International Journal of Contemporary Pediatrics
Thaddanee R et al. Int J Contemp Pediatr. 2017 Nov;4(6):2103-2108
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20174740

Original Research Article

Antibiotic sensitivity pattern of pathogens in children with urinary tract infection in a tertiary care hospital in Kachchh, Gujarat, India

Rekha Thaddanee[1], Gurudas Khilnani[2], Nupur Shah[3], Ajeet Kumar Khilnani[4]*

[1]Department of Paediatrics, Gujarat Adani Institute of Medical Sciences, Bhuj, Kachchh, Gujarat, India
[2]Department of Pharmacology, Gujarat Adani Institute of Medical Sciences, Bhuj, Kachchh, Gujarat, India
[3]Final year MBBS student, Gujarat Adani Institute of Medical Sciences, Bhuj, Kachchh, Gujarat, India
[4]Department of Otorhinolaryngology, Gujarat Adani Institute of Medical Sciences, Bhuj, Kachchh, Gujarat, India

Received: 11 August 2017
Accepted: 09 September 2017

***Correspondence:**
Dr. Ajeet Kumar Khilnani,
E-mail: ajeetkhilnani@gmail.com

ABSTRACT

Background: This prospective observational study was conducted in a tertiary care hospital in Kachchh, over a period of 6 months, to know the antibiotic sensitivity pattern of pathogens in children less than 18 years old with Urinary Tract Infection (UTI).
Methods: Between December 2016 to June 2017, 186 children met the inclusion criterion. Urine samples were collected and processed for urine routine microscopy, culture and antibiotic sensitivity as per the standard laboratory guidelines. Urine culture was positive in 50 cases, which were further evaluated to find out any renal disease. All patients were given 10-14 days antibiotics course and follow-up urine reports were done. Patients were considered cured when the follow-up urine reports were normal.
Results: *E. coli* was the commonest organism (34%) isolated, found mainly in 1-5 years age group (20%). *Enterococci* were isolated in 32% cases, most of which were less than 5 years of age (28%). *Klebsiella* (12%), Methicillin Resistant Staphylococcus Aureus (MRSA) (10%), Coagulase negative staphylococci (6%), Pseudomonas (2%) and Budding yeast cell (4%) were the less frequent organisms isolated. *E. coli* were found to be less sensitive to different Aminoglycosides (11.7% - 23.5%), Cephalosporins (11.7% - 52.9%), Fluoroquinolones (5.8% - 11.7%), Co-trimoxazole (17.6%) and Piperacillin (17.6%), but were more sensitive (70.6%) to Imipenems. *Enterococci* were also partially sensitive to Aminoglycosides (6.2-18.7%), Cephalosporins (25-37.5.7%), Fluoroquinolones (6.25-12.5%), Penicillin-G (50%), Piperacillin (31.25%) and Co-trimoxazole (43.75%), but had good sensitivity for Imipenems (68.7%), Linezolid (75%) and Vancomycin (81.2%). Similarly, *MRSA* was 100% sensitive to Linezolid and Imipenem but partially sensitive (20-60%) to other antibiotics. *Klebsiella* showed 16.65-33.3% sensitivity to all antibiotics except Imipenem (83.3%) and was 100% resistant to Co-trimoxazole. Coagulase negative *Staphylococci* (CONS) remained 100% sensitive to all antibiotics and *Pseudomonas* was resistant to all antibiotics.
Conclusions: The study concludes that pathogens for UTI in children have developed resistance, even to the newer generation antibiotics, probably due to the irrational use of antibiotics. In view of emergence of multi drug resistant pathogens, which carry considerable morbidity and mortality, every effort must be taken to use antibiotics judiciously.

