# PREVALENCE OF BREAKTHROUGH URINARY TRACT INFECTION AMONG PATIENT ON PROPHYLACTIC ANTIBIOTICS FOR RECURRENT UTI ON FOLLOW UP AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

A RESEARCH THESIS TO BE SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, PEDIATRICS AND CHILD HEALTH DEPARTMENT IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE SPECIALITY CERTIFICATE PROGRAM IN PEDIATRICS AND CHILD HEALTH.

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ADDIS ABABA, ETHIOPIA

# ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

**I, the undersigned Pediatrics and Child health resident declare that I have submitted my original Paper on the title prevalence of breakthrough urinary tract infection among patient on prophylactic antibiotics for recurrent uti on follow up at tikur anbessa specialized hospital, addis ababa, ethiopia in partial fulfillment of the specialty program.**

**Submitted by:**

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**This proposed work has been submitted with my approval as an advisor,**

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2. **Dr. Bezaye Abebe**

**Co-Advisor name** **Signature** **Date**

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## Acronym

UTI- ……. Urinary Tract Infection

CAKUT----------Congenital Anomalies of Kidney and Urinary tract

VUR----------Vesicoureteral reflux

BBD----------Bladder and Bowel dysfunction

TMP-SMX----------Trimethoprim-sulfamethoxazole

CKD----------chronic kidney disease

ESRD----------End-Stage Renal Disease

BUTI----------Breakthrough Urinary Tract Infection

DMSA----------Dimercaptosusscinic acid

OPD----------Out Patient Department

TASH----------Tikur Anbessa Specialized Hospital

SPSS----------statistical Package for Social Science

USA----------United State of America

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# Acknowledgment

I would like to express my deepest gratitude to Addis Ababa University College of Health Sciences, Department of Pediatrics and Child Health for allocating the budget and giving me the chance to do this research. I would like to express my respect to my advisors Dr. Semhal Getachew and Dr. Bezaye Abebe for their invaluable comments and guidance's throughout this research and their interest and readiness to help me until the end of the study.

**SUMMARY**

**Background:** Urinary tract infections (UTIs) are the most common infectious diseases diagnosed around the globe, particularly in developing countries. It is one of the most common microbial diseases encountered in medical practice. Risk factor for Recurrent UTI can be Anatomic factors, toileting habits, constipation, and other factors may contribute to an elevated risk of reinfection. Vesicoureteral reflux (VUR), urinary obstruction, or bladder and bowel dysfunction (BBD) are some of anatomical factor that predispose to recurrent UTI.

**Objectives:** To assess the prevalence of breakthrough urinary tract infection among patient on prophylactic antibiotics for recurrent UTI on follow up at Tikur Anbessa specialized hospital

**Methods:** This study was conducted using a hospital-based Cross-sectional study design from August 2023 to January 2024 at Tikur Anbessa specialized Hospital Renal, Neurology and Pediatric surgical follow-up unit. The sample size required was 277. Data was entered into Statistical Package for Social Sciences version 25 (SPSS) for subsequent descriptive and analytical statistics where applicable. Statistically, a significant association was taken for a p-value of <0.05.

**Result:** The overall prevalence of BUTI was 27%. The average age was 1-4 years of age and 74.2% were males. 35.3% of the male participant were uncircumcised. The most common indication for prophylactic antibiotic was CAKUT. 69.2% of the children were on prophylactic antibiotic for more than 12 months. 91.2% of the children in the study used trimethoprim-sulfamethoxazole as prophylactic. The most common etiology identified was E.coli (42%). Males that were uncircumcised, neurogenic bladder and urine WBC more than 5 were associated with increased risk for recurrent UTI. 37% of the organism that grew were resistant to more than 3 classes of antibiotics. 70% of the organisms that grew were resistant to trimethoprim-sulfamethoxazole.

