



Is Empirical antibiotic treatment in UTI justified in resource constraint settings in India

Balamma Sujatha*, Lal D V, Sulochana G

Department of Pediatrics, Saveetha Medical College, Chennai, Tamil Nadu, India

Article History:

Received on: 01 Nov 2019

Revised on: 09 Dec 2019

Accepted on: 06 Jan 2020

Keywords:

Antibiotic resistance,
Community-acquired
ESBL,
Enterococci,
Klebsiella

ABSTRACT

UTI, one of the most common infections noted in children, is reported with incidence of 2% in boys and 8% in girls of less than 8 year. Absence of specific signs of UTI in younger children and increased risk for complications make it almost mandatory to test for UTI in very young children with fever. Fairly common genitourinary tract abnormalities in young children makes it even more important to screen for UTI as it can lead to chronic kidney injury later. Empiric antibiotic treatment in suspected UTI in children is rampant in our community; equally high is the possibility of antibiotic resistance, which is not studied due to cost limitations. Hence the need for identifying the change in microbial flora causing UTI and their changes in resistance pattern at community level, making it an important tool for preventing and addressing the growth issues, complications like CKD, etc. The study aims at addressing this infelt need of the community. Analysis of culture-positive UTI cases referred as suspected UTI from the community for evaluation from April 2017-March 2018 were done. Demographic data, organisms, their susceptibility to common antibiotics prescribed in our community settings were analysed. UTI was common in boys between 1-5 years. The common organism isolated was E.coli and Enterococcus species, followed by Klebsiella in girls and Proteus in males. Nearly 40% of GNB isolates were ESBL producing organisms with E.coli being highest. 70% of E.coli were resistant to commonly used 1stline antibiotics-Ampicillin and cephalexin. 50% of other isolates were resistant to common antibiotics. This may lead to failure of treatment in UTI, leading to long-term complications. Hence empirical antibiotic therapy is not advised even in resource constraint community settings.



*Corresponding Author

Name: Balamma Sujatha
Phone: +91-9677275477
Email: suja1973@gmail.com

ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11iSPL2.2264>

Production and Hosted by

IJRPS | www.ijrps.com

© 2020 | All rights reserved.

INTRODUCTION

Urinary tract infection (UTI) is one of the most common infections worldwide, which can occur in any time in the life of an individual. UTI can affect both lower and upper urinary tract. Lower UTI includes cystitis, urethritis and prostatitis, while upper UTI can affect the ureter or kidney causing pyelitis or pyelonephritis, respectively (Nicolle, 2008).

By the age of seven, 8% of the girls and 2% of the boys will have had UTI (White, 2011). In the first year of life, UTIs are more common in boys and 10 times higher in uncircumcised. The incidence of UTIs, however, falls below 1% in school-aged boys in contrast to its increase by 1-3% in school-aged girls.

Sexual activity increases the risk of UTI in teenage girls (Ronald, 2002).

The classical triad of fever with chills and rigors, suprapubic pain and vomiting occurs only after 5 years (Sargiary et al., 2016). So all the children between 2 and 24 months having a febrile illness should be tested for UTI. The other symptoms seen are dysuria, increased urgency and frequency of voiding (Singh et al., 2015). UTI is said to be complicated when the child presents with high fever, systemic vomiting, dehydration, renal angle tenderness, or raised serum creatinine (Carmeli et al., 2016).

Often, UTIs develop when uropathogens ascend from periurethral colonisations to the bladder (cystitis). From the bladder, uropathogens may ascend the urinary tract (pyelonephritis) or invade the bloodstream (urosepsis), which is a very rare scenario. Uropathogens gain entry through catheterisation, genital manipulation, or turbulent voiding patterns. The susceptibility to UTI depends on the anatomical variances (Vesicourethral reflex, circumcision and gender), bacterial virulence, bowel or bladder dysfunction resulting in urinary stasis (constipation and neurogenic bladder) and host defences (genetics and flora of periurethral and gastrointestinal tracts) (Desai et al., 2016).

