	2	1	0
Imipenem	27	0	7	0	0	0
Meropenem	17	0	3	0	0	0
Nitrofurantoin	8	1	1	3	0	0
Tigecycline	14	0	3	0	0	0
Piperacillin	0	0	4	3	1	0
Cefoperazone	5	0	1	0	0	0
Cefuroxime	6	8	1	4	1	0
Amoxyclav	7	5	2	6	0	1

Table.8 Antibiotic susceptibility pattern of the Non-fermenting Gram-negative bacilli

Antibiotics	<i>Salmonella typhi</i>		<i>Pseudomonas aeruginosa</i>		<i>Proteus mirabilis</i>	
	S	R	S	R	S	R
Amikacin	1	2	0	3	0	2
Ampicillin	2	1	0	0	0	0
Cefepime	2	1	0	3	0	2
Ceftriaxone	2	1	0	0	0	0
Ciprofloxacin	0	3	0	0	0	0
Cotrimoxazole	3	0	0	3	0	2
Erythromycin	2	0	0	0	0	0

Gentamycin	1	2	0	3	0	2
Imipenem	3	0	0	0	2	0
Meropenem	6	0	0	0	0	0
Nitrofurantoin	1	1	0	0	0	0
Tigecycline	3	0	0	0	0	0
Piperacillin	2	1	2	1	2	0
Cefoperazone	2	1	0	0	0	0
Cefuroxime	2	1	2	1	0	0
Amoxyclav	2	1	1	0	0	0

Fig.3 Age-wise distribution of culture positive cases of febrile illnesses based on Gram's stain

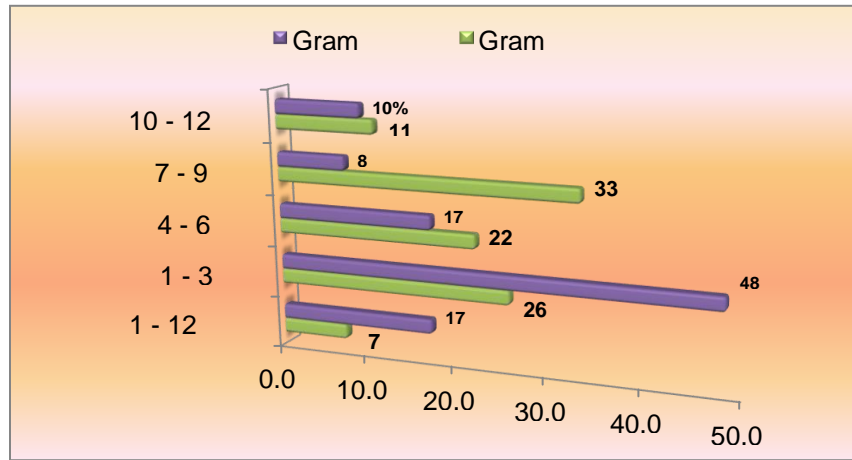


Fig.4 Sex-wise distribution of culture positive cases of febrile illnesses based on Gram's stain