Keywords: Antibiotic sensitivity, Resistance, Urinary tract infection

INTRODUCTION

Urinary Tract Infection (UTI) is a common disease in pediatric practice. Early diagnosis and prompt treatment can reduce the risk of renal scarring and its long-term sequelae such as hypertension and end stage renal failure.[1]

UTI is the term applied to all conditions, irrespective of localization of infection, characterized by invasion of urinary tract with pathogens and associated with the presence of significant bacteriuria. Significant bacteriuria means colony count $>10^5$ colony forming units (CFU)/ml of single species on clean catch specimen and >50,000 CFU/ml in transurethral specimens.[2]

Adequate treatment of acute UTI depends on knowledge of the local pattern of causative pathogens, their antimicrobial resistance and the associated underlying risk factors. The changing pattern of antimicrobial susceptibility of bacterial pathogens causing acute UTI is a growing problem. Consequently, many organisms including those causing acute UTI may ultimately develop high resistance to many antibiotics in current use. Moreover, organisms not known to be common in causing acute UTI may emerge as important causative pathogens. Therefore, the knowledge of the local pattern of urinary pathogens and their susceptibility to various antimicrobials are essential for selection of the appropriate empiric therapy for children with acute UTI.[3,4]

METHODS

The present study was carried out at a tertiary care teaching hospital at Bhuj, Kutch (Gujarat) for a period of 6 months from December 2016 to June 2017. In this prospective study, 186 children, less than 18 years of age, diagnosed with UTI were included, after obtaining written informed consent from parents/guardians. IEC approval was taken before starting this study.

Inclusion criteria

- Children with complaints of burning micturition, straining, poor urinary stream, dribbling, frequency, change in urine color, urgency, change in urine odor, blood in urine, and diurnal incontinence
- Children with fever without a discernible cause and failure to thrive, where no other cause is ascertained.

Exclusion criteria

- Critically ill children with diabetic ketosis, coexistence of any other systemic disorder requiring close monitoring
- Those children for whom consent was not given by the parents.

Once a child was selected for the study a detailed history and clinical examination were performed with emphasis on the present and past urinary complaints.

Urinalysis

To get a clean uncontaminated urine sample, precautions were taken. In girls, labia were separated and introitus was washed with plain water. In boys, the prepuce was retracted and glans cleaned beforehand.

Only midstream urine was used for routine urine examination and culture sensitivity testing. 50 ml of urine collected in a sterile container, was examined grossly for turbidity, color and sediment, pH, sugar and protein (albumin). About 10 ml sample was centrifuged at 5000 RPM and the supernatant discarded. The remaining 0.5 ml was placed on a slide and examined under high power (X 100) objective of microscope to find out pus cells, casts, debris, epithelial cells, RBCs, crystals and microbes.

Urine culture and sensitivity

Uncentrifuged sample was subjected to culture and sensitivity. The culture was done as early as possible (within 2 hours of collection) on 5% blood agar, nutrient agar and MacConkey agar. Antibiotic susceptibility testing was done by modified Kirby-Bauer disc diffusion method as per the National Committee recommendations.[5,6] As per the protocol followed by Microbiology Department, a battery of antibiotic discs was used, depending on the gram staining nature of bacteria grown. At least 10 antibiotic discs were used for finding antibiotic susceptibility.

Other tests done were routine blood investigations, flat plate abdomen X-Ray and abdominal ultrasound to delineate anatomical details of urinary system. MCU and DMSA scans were performed in certain cases if required.

In this study, urine culture was positive in 50 patients who were further evaluated for their antibiotic sensitivity patterns.

RESULTS

E. coli was the commonest organism (34%) isolated, predominantly in 1-5 years age group (20%); *Enterococci* were revealed in 32% cases, mostly in <5 years age (28% cases); *Klebsiella* were isolated in 12% cases, mainly in 1-12 months age group (6%).

MRSA and CONS were isolated in 10% and 6% cases respectively; *Pseudomonas* was isolated in a single case of 1-12-month age group; Budding yeast cells were isolated from 4% cases, of which 2% were newborns and 2% between 1 and 2 years age group.

Table 1: Age and sex wise distribution of pathogenic organisms.

Age	Pathogens											
	E. Coli (%)		*Enterococci* (%)		*Klebsiella* (%)		*MRSA* (%)		*Pseudomonas* (%)		*CONS* (%)	
	M	F	M	F	M	F	M	F	M	F	M	F
<1 month*		2	2	2								
1-12 months	2	4	2	4	6			2		2		2
1-2 years	6			6				4			2	2
2-5 years	4	10	6	6		4	2					
5-18 years	4	2	2	2	2			2				
Total	16	18	12	20	8	4	2	8	0	2	2	4

* In 4% patients yeast was cultured

Table 2: Sensitivity patterns of the pathogens to Aminoglycosides.