E.coli accounts of 85% of the UTI cases in children (Shaikh et al., 2007). Other organisms include Klebsiella, Proteus mirabilis, and Pseudomonas aeruginosa. Enterococci and coagulase-negative Staphylococci are the most frequently implicated gram-positive organisms (Rushton, 1997). Extended-spectrum beta-lactamases (ESBL) producing organisms are now more frequently being isolated from community-acquired UTI (Rawat and Nair, 2010). ESBL are enzymes produced by certain types of bacteria which can break down the beta lactam ring of beta lactam antibiotics, making them ineffective. Bacterial groups known to produce ESBLs include Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Proteus mirabilis, Enterobacter species. Commonly used medications to treat ESBL-involved infections include Carbapenems, Fosfomycin, Nitrofurantoin, Beta-lactamase inhibitors (e.g., Clavulanic acid), non-beta-lactamases, Colistin, if all other medications have failed.

The diagnosis of UTI is based on the growth of a significant number of organisms of a single species in a clean catch sample. The reference standard for suprapubic aspiration specimen, greater than 1,000 colony-forming units/ml; catheter specimen, greater than 10,000 colony-forming units/ml;

clean-catch, midstream specimen, 100,000 colony-forming units/ml or greater (Zorc et al., 2005). The urine specimen is cultured on blood agar and Macconkey agar and quantified (Representatives, 1999) several biochemical tests such as Coagulase, Catalase, Urease, Oxidase, etc. to further identify the organisms.

Since several organisms cause, UTI empiric antibiotic treatment is adopted. Although amoxicillin has traditionally been the first-line antibiotic for UTI, increased rates of E. coli resistance have made it a less acceptable choice. Other choices include amoxicillin/clavulanate or cephalosporins, such as cefixime, cefpodoxime, or cephalexin (Schlager, 2016). Infants and children with complicated UTI should initially receive parenteral antibiotics, which is then followed by oral doses after 48-72 hours (Becknell et al., 2015).

The selection of antibiotics against UTI is done by performing antibiotic sensitivity tests as antimicrobial resistance remains the major problem in the therapy for UTI throughout the world. Fundamental mechanism of antibiotic resistance may be due to enzymatic degradation of antibiotics, alteration of bacterial proteins, or changes in the membrane permeability to antibiotics. Periodic evaluation of pathogens epidemiology is recommended in order to revise treatment advice (Rosello et al., 2017).

MATERIALS AND METHODS

The study was conducted in the Department of Paediatrics Saveetha Hospital over 1 year from April 2017 to end of March 2018, to determine the sensitivity pattern of microorganism causing UTI to commonly used antibiotics in the community and to determine the possibility of effective empirical antibiotic for UTI in resource constraint community setting. Of the 230 children referred to as suspected UTI cases from community, urine cultures were done and 96 culture-positive samples were included for study.

RESULTS AND DISCUSSION

Sex distribution was equal with 48 in each group. In the first year of life, girls were more affected and between 1-5 years, boys were more affected. After that, sex distribution was nearly equal, as in Figure 1.

Commonest organism isolated was GNB (81.25%), followed by GPC.

E.coli was the commonest isolate from both groups, followed by Enterococcus and Klebsiella in females

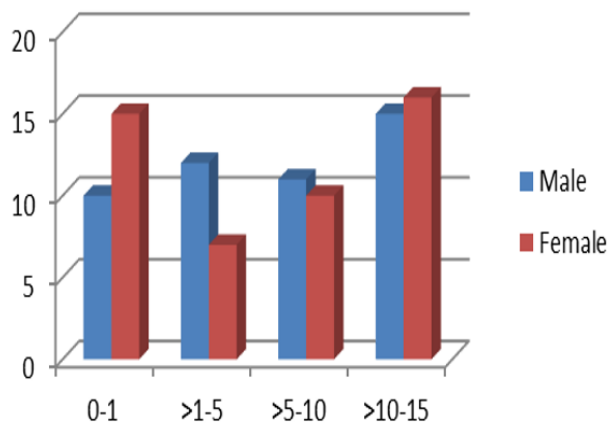


Figure 1: Age and Sex distribution

and Enterococcus and Proteus in males. Distribution of other organisms are as in Figure 2.