**Conclusion:** our finding revealed that there is significant burden of breakthrough UTI and uncircumcised male children, neurogenic bladder are higher risk for breakthrough UTI and there is high resistance pattern for the most commonly used antibiotic in our setup which is Trimethoprim-Sulfamethoxazole

# 1. INTRODUCTION

## 1.1.Background of the study

Urinary tract infection is defined as an infection of the urinary tract that include the upper urinary tract with pyelonephritis up to the lower urinary tract with cystitis. It is usually classified as complicated UTI and uncomplicated UTI. Uncomplicated UTI defined as infection in a structurally and neurologically normal urinary tract and complicated UTI defined as infection in the presence of factors that predispose to persistent or relapsing infection, such as foreign bodies (e.g., calculi, indwelling catheters or other drainage devices), obstruction, immunosuppression, renal failure, renal transplantation, and urinary retention from neurologic disease.

Urinary tract infections are one of the most common infectious disease around the world, especially more common in developing countries. It can occur in children of all age groups, but the prevalence varies with age.

The prevalence of UTI is 1.25 per 1000 live births. Symptomatic and asymptomatic UTIs are seen in 1-2% of school-age and are more common in girls and between the ages of 7 and 11, but they are rare in boys in these age ranges. (2)

In the first year of life, male: female ratio is 2.8: 5.4 but after year of life, there is a female preponderance, with a male: female ratio of 1:10. In males, most UTIs occur during the first year of life; UTIs are more commonly found in uncircumcised males, especially in the first year of life, where the rate is 20% in febrile uncircumcised males under age 1 yr. In females, the first UTI usually occurs by the age of 5 year, with peaks during infancy, toilet training, and onset of sexual activity. (2)

The usual bacteria found include Proteus, Enterococcus, Klebsiella, and Staphylococcus. But the most commonly found bacteria is Escherichia Coli accounting for more than 80% of cases.

UTIs may be suspected based on symptoms or findings on urinalysis, or both; a urine culture is necessary for confirmation (urine culture results of $>10^5$ colony forming units of a single organism/ml of a midstream urine sample).

Risk factor for Recurrent UTI can be Anatomic factors, toileting habits, constipation, and other factors may contribute to an elevated risk of reinfection. vesicoureteral reflux (VUR), urinary obstruction, or bladder and bowel dysfunction (BBD) are some of anatomical factor that predispose to recurrent UTI.

Regarding prophylaxis use, there is still misunderstanding and there is no clear guideline but most recommended prophylaxis in high risk conditions for development of renal scarring or urosepsis (dilated VUR, severe obstruction, recurrent symptomatic UTI, especially with bladder instability or voiding dysfunction and girls with frequent UTIs for symptomatic relief, infective stones(9)

Trimethoprim-sulfamethoxazole (TMP-SMX) 2 mg TMP/kg as a single daily dose or Nitrofurantoin 1 to 2 mg/kg as a single daily dose are some of the commonly used prophylactic antibiotic used as a prevention of recurrent UTI. (14) In our setup we often use Trimethoprim-sulfamethoxazole due to availability and cost.

The use of nitrofurantoin, trimethoprim and sulfamethoxazole is safe in children for long-term prophylactic therapy. (11)

Based on many experts, when using prophylaxis antibiotic it is recommended to not exceed the duration for more than 6 month due to risk of resistance and complication. (15)

Several interventions, other than antibiotic prophylaxis, for the prevention of recurrent UTI have been tried and, although showing some promise, they do not provide so far a definitive effective answer. Cranberry juice appears to be a promising and safe alternative with no serious adverse events. However, its efficacy remains questionable in the pediatric population. Few studies are available on probiotics, but their efficacy is still debated for UTI prevention. Circumcision, a largely popular choice in certain countries, lacks good quality studies to prove its safety, and effectiveness. (10)

## 1.2 Statement of the Problem

Urinary Tract Infection (UTI) is the most common childhood bacterial infection associated with high morbidity and long-term complications like renal scarring, hypertension, and chronic renal Failure. The global prevalence of UTI is 1.25 per 1000 live births. Children who were treated within 3 days of their symptoms starting were one-third as likely to scar as those whose symptoms lasted longer. (12)