Aminoglycosides	Pathogen											
	E. coli (n=17) Number (%)		*Enterococci* (n=16) Number (%)		*Klebsiella* (n=6) Number (%)		*MRSA* (n=5) Number (%)		*Pseudomonas* (n=1) Number (%)		*CONS* (n=3) Number (%)	
	S	R	S	R	S	R	S	R	S	R	S	R
Gentamicin	4 (23.5)	13 (76.4)	3 (18.7)	8 (50)	2 (33.3)	4 (66.6)	-	5 (100)	-	-	3 (100)	-
Amikacin	-	13 (76.4)	1 (6.2)	8 (50)	1 (16.6)	4 (66.6)	-	1 (20)	-	-	-	-
Netilmicin	3 (17.6)	12 (70.5)	4 (25)	9 (56)	2 (33.3)	1 (16.6)	2 (40)	3 (60)	-	1 (100)	3 (100)	-
Tobramycin	2 (11.7)	14 (82.3)	-	1 (6.2)	2 (33.3)	4 (66.6)	-	-	1 (100)	-	-	-

S: Sensitive; R: Resistant

Table 3: Sensitivity patterns of the pathogens to Cephalosporins.

Cephalosporins	Pathogen											
	E. coli (n=17) Number (%)		*Enterococci* (n=16) Number (%)		*Klebsiella* (n=6) Number (%)		*MRSA* (n=5) Number (%)		*Pseudomonas* (n=1) Number (%)		*CONS* (n=3) Number (%)	
	S	R	S	R	S	R	S	R	S	R	S	R
Cefepime	2 (11.7)	1 (5.8)	5 (31.2)	8 (50)	1 (16.6)	5 (83.3)	-	-	-	1 (100)	-	-
Cefixime	3 (17.6)	-	6 (37.5)	7 (43.7)	-	6 (100)	-	-	-	-	-	-
Cefoperazone	2 (11.7)	1 (5.8)	-	4 (25.0)	1 (16.6)	-	-	-	-	1 (100)	-	-
Cefotaxime	9 (52.9)	8 (47.05)	-	-	4 (66.6)	2 (33.3)	-	-	-	-	-	-
Ceftazidime	2 (11.7)	10 (58.8)	-	7 (43.7)	1 (16.6)	5 (83.3)	-	-	-	1 (100)	-	-
Ceftriaxone	2 (11.7)	2 (11.7)	4 (25.0)	8 (50)	2 (33.3)	4 (66.6)	-	-	-	1 (100)	-	-
Cefazolin	-	2 (11.7)	4 (25.0)	7 (43.7)	2 (33.3)	4 (66.6)	-	-	-	-	-	-
Cefalexin	-	-	-	13 (81.2)	-	-	1 (20)	4 (80)	-	-	1 (33.3)	2 (66.6)
Cefoxitine	-	2 (11.7)	4 (25.0)	10 (62.5)	2 (33.3)	4 (66.6)	1 (20)	3 (60)	-	-	1 (33.3)	1 (33.3)

Enterococci were found to be associated with UTI more commonly in females (20%); *E. coli* was equally seen in both genders.

All organisms were showed resistance to the most of Aminoglycosides, which are the common drugs used in UTI. Only 11.7%-23.5% *E. coli*, 6.2%-18.7% *Enterococci*, 16.6%-33.3% *Klebsiella* and 40% MRSA isolates were sensitive to Aminoglycosides. Interestingly, CONS were 100% sensitive to Aminoglycosides. *Pseudomonas* was resistant to Netilmicin but showed sensitivity to Tobramycin.

Table 4: Sensitivity patterns of the pathogens to Fluoroquinolones.