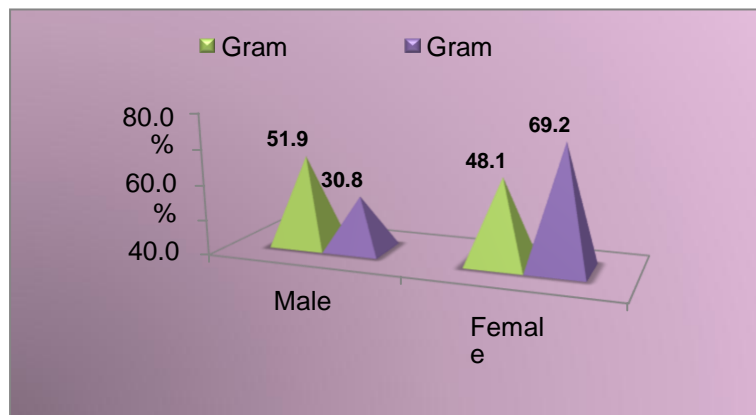


Fig.5 Distribution of culture positives in different samples

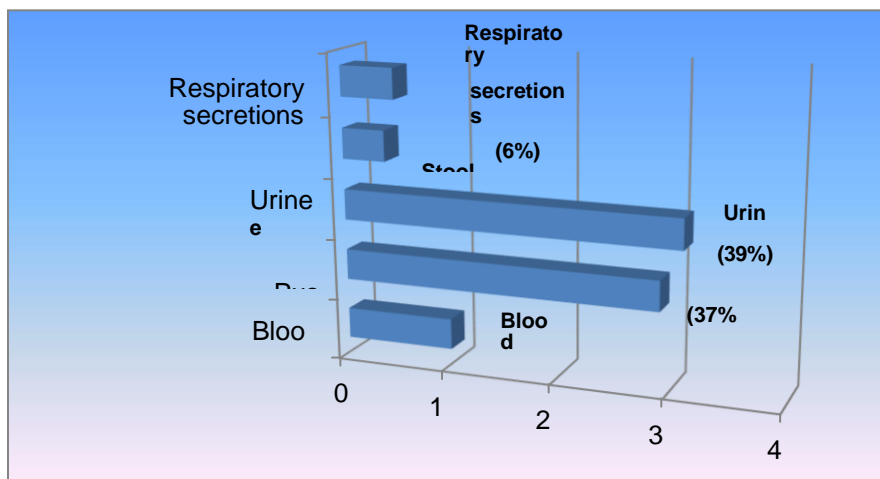
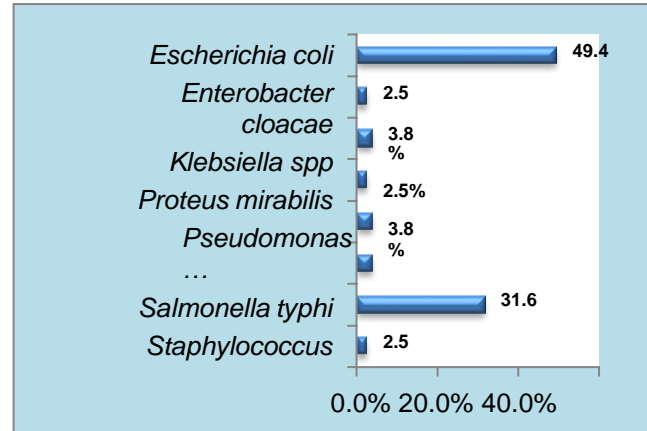


Fig.6 Distribution of organisms in all samples



The evaluation of young febrile children is a major management dilemma worldwide and has attracted considerable research and policy attention. Febrile illness is the single most common reason for young children to be seen by primary care practitioners and to present to emergency departments for acute care. Parental anxiety over fever is common. There is a need for an accurate acute clinical decision making tool that takes into account all the signs and symptoms along with the laboratory investigations associated with serious causes of febrile illnesses.

In the present study, an attempt was made to study the bacterial agents causing febrile illnesses in children between 1 month to 12 years of age and antibiotic susceptibility of the isolates. The results obtained in this study were compared and analysed with other previous

studies. It was noted that febrile illnesses was highest among the younger age group of 1 year-3 years and majority of children suffering from febrile illnesses, the bacterial growth was seen in 79 samples (culture positivity was observed to be 15%). Similarly, Kheng Chheng *et al.*,⁽¹¹⁾ in a prospective study of febrile illnesses requiring hospitalization in children in Cambodia

(2013) observed that the median (IQR) age was 2.0 (0.8–6.4) years, whereas Johnson *et al.*⁽¹²⁾ in a prospective cohort study in Northern Tanzania (2013), observed out of the 870 febrile admissions to two hospitals in Northern Tanzania enrolled in the study, 484 (55.6%) were females and among the participants, 467 (53.7%) were infants.