In Ethiopia a cross-sectional study done in southern Ethiopia which was published in 2018 showed that UTI accounted for 31.2% of OPD patients. [8] As research shows prevalence of UTI in CAKUT patients reached 64% in which 52% is the obstructive type and 12% non-obstructive type. (4) Recurrent UTI as a result of CAKUT may predispose children to renal scarring, hypertension and CKD, which carries the risk of progression to ESRD requiring renal replacement therapy

## 1.3 Significance of the study

To date, there is a lack of adequate research regarding the occurrence of breakthrough Urinary Tract Infections (UTIs) and the resistance patterns of antibiotics used for prophylactic treatment. This study aims to fill this gap by investigating the prevalence and risk factors associated with breakthrough UTIs, as well as the patterns of antibiotic resistance. The findings of this research will provide valuable insights into the extent of this issue and guide the development of national guidelines for prophylactic antibiotic use in cases of recurrent UTIs.

## 2. Literature Review

Urinary Tract Infection (UTI) poses a global burden, impacting children across the world. Extensive research has been conducted globally, highlighting the significant importance of addressing this issue.

According to metanalysis done on 2008 it was found that out of infants who presented with fever, he overall prevalence of UTI was 7.0%. Among those febrile male infants less than 3 months of age, 2.4% of circumcised males and 20.1% of uncircumcised males had a UTI. Among older children (<19 years) with urinary symptoms, the pooled prevalence of UTI (both febrile and afebrile) was 7.8%. The conclusion of the study was prevalence rates of UTI varied by age, gender, race, and circumcision status. Uncircumcised male infants less than 3 months of age and females less than 12 months of age had the highest baseline prevalence of UTI. (1)

Another cross-sectional study done in Iran showed the prevalence of UTIs was higher in girls (77.2%). The highest prevalence of UTIs was in the age group of 0-1 years (38.6%). In this study, 79.8% of the participants in the non-infected group were breastfed. There was a significant relationship between breastfeeding and not getting a UTI.(2)

Another systematic review done on 2013 showed that, up to 11% of girls and 7% of boys will have had a urinary tract infection (UTI) by the age of 16 years, and recurrence of infection is common. It also showed that Vesicoureteric reflux (VUR) is identified in up to 40% of children being investigated for a first UTI, and it is a risk factor for, but weak predictor of, renal scarring. Another finding on this study was that prophylactic antibiotics may be more effective than placebo at reducing the risk of recurrent UTI; however, they may increase microbial resistance to the prophylactic drug. The final finding on this study was Nitrofurantoin appears to be more effective than other prophylactic antibiotics, but this is balanced by the increased risk of side-effects and treatment drop-out(3)

In a retrospective descriptive study done in Iran on resistance pattern of breakthrough UTI in children on antibiotic prophylaxis, showed that 57 patient had breakthrough UTI. Of which sixty-one percent of them were female and the mean age was 4.2 years. The duration of prophylaxis was 1-2 month for half of the children. The commonest indication for prophylaxis was vesicoureteral reflux followed by neurogenic bladder.

The commonest organisms identified were E.coli, staphylococcus saprophyticus, Pseudomonas species, Enterobacter species and Klebsiella species. The most common antibiotic prophylaxis agent used were cefixime and cephalexin. 59 of the patients with organisms that were resistant to the prophylactic antibiotic that they were using (14)

In a Prospective Cohort done in Indonesia on 2018, showed that the prevalence of UTI in CAKUT patients reached 64% in which half of them had obstructive type and 12% non-obstructive type. Pelvic ureteric junction obstruction was the commonest cause. Children with known urinary tract problems such as CAKUT were very prone to developing recurrent UTI. And it also showed that E. coli was the most common isolated organism(4)