Fluoroquinolones	Pathogen											
	***E. coli* (n=17) Number (%)**		***Enterococci* (n=16) Number (%)**		***Klebsiella* (n=6) Number (%)**		***MRSA* (n=5) Number (%)**		***Pseudomonas* (n=1) Number (%)**		***CONS* (n=3) Number (%)**	
	S	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Norfloxacin	-	17 (100)	-	-	-	6 (100)	-	-	-	-	-	-
Ciprofloxacin	1 (5.8)	16 (94.1)	2 (12.5)	14 (87.5)	2 (33.3)	4 (66.6)	3 (60)	2 (40)	-	1 (100)	3 (100)	-
Ofloxacin	2 (11.7)	15 (88.2)	1 (6.25)	15 (93.7)	2 (33.3)	4 (66.6)	-	-	-	1 (100)	-	-
Gatifloxacin	-	-	1 (6.25)	15 (93.7)	-	-	-	-	-	-	-	-
Nalidixic acid	-	15 (88.2)	-	-	-	6 (100)	-	-	-	-	-	-

Table 5: Sensitivity patterns of the pathogens to other antibiotics.

Other Antibiotics	Pathogen											
	***E. coli* (n=17) Number (%)**		***Enterococci* (n=16) Number (%)**		***Klebsiella* (n=6) Number (%)**		***MRSA* (n=5) Number (%)**		***Pseudomonas* (n=1) Number (%)**		***CONS* (n=3) Number (%)**	
	S	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Linezolid	-	-	12 (75.0)	4 (25.0)	-	-	5 (100)	-	-	-	3 (100)	-
Vancomycin	-	-	13 (81.2)	3 (18.75)	-	-	2 (40)	3 (60)	-	-	3 (100)	-
Penicillin-G	-	-	8 (50.0)	8 (50.0)	-	-	1 (20)	4 (80)	-	-	-	-
Piperacillin	3 (17.6)	14 (82.3)	5 (31.25)	11 (68.7)	1 (16.6)	5 (83.3)	-	-	-	1 (100)	-	-
Imipenem	12 (70.5)	5 (29.41)	11 (68.7)	5 (31.25)	5 (83.3)	1 (16.6)	5 (100)	-	-	1 (100)	-	-
Co-trimoxazole	3 (17.6)	14 (82.3)	7 (43.75)	9 (56.25)		6 (100)	-	5 (100)	-	-	-	-

Most of the organisms showed resistance to commonly used oral Cephalosporins; Cefixime and Cefalexin. 11.7%-52.9% *E. coli*, 25%-37.5.7% *Enterococci*, 16.6%-66.6% *Klebsiella*, 20% *MRSA* and 33.3% *CONS* isolates were sensitive to most of the Cephalosporins. *Pseudomonas* was 100% resistant to Cephalosporins.

The common pathogens, *E. Coli* and *Enterococci*, were resistant to most of the Fluoroquinolones. Only 5.8%-11.7% *E. coli*, 6.25%-12.5% *Enterococci*, 33.3% *Klebsiella* and 60% *MRSA* isolates were sensitive to most of the Fluoroquinolones. CONS were sensitive to Fluoroquinolones, while *Pseudomonas* was resistant to Fluoroquinolones.

E. coli showed 70.5% sensitivity to Imipenem, only partial sensitivity to Pipericillin (17.6%) and Co-trimoxazole (17.6%). Most of Enterococci were sensitive to Imipenem (68.7%), Linezolid (75%) and Vancomycin (81.2%); partially sensitive to Penicillin-G (50%), Piperacillin (31.25%) and Co-trimoxazole (43.75%).

Klebsiella showed sensitivity to Imipenem (83.3%), but were resistant to Co-trimoxazole. *MRSA* were 100% sensitive to Linezolid and Imipenem. *CONS* were 100% sensitive to Linezolid and Vancomycin.

DISCUSSION

Although *E. coli* is the commonest organism isolated in the present study (34 % cases), the prevalence is low as compared to some other studies such as that of Rai et al and Bagga et al, where they found *E. coli* in 93.3% and 90% of cases respectively.[7,8] However, some studies, such as, Ashteiani H et al (38.6%), Ejaz et al (37%), Akram M et al (21.4%), have shown less prevalence of *E. coli* as compared to the present study.[9-11]

In the present study, *E. coli* showed less sensitivity to Aminoglycosides (11.7%-23.5%), Cephalosporins (11.7%-52.9%), Fluoroquinolones (5.8%-11.7%), Co-trimoxazole (17.6%) and Piperacillin (17.6%) but was 70.6% sensitive to Imipenems. The sensitivity pattern varies with the local prevalent level of resistance and extent of use of a particular drug. In 2002, Amikacin was the most sensitive drug for *E. coli*, but now in 2017, Imipenem has replaced it. High sensitivity of *E. coli* to Imepenem has also been documented by Patel et al (100%), Gupta et al (96%) and Sharan et al (58%).[12-14]