On Gram staining, 27 samples (34.2%) were found to be Gram-positive and 52 samples (65.8%) were found to be Gram-negative. Majority of the samples from Gram-negative belonged to the age group of 1-3 years. In case of Gram-positive, more samples belonged to the age group 7-9 years (33%). Most of the isolates belonged to the age groups of 1 year-3 years and 4-6 years and 7-9 years. *E.coli* (56.3%) followed by *S.aureus* (21.9%) and *Salmonella typhi* (9.4%) were the most common isolates in the younger age group (1 year-3 years) whereas *S.aureus* (53.8%) followed by *E.coli* (30.8%) predominated the older age group (7-9 years). Similar observations were also made by Robson *et al.*,⁽¹³⁾ who found that 56.7% of those affected were males and 43.3% were females. Blood (47%) sample was found to be the most common sample. Among 10 positive blood samples, the most common organisms isolated was *S.aureus* (40%) followed by

S.typhi (30%). In a similar study, Samuel et al.⁽¹⁴⁾ in a hospital based retrospective analysis of blood cultures from infants to children up to 14 years of age with preliminary diagnosis of sepsis in Tamale teaching hospital observed Gram positive cocci (GPC) were the predominant isolates with Coagulase positive (32.2%) and Coagulase- negative (28.7%). *Staphylococci* account for 60.9% of the total isolates. Gram negative rods (GNR) comprised 39.1% of all isolates with *Klebsiella*, *E.coli* and *Salmonella* being the most common organisms isolated.

Staphylococcus aureus showed high level resistance to Penicillin (63.6%) whereas they were sensitive to Vancomycin (45.45%) which are in accordance to the study of Rahbar et al.⁽¹⁵⁾ found that *S. aureus* were resistant to penicillins (82.6%) but sensitive to Cotrimoxazole and Vancomycin. In this study, *E.coli* showed high resistance to Cotrimoxazole (46.4%), Ceftriaxone (39.3%) and showed sensitivity to Amikacin (78.57%) whereas *Klebsiella pneumoniae* showed similar trends except that it was also resistant to Amoxicillin- Clavulanic acid (60%). *Salmonella typhi* showed high resistance to Amikacin (21.4%), while it showed sensitivity to Imipenem (78.57%) and all these results agreed to the results of Usha

Arora et al.,⁽¹⁶⁾ in their study also found that most of the GNB were multidrug resistant. Resistance was especially high to Ampicillin (89.96%) and low in respect to Amikacin (25%) which is similar to our study. However, in their study, they did not test the sensitivity pattern in higher antibiotics like Carbapenem, Tigecycline and Colistin hence their sensitivity pattern could not be compared. Fluit et al.,⁽¹⁷⁾ also found that aminoglycosides provided good coverage to all the Enterobacteriaceae, with atleast 93.4% of isolates being sensitive to them.

In conclusion there is urgent need for strict aseptic precautions on part of the community and health care workers in order to curb the fast growing incidence of febrile illnesses. Efforts should also be made to decrease the duration of hospital stay of children. It is thus concluded that in order to bring down the fast developing antibiotic resistance, rational and judicious use is essential according to the antibiotic resistance pattern of that particular institution. Frequent hand washing and good aseptic techniques should be reinforced for all health care personnel. A regular epidemiological study of blood culture isolates and determination of susceptibility to antibiotics is necessary in order to guide the clinicians to and choose the appropriate empirical therapy and switch over to the best regime based on the antibiotic susceptibility pattern to improve the overall outcome of the patient's health.

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How to cite this article:

Krishna Agarwal, Jyotsna Kapil and Pilli Hema Prakash Kumari. 2020. Study of Bacterial Agents Causing Febrile Illnesses in Children between 1 Month to 12 Years of Age in a Tertiary Care Hospital in Sikkim. *Int.J.Curr.Microbiol.App.Sci.* 9(10): 1310-1323.
doi: <https://doi.org/10.20546/ijcmas.2020.910.158>