Another research done in Duke University, USA, on incidence of Breakthrough UTI in hospitalized infant taking prophylactic Antibiotic showed, 60 infants (9.5%) suffered a total of 65 BUTIs. Of all prophylactic antibiotic courses, 65/821 (7.9%) were complicated by BUTI. Klebsiella, Enterobacter, and Escherichia coli species were the most common causes of BUTI. There was no statistically significant difference in BUTI incidence among the four antibiotics assessed (amoxicillin, cephalexin, nitrofurantoin, or trimethoprim-sulfamethoxazole) ($p=0.78$) (5)

Another single center cohort study done on Risk factors for breakthrough urinary tract infection in children with vesicoureteral reflux receiving continuous antibiotic prophylaxis showed BT-UTI occurred in 81 out of 256 children with grade I–V VUR who received CAP, an incidence of 31.64%. It also showed that younger age at the initial diagnosis of UTI, bilateral VUR, renal scarring on the dimercaptosuccinic acid (DMSA) scan at the initial diagnosis of UTI and BBD were correlated with the occurrence of BT-UTI. Multivariate analysis showed that younger age at the initial diagnosis of UTI, bilateral VUR and BBD were independent risk factors for the occurrence of BT-UTI(6)

When we come to our continent there was a systematic review published on 2022 showed Overall, the overall prevalence of UTIs in the nine countries of sub-Saharan Africa was 32.12% with South Africa ranking high (67.6%); followed by Nigeria (43.65%); Zambia (38.25); Uganda (35.66%); Ethiopia (37.47%); Tanzania (23.7%); Ghana (19.2%); Kenya (18.53%); and Senegal (5.1%) with Escherichia coli being the most commonly isolated bacteria accounting for 86.4%, followed by Klebsiella pneumoniae (10.53%) and Staphylococcus aureus(5.26%)(7)

When we come to our country there was a cross-sectional study done on Pediatric Urinary Tract Infection as a Cause of Outpatient Clinic Visits in Southern Ethiopia, a total of 863 children visited the OPD during the study period among which 31.2% fulfilled the predefined eligibility criteria. Urine culture was positive for 27.5% of the clinically suspected children. Male uncircumcision and under nutrition were independent predictors of culture positivity. More than 5 WBC per high power field on microscopy, urine PH > 5, and positive leukocyte esterase independently predicted positive growth on urine culture. Escherichia coli (34/74, 45.9%) and Klebsiella species (24.3%) were the most frequent isolates. High resistance was noted against amoxicillin (70.6%) and cotrimoxazole (97.1%) by E. coli. (8)

In our country there is no literature on the incidence of Breakthrough UTI or prevalence of Recurrent UTI.

# 3. Objectives

## 3.1. General Objectives

- To assess the prevalence of breakthrough urinary tract infection among patient on prophylactic antibiotics for recurrent UTI from age 1 month to 12 years on follow up at Tikur Anbessa Specialized Hospital

## 3.2. Specific Objectives

- To assess the prevalence of breakthrough Urinary Tract Infection among patient of prophylactic antibiotic
- To assess the risk factor associated with breakthrough UTI
- To identify the common microorganisms associated with breakthrough UTI
- To assess the resistance pattern of common microorganism.
- To assess the practice/ use of prophylactic antibiotics

# 4. Methodology

## 4.1.Study setting

The study was conducted at Tikur Anbessa specialized hospital pediatric Ward, pediatric Renal, pediatric Neurology, pediatric surgical and neurosurgical follow up clinic, Addis Ababa, Ethiopia. Established in 1974, Tikur Anbessa specialized hospital is the largest tertiary hospital in Ethiopia. Administered by Addis Ababa University, it serves as the country's largest and oldest teaching hospital. Every year, Tikur Anbessa provides education and training to approximately 300 medical students and 350 residents, solidifying its role as a leading institution for medical education in Ethiopia. TASH provides diagnosis and treatment for approximately 400,000 patients each year. The pediatric department currently have more than 100 residents with multiple subspeciality programs. One of these units is the pediatric renal unit which provides comprehensive care to over 300 children with the predominant cases being CKD, Nephrotic syndrome and Recurrent UTI with CAKUT.