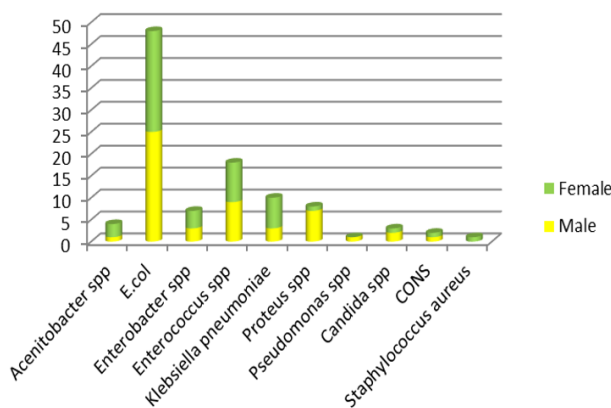


Figure 2: Distribution of isolates with respect to sex

In girls, E.coli infection is prevalent throughout the age spectrum, whereas Enterococcus is more common in the first year of life and later in the 10-15 age group. Klebsiella is common in the age group 1-5 and 10-15, as in Figure 3.

In boys, E.coli is the commonest isolate in all age groups. Enterococcus, followed by Enterobacter, is common in 10-15 age groups- Figure 4.

Of the total of 78 GNB community isolates, 32 (39.7%) were ESBL producing organism. The 41.6% of E.coli and 50% Proteus were ESBL producing organisms- Figure 5.

All GNB isolates in our study except for E.coli are intrinsically resistant to ampicillin and cephalixin. Among the E.coli isolates, 70% of them are also resistant to Ampicillin and Cephalixin. 75% of Klebsiella isolates are sensitive to Cefataxime and Cefuroxime. Proteus is resistant to them. Rest of the GNB isolates are 50% resistant to these antibiotic. Cefaperazone, Cefepime, Piperacillin and Amikacin