In present study, the pathogens which were commonly seen below 1 month of age were either Enterococci (2 cases) or *E. coli* (1 case). These neonates were in septicemia with intravenous lines that predisposed them to Enterococcal infection. Gokce et al studied 513 children (newborn to 16 years of age) and reported Enterococci in 2.9% cases.[15] Taneja et al studied 1974 children <12 years of age and found Enterococci in 8.7% cases.[3] Mortazavi F et al studied 232 children from 2 months to 14 years of age and isolated Enterococci in 2.2% cases.[16] Enterococci belong to Lancefield group-D pathogens, resemble streptococci and tend to cause UTI in debilitated and hospitalized individuals. Enterococci are a frequent cause of UTI in patients with intravascular line. The ability to form biofilms facilitates the colonization of urinary and vascular catheters, according to Sing-Naz N et al.[17] The reason why Enterococcal UTI occurs more commonly in females is because of proximity of the urethra to anal canal with more chances of retrograde movement of bacteria into lower urinary tract.[17] Use of superabsorbent diapers and faulty toilet training can lead to infection of urinary tract with fecal organisms as *E. coli* and *Enterococci*.

According to Subbalaxami et al, Enteroccocal infection is increasingly reported in hospital settings from India.[18] These isolates are reported to be sensitive to Vancomycin and Ampicillin. In the present study, Enterococci was more sensitive to Vancomycin (81.2%), Linezolid (75%) and Imipenem (68.7%) and partially sensitive to Aminoglycosides (6.25-18.7%), Cephalosporins (25%-37.5.7%), Fluoroquinolones (6.25%-12.5%), Penicillin-G (50%), Piperacillin (31.25%) and Co-trimoxazole (43.75%).

In present study, *Klebsiella* were isolated in 12% cases, mainly in 1-12 months age group (6%). Majority of *Klebsiella* infections now occur in long-term-care facilities and hospitals. *Klebsiella* infection at any site can result in bacteremia. Infection of urinary tract accounts for 15%-30% of *Klebsiella* bacteremia. Ashteiani H et al and Gokce et al found *Klebsiella* in 17.2% and 22.5% of cases respectively.[9,15]

It has been shown in a study from a tertiary care hospital, Karnataka, that 50% of *E. coli* and *Klebsiella* strains are resistant to commonly used anti gram negative antibacterials.[19]

MRSA was isolated in 10% cases in present study. Of these, 6% cases were in 1-5 years age group. *CONS* were isolated in 6% cases of 6 to 24 months age groups. Wattal et al reported high prevalence of MRSA (35% cases) in wards and (43% cases) in ICU, which were sensitive to Vancomycin, Linezolid and newer antibacterial such as Daptomycin.[20] In the present study MRSA was 100% sensitive to Linezolid and Imipenem but partially sensitive (20%-60%) to other antibiotics.

These results show that there is a threat of emergence of multidrug resistant Enterobacteriaceae organisms. The resistance is purported to be due to production of Extended Spectrum Beta Lactamases (ESBLs) by this group of pathogens. ESBLs confer resistance to all the beta-lactam antibiotics except Carbepenem. There is a also cross resistance to Sulphonamides, Fluoroquinolones and Aminoglycosides.[21] This means very limited number of antibiotics are available at our disposal.

CONCLUSION

This study concludes that pathogens causing UTI have developed resistance, even to the newer generation antibiotics, probably due to the overuse of antibiotics. In view of emergence of multi drug resistant pathogens, which carry considerable morbidity and mortality, every effort must be taken to curtail these pathogenic infections. Some of the measures suggested are:

- Proper antibiotic selection based on culture and sensitivity
- Optimizing antimicrobial use by antibiotic stewardship
- Formulation of standard treatment protocols for infections
- Developing hospital infection control program
- Avoiding antimicrobial fixed dose combinations.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Hellersteim S. Urinary tract infection, old and new concepts. Pediatr Clin North Am. 1995;42(6):1433-57.
2. Shrivastava RN, Bagga A. Urinary Tract Infection. In; Paediatric Nephrology. 4th edition, New Delhi. Jaypee Brothers; 2005:235-64.
3. Taneja N, Chatterjee SS, Singh M, Singh S, Sharma M. Paediatric urinary tract infection in a tertiary care centre from north india. Indian J Med Res. 2010;131:101-5.
4. Sharan R, Kumar D, Mukherjee B. Bacteriological and antibiotic resistance pattern in community acquired urinary tract infection. Indian Pediatr. 2013;50:707.
5. Friedman S, Reif S, Assia A, Levy I. Clinical and laboratory characteristics of non *E. coli* urinary tract infections. Arch Dis Child. 2006;91(10):845-6.
6. Gafencu M, Doros G, Sandru R, Serban M. Investigational limit and multi-drug resistance among children's urinary tract infection-our recommendations. Pediatr J. 2007;10:39-40.
7. Rai GK, Upreti HC, Rai SK, Shah KP, Shrestha RM. Causative agents of urinary tract infections in children and their antibiotic sensitivity pattern: a hospital based study. Nepal Med Coll J. 2008;10(2):86-90.
8. Bagga A. Urinary Tract Infection: In: Ghosh TK et al, eds. Speciality series on paediatric infectious diseases. IAP; 2006:138-145.
9. Haghi-Ashteiani M, Sadeghifard N, Abedini1 M, Soroush S, Taheri-Kalanim. Etiology and antibacterial resistance of bacterial urinary tract infection in children's medical centre, Tehran, Iran. Acta Medica Iranica. 2007;45(2):153-7.
10. Ejaz H, Zafar A, Anwar N, Cheema TA, Shehzad H. Prevalence of bacteria in urinary tract infections among children, The Children's Hospital and Institute of Child Health, Lahore. Biomedica. 2006;22:139-42.
11. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in JNMC Hospital Aligarh. Ind An Clin Microbiol Antimicrobials. 2007;6:4.
12. Patel AH, Bhavsar RH, Trivedi P, Mehta SR. Urinary tract infection in children: Clinical profile, bacteriology and antibiotic sensitivity pattern. GCSMC J Med Sci. 2015;(4):75-81.
13. Gupta S, Agarwal R, Bhooshan S, Agrawal A, Goyal A. Urinary tract infection in pediatrics patients in north India. IOSR JODMS. 2013;11(3):58-62.
14. Sharan R, Kumar D, Mukherjee B. Bacteriology and Antibiotic Resistance pattern in Community Acquired Urinary tract infection. Indian Pediatr.2013;50:707.
15. Gokce I, Alpay H, Biyikh N, Ozdemir N. Urinary tract pathogen and there antimicrobial resistance patterns in Turkish children. Pediatric J. 2006;21:1327-8.
16. Mortazavi F, Shahin N. Changing patterns in sensitivity of bacterial uropathogens to antibiotics in children. Pak J Med Sci. 2009;25(5):801-5.
17. Sing-Naz N, Rakowsky A, Cantwell E: Nosocomial enterococcal infection in children. J infect. 2000;40:145-9.
18. Subbalaxami MV, Lakshmi V, Lavalnya V. Antibiotic resistance: experience in tertiary care hospital in south India. JAPI. 2010;58:18-22.
19. Verghese GK, Mukhopadhyaya C, Bairy I, Vandana KE, Verma M. Bacterial organism and antimicrobial resistance pattern. JAPI. 2010;58:23-4.
20. Wattal C, Goel M, Oberoi JK, Ravindran R, Datta S, Prasad KJ. Surveillance of multidrug resistant organisms in a tertiary care hospital in Delhi. JAPI. 2010;58:32-6.
21. Medeiros AA. Evolution and dissemination of betalactamses accelerated by generations of beta lactam antibiotics. Clin Infect Dis. 1997;24(1):S19-45.

Cite this article as: Thaddanee R, Khilnani G, Shah N, Khilnani AK. Antibiotic sensitivity pattern of pathogens in children with urinary tract infection in a tertiary care hospital in Kachchh, Gujarat, India. Int J Contemp Pediatr 2017;4:2103-8.