### 4.2. Study design

The study was conducted using a hospital-based cross-sectional study design.

### 4.3. Study Period

The study included all patients age from 1 month to 12 years on prophylactic antibiotics for prevention of recurrent UTI seen at pediatric ward, Renal, Neurology, neurosurgery and pediatric surgical follow-up clinic at Tikur Anbessa Specialized hospital from the period August 2023 to January 2024.

### 4.4. Source population

All children between 1-month to 12 years of age who were at risk for recurrent UTI on follow up at pediatric clinic at TASH hospital

### 4.5. Study Population

All children aged 1 month to 12 years who were on prophylactic antibiotic on follow up at TASH that full filled the inclusion criteria.

### 4.6. Sample size

With the general assumption that this study presented with a level of confidence interval of 95% and 5% precision, the single population proportion formula was used to calculate the minimum sample size for this study. Due to absence of studies in Ethiopia the prevalence was considered to be 50%.

Sample size: $n=\frac{Z^2P(1-P)}{d^2}=\frac{1.96^2*0.17*(1-0.5)}{0.05^2}=384$

then using the correction formula, since the sample population is small, the final sample size was 277.

where: n= the minimum sample size

P=the expected prevalence of psychiatric disorders

d= the level of precision (margin of error)

Z= the value at 95% confidence level

### 4.7. Inclusion and exclusion criteria

- Inclusion criteria
    - All patients who are aged between 1 month and 12 years on prophylactic antibiotic, for prevention of recurrent UTI, on follow up at TASH
- Exclusion criteria
    - Those patients who are aged less than 1 month and above 12 years
    - Patients who don't have regular follow up at TASH
    - Patient who are not willing to take the prophylactic antibiotic

### 4.8. Sampling technique and procedure

A total of 202 children aged from 1 month to 12 year who are taking prophylactic antibiotic for different indication and who are on follow up at Tikur Anbessa specialized hospital were selected for the study and sociodemographic data and consent was collected and they were followed for a period of 6 month with follow up every 3month and data was collected via prepared questioner and urine analysis in each follow up and culture was sent for those who had sign and symptom and for those whose urine analysis suggested urinary tract infection due to financial issue.

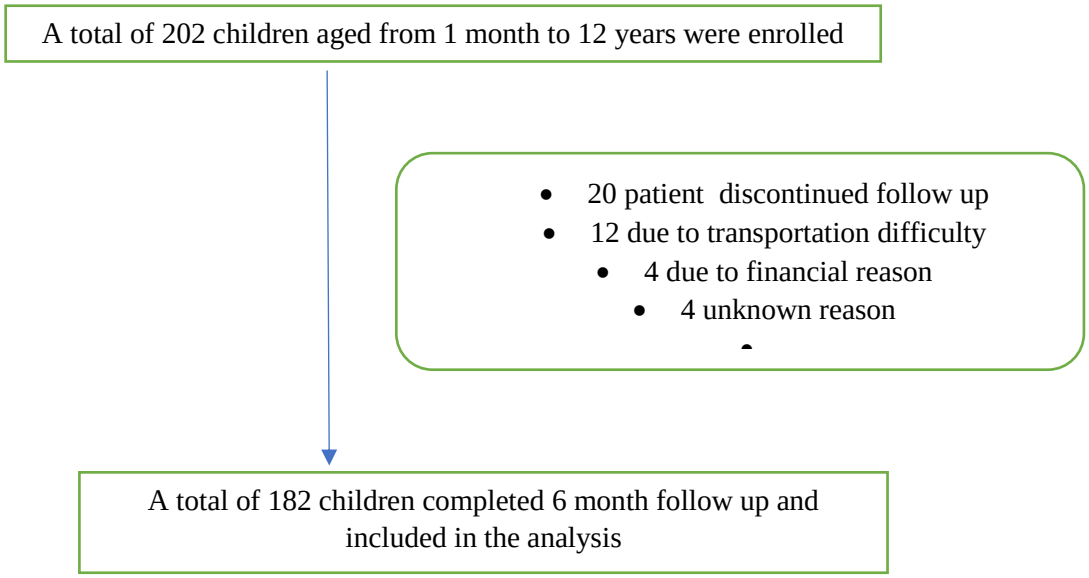


Figure 1 Schematic presentation of sampling procedure in Tikur Anbessa Specialized Hospital pediatric renal, surgical, neurology, neurosurgical follow up clinic