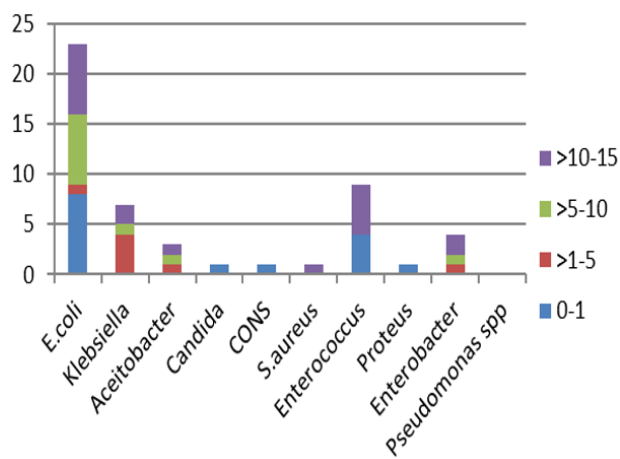


Figure 3: Distribution of organism in girls according to age

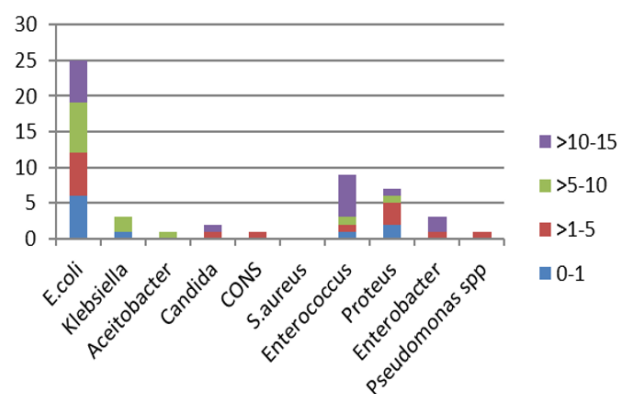


Figure 4: Distribution of organism in boys according to age

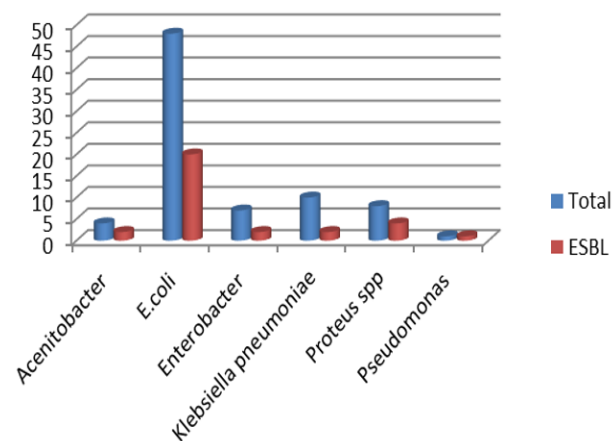


Figure 5: ESBL distribution in various GNB isolates

have a high sensitivity against GNB, ranging from 84-85%.

Acinetobacter has 75% resistance to Norfloxacin and Levofloxacin. 60% of Proteus isolates are resistant to Norfloxacin, 60% sensitive to Levofloxacin. E.coli and Enterobacter isolates are resistant in 40% of the cases. 50% of GNB isolates are resistant to Cotrimoxazole.

75-100% of E.coli, Acinetobacter, Enterococcus and Klebsiella are sensitive to Nitrofurantoin. Proteus and Pseudomonas are intrinsically resistant to it. Imepenem and Meropenem have a high sensitivity of 95% against all GNB isolates. Polymyxin B has 100% sensitivity to GNB except for Proteus, to which it is intrinsically resistant.

Among the Gram-positive organisms, Staphylococcus is 100% sensitive to all the antibiotics tested. CONS isolates were 50% resistant to the currently used first-line of drugs like Ampicillin, cephalixin, cefoxitime and cefotaxime. They are 100% sensitive to Ciprofloxacin, Vancomycin, Linezolid and Nitrofurantoin. Enterococcus, isolates were 100% sensitive to Linezolid and Vancomycin, 70% sensitive to Ampicillin and Nitrofurantoin and 60% sensitivity for Gentamycin and Ciprofloxacin.

Overall we find that Ampicillin, Cephalexin, Cefataxime and Nitrofurantoin can be used for both GNB and GPC infection. 70% GNB and 30% GPC isolates are resistant to Ampicillin and Cephalexin. Cefotaxime is sensitive in 50% GNB and 70% GPC. Nitrofurantoin has 80% sensitivity for both groups, as in Figures 6 and 7.

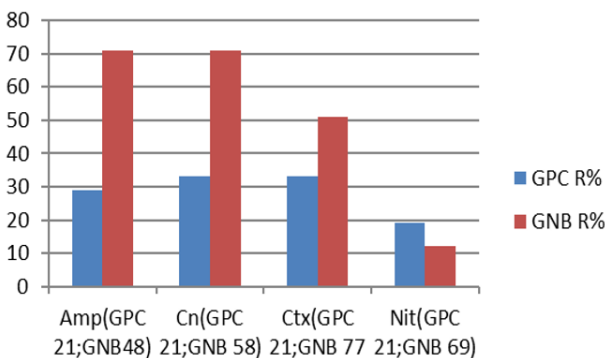


Figure 6: Resistance pattern to commonly used drugs

Imepenem, Meropenem and Polymyxin B have 90-98% and Cefaperazone, Piperacillin, Cefepime and Amikacin have 85-88% sensitivity against GNB. Norfloxacin, Levofloxacin and Cotrimoxazole have 40-50% resistance, as in Figure 8.