## 4.9. Data quality control and Management

To ensure the quality of data, The Structured checklists were tested on 5% of the sample. Problems highlighted during the pre-test were corrected before the start of the data collection. Each question was properly coded; continuous supervision was done both during the pre-test and data collection period by the principal investigator. The collected data were checked for completeness and consistency on each day of data collection

## 4.10. Study Variables

**Independent Variables**

- Sociodemographic data: Age, Sex, Residency
- Caregivers Economic status of parents, educational status, and religious status
- Male Circumcision
- CAKUT
- Neurologic bladder
- Other congenital anomalies

**Dependent Variables**

- Breakthrough UTI

## 4.11. Data Analysis

After a thorough cleaning and checking for its completeness data was entered into the statistical package for Social Science ver.25 (SPSS) for subsequent descriptive analysis such as Mean frequencies and percentages as appropriate. Chi-square and multiple logistic regression analysis was used to analyze the association between variables where applicable. Statistical significance was taken for a p-value of $< 0.05$ for all statistical tests.

## 4.12. Ethical Consideration

Ethical clearance to conduct this study was obtained from the pediatrics and child health Department's Research and Publications Committee of the School of Medicine, College of Health Sciences, Addis Ababa University. Then an official letter of support and a copy of ethical clearance was submitted to pediatric renal, neurology, surgical and neurosurgical clinic. Confidentiality was fully maintained during Data collection and further analysis and dissemination of results.

## 4.13. Dissemination of findings

The result of the study will be submitted to Addis Ababa University, College of Health Sciences, School of medicine, Department of Pediatrics and Child Health for the requirement of partial fulfillment of specialty certificate in pediatric and child health. The finding of the study will also be shared to other concerned bodies. Furthermore, the manuscript will be published on peer reviewed journals.

### 4.14. Operational Definition

**Urinary Tract Infection-** a patient who came with symptom and sign of Urinary infection and Urinary culture positive (More than $10^5$ colony forming units per milliliter of urine (cfu/mL) and growth of a single organism was considered as culture positive).

**Recurrent UTI-** those who present with symptomatic UTI more than 3 episodes per year or more ever.

**Multidrug resistant (MDR**)-was defined as acquired nonsusceptibility to at least one agent in three or more antimicrobial categories

**Extensively drug resistant (XDR)**- was defined as nonsusceptibility to at least one agent in all but two or fewer antimicrobial categories

**CAKUT-** are embryonic disorders that arise during development and result in a spectrum of defects in the kidneys and outflow tracts which include the ureters, the bladder, and the urethra

**Neurogenic Bladder-** are embryonic disorders that arise during development and result in a spectrum of defects in the kidneys and outflow tracts which include the ureters, the bladder, and the urethra

**VUR-** a condition in which urine flows backward from the bladder to one or both ureters and sometimes to the kidneys

**Adherence**- good adherence was defined as missing less than 2 dose in 30 days, Fair if they miss 2-4 doses in 30days and poor adherence if they muss more than 5 doses in 30 days

# 5. Result

## 5.1 Sociodemographic characteristic of the study participants

The Study included initially 202 patient who fulfilled the inclusion criteria at pediatric Renal, Neurology, Surgery and neurosurgical clinic. Out of this 20 patient didn't finish the 6 month follow up so they were excluded from the study. So 182 patients were included in the analysis. Majority (43.4%) of the children were in the age group of 1-4 years and 74.2% of the children were male. Sixty-one percent of the children were from Addis Ababa and 71.4% were urban in residence. Majority (44.5%) were of the children's parent were orthodox in religion and 29.5% of the parents or guardians completed primary education level.

Table 1. The sociodemographic characteristics of study participants among patient on prophylactic antibiotics for recurrent UTI, TASH, 2023.

| Variable | frequency | Percent |
|---|---|---|
| Age in years | | |
| <1 | 23 | 12.6 |
| 1-4 | 79 | 43.4 |
| 5-10 | 43 | 23.6 |
| >10 | 37 | 20.3 |
| Sex of the study participants | | |
| Male | 135 | 74.2 |
| Female | 47 | 25.8 |
| Region | | |
| Addis Ababa | 111 | 61.0 |
| Oromia | 41 | 22.5 |
| Amhara | 7 | 3.8 |
| SSNPR | 12 | 6.6 |
| Afar | 5 | 2.7 |
| Benishangul-Gumuz | 2 | 1.1 |
| Dire Dewa | 1 | .5 |
| Somali | 3 | 1.6 |
| Residence | | |
| Urban | 130 | 71.4 |
| Rural | 52 | 28.6 |
| Religion of the Parent | | |
| Orthodox | 81 | 44.5 |
| Muslim | 49 | 26.9 |
| Protestant | 52 | 28.6 |
| Educational background of the Parent | | |
| Uneducated | 32 | 17.6 |
| Primary | 54 | 29.7 |
| High school | 46 | 25.3 |

| | | |
|---|---|---|
| College graduate | 50 | 27.5 |
| If male circumcised | | |
| Yes | 88 | 64.7 |
| no | 47 | 35.3 |

## 5.2 Clinical characteristics of the study participants

Almost half (46.7%) of the indication for prophylaxis were CAKUT and 69.2% of the study participant used antibiotic for more than 12 months and 91.2% were using Trimethoprim-sulfamethoxazole. Thirty five percent of the participants had good level of medication adherence and 68.7% had 1-3 episode of UTI after starting prophylactic antibiotic and 73.6% of the participates had 1-3 times hospitalized due to UTI.

Table 2. Clinical characteristics of the study participants

| variable | frequency | Percent |
|---|---|---|
| The indication for prophylactic antibiotics | | |
| CAKUT | 85 | 46.7 |
| VUR | 41 | 22.5 |
| Neurogenic Bladder | 45 | 24.7 |
| Other | 11 | 6.0 |
| Duration of antibiotic use in month | | |
| >1 | 3 | 1.6 |
| 1-3 | 13 | 7.1 |
| 3-12 | 40 | 22.0 |
| > 12 | 126 | 69.2 |
| Types of prophylactic antibiotic used | | |
| Trimethoprim-sulfamethoxazole | 166 | 91.2 |
| Amoxicillin | 13 | 7.1 |
| Nitrofurantoin | 2 | 1.1 |
| Other | 1 | .5 |
| Level of the adherence to the prophylactic antibiotic | | |
| Good | 64 | 35.2 |
| Fair | 96 | 52.7 |
| Poor | 22 | 12.1 |
| Episode of UTI after starting prophylactic antibiotic | | |
| None | 1 | .5 |
| 1-3 | 125 | 68.7 |
| 3-5 | 55 | 30.2 |
| > 5 | 1 | .5 |
| Number of hospitalization for UTI | | |
| None | 48 | 26.4 |
| 1-3 | 134 | 73.6 |

## 5.3 UTI characteristics of the study participants during follow up visit

Forty-six percent of the study participants had fair prophylactic adherence at the first and 46.7% had good adherence at third month follow up and 57.7% at sixth month follow up. In this study fever, urinary frequency and urgency were the most common symptom reported.

Table 3. UTI characteristics of the study participants during follow up visit

| Variable | First | Third month | Sixth month follow up |
|---|---|---|---|
| The adherence to the prophylactic antibiotic | | | |
| good | 61(33.5%) | 85(46.7%) | 105(57.7%) |
| fair | 110(46.4%) | 84(46.2%) | 75(