In a surveillance study conducted by (Mirsoleymani et al., 2009) from 2009-2012, it was found

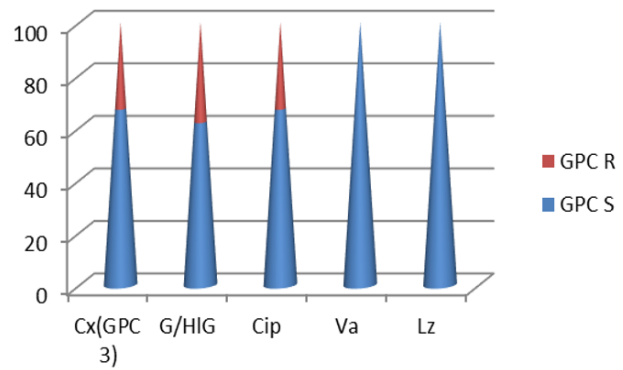


Figure 7: Sensitivity and resistance pattern for GPC

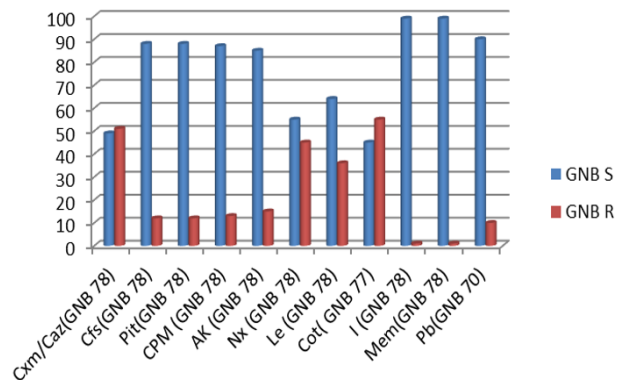


Figure 8: Sensitivity and resistance pattern for GNB

that the predominant agents causing UTI were E.coli (65.2%),Klebsiella spp. (26%), Pseudomonas aeruginosa (3.6%), Staphylococcus- cogulase positive (3.7%). E.coli was more prevalent in females (70.8%) compared to males (60.5%) whilst Klebsiella spp. was observed increasingly in males (28.3%) than females (21.3%) (Mirsoleymani et al., 2009). In the study conducted in north India by Charoo hans et al observed that in infants the organisms commonly found were E.coli, Klebsiella and Candida albicans in constrast to Klebsiella, E.coli and proteus in children less than 12 years (Kaur, 2014). But in our study, we found that community-acquired infection with E coli, Enterococcus species and Enterobacter is almost equitably distributed in males and females. Klebsiella was isolated twice more from girls and Proteus was 90% of time isolated from boys.

(Shrestha et al., 2019) found E coli had 87% resistance to Ampicillin, 62% to Ceftriaxone and Ofloxacin (Shrestha et al., 2019). E coli were sensitive to Amikacin, CPS and Nitrofurantoin 90-100% (Mandal et al., 2015). Meropenem was sensitive in 75% of isolates. Ceftazidime and Ceftriaxone were resistant in 70 and 75% of the isolates, respectively. In our study, 70% E coli isolates were

resistant to Ampicillin and Cephalexin, 50% to Cotrimoxazole, Cefataxime and Cefuroxime. Norflox was resistant in 40% of isolates (Mandal et al., 2015).

In their study, they (Mandal et al., 2015) found that 86% of Klebsiella were sensitive to Nitrofurantoin. Resistance was high to Amikacin, Cefazidime, Meropenem, Cefoperazone, Ceftriaxone, Ciprofloxacin and gentamicin. Whereas in our study, we found that Klebsiella was sensitive to Cefuroxime, Cefataxime and Cefaperazone in 70-80% of isolates. This could be due to the fact that (Mandal et al., 2015) study included children admitted in PICU and pre existing renal disease. Whereas others (Shrestha et al., 2019) found that Klebsiella isolated in their study were resistant to Ceftriaxone, Cotrimoxazole in 40% of cases and 10-20% resistant to Imipenem, Nitrofurantoin and Amikacin.

In our study, Enterobacter isolates were highly sensitive to Amikacin, Cefaperazone, Piperacillin, Nitrofurantoin, Imepenem and Cefipime as in the study done by (Shrestha et al., 2019).

Similar to the study by (Shrestha et al., 2019), we found that gram positive isolates Enterococcus species were 100% sensitive to Vancomycin and Linezolid. 70% were sensitive to Ampicillin and Nitrofurantoin and 50-60% sensitivity to HL Gentamycin and Ciprofloxacin. (Mandal et al., 2015) found in their study that Enterococcus isolates were 96% sensitivity to Nitrofurantoin, 80% to Vancomycin and 62% for ampicillin. With regards to Ciprofloxacin only 25% were sensitive. HL Gentamycin also had similar sensitivity (60%) as our study. However, Nitrofurantoin sensitivity was 90% as against 60% in our study.

Staphylococcus isolates were 100% sensitive to all antibiotics tested like Ampicillin, Cefataxime, HL Gentamicin, Ciprofloxacin, Linezolid and Vancomycin. (Shrestha et al., 2019; Mandal et al., 2015) also found that staphylococcus isolates were 100% sensitive to Nitrofurantoin, Vancomycin and Linezolid. But the rest of the antibiotics tested had varying degrees of resistance from 20% to Amikacin, 60% to Cephalexin, 40% to Ceftriaxone, Cefoxitin and Ofloxacin.

With respect to isolation of ESBL organisms, we found comparable results with the study done by others (Patwardhan et al., 2017) in Northern India, where they found that the prevalence of ESBL isolates was 33.2% in the year 2014. Similarly, (Shrestha et al., 2019) found 40% of the isolates to be ESBL in their study conducted in 2018 in Nepal. This shows there is a high incidence of infection with ESBL producing organisms from the community. This could lead to treatment failure to com-

monly used first-line drugs. The increasing ESBL isolates could be due to Antibiotic abuse in the community since over the counter medications are easily available. Moreover, the use of antibiotics without doing culture and sensitivity for suspected UTI, pneumonia and other infections or noncompliance of antibiotic course lead to this scenario. Hence we find that commonly used first-line antibiotics are no more effective in more than 50% of UTI infections.

CONCLUSION

The organisms which were commonly seen in our settings were Ecoli, enterococcus, Klebsiella. Out of these, there was a high percentage of ESBL producing organisms. Culture and sensitivity pattern showed that they are resistant to common antibiotics prescribed like Amoxycillin, Cephalexin, Cefixime. We report that almost 50% of them are resistant to these antibiotics. This may lead to failure of treatment in UTI, which may lead to long-term complications. Hence empirical antibiotic therapy is not advised even in resource constraint community settings.

REFERENCES

- Becknell, B., Schober, M., Korbel, L., Spencer, J. D. 2015. The diagnosis, evaluation and treatment of acute and recurrent pediatric urinary tract infections. *Expert Review of Anti-infective Therapy*, 13(1):81-90.
- Carmeli, Y., Armstrong, J., Laud, P. J., Newell, P., Stone, G., Wardman, A., Gasink, L. B. 2016. Ceftazidime-avibactam or best available therapy in patients with ceftazidime-resistant Enterobacteriaceae and Pseudomonas aeruginosa complicated urinary tract infections or complicated intra-abdominal infections (REPRISE): a randomised, pathogen-directed, phase 3 study. *The Lancet Infectious Diseases*, 16:661-673.
- Desai, D. J., Gilbert, B., McBride, C. A. 2016. Paediatric urinary tract infections: Diagnosis and treatment. *Australian Family Physician*, 45(8):558-563.
- Kaur, N. 2014. Urinary Tract Infection: Aetiology and Antimicrobial Resistance Pattern in Infants From A Tertiary Care Hospital in Northern India. *Journal of Clinical and Diagnostic Research*, 8(10).
- Mandal, J., Krishnamurthy, S., Barathi, D., Pandit, N., Gupta, P. 2015. Profile of urinary tract infections in paediatric patients. *Indian Journal of Medical Research*, 141(4):473-473.
- Mirsoleymani, S. R., Salimi, M., Brojeni, M. S., Ranjbar, M., Mehtarpoor, M. 2009. Bacterial Pathogens and Antimicrobial Resistance Patterns in Pediatric

- Urinary Tract Infections: A Four-Year Surveillance Study. *International Journal of Pediatrics*, pages 1–6.
- Nicolle, L. E. 2008. Uncomplicated Urinary Tract Infection in Adults Including Uncomplicated Pyelonephritis. *Urologic Clinics of North America*, 35(1):1–12.
- Patwardhan, V., Kumar, D., Goel, V., Singh, S. 2017. Changing prevalence and antibiotic drug resistance pattern of pathogens seen in community-acquired pediatric urinary tract infections at a tertiary care hospital of North India. *Journal of Laboratory Physicians*, 9(04):264–268.
- Rawat, D., Nair, D. 2010. Extended-spectrum β -lactamases in gram negative bacteria. *Journal of Global Infectious Diseases*, 2(3):263–263.
- Representatives, L. 1999. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. *American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. Pediatrics*, 103(4):843–52.
- Ronald, A. 2002. The etiology of urinary tract infection: traditional and emerging pathogens. *The American Journal of Medicine*, 113(1):14–19.
- Rosello, A., Hayward, A. C., Hopkins, S., Horner, C., Ironmonger, D., Hawkey, P. M., Deeny, S. R. 2017. Impact of long-term care facility residence on the antibiotic resistance of urinary tract *Escherichia coli* and *Klebsiella*. *Journal of Antimicrobial Chemotherapy*, (4):dkw555–dkw555.
- Rushton, H. G. 1997. Urinary Tract Infections in Children. *Pediatric Clinics of North America*, 44(5):1133–1169.
- Sargiary, P., Baro, L., Choudhury, G., Saikia, L. 2016. Bacteriological Profile and Antimicrobial Susceptibility Pattern of Community Acquired Urinary Tract Infection In Children: A Tertiary Care Experience. *Journal of Dental and Medical Sciences*, 15(6):61–66.
- Schlager, T. A. 2016. Urinary Tract Infections in Infants and Children. *Microbiology Spectrum*, 4.
- Shaikh, N., Morone, N. E., Lopez, J., Chianese, J., Sangvai, S., D'Amico, F., Hoberman, A., Wald, E. R. 2007. Does This Child Have a Urinary Tract Infection? *JAMA*, 298(24):2895–2895.
- Shrestha, L. B., Baral, R., Poudel, P., Khanal, B. 2019. Clinical, etiological and antimicrobial susceptibility profile of pediatric urinary tract infections in a tertiary care hospital of Nepal. *BMC Pediatrics*, 19(1):36–36.
- Singh, Y. R., Devi, O. P., Singh, T. H. 2015. Clinical and laboratory profile of children birth to 12 years presenting with first urinary tract infection (UTI) at a tertiary care hospital. *Journal of Evolution Of Medical And Dental Sciences-J EMDS*, 4(83):14486–92.
- White, B. 2011. Diagnosis and treatment of urinary tract infections in children. *American family physician*, 83(4).
- Zorc, J. J., Kiddoo, D. A., Shaw, K. N. 2005. Diagnosis and Management of Pediatric Urinary Tract Infections. *Clinical Microbiology Reviews*, 18(2):417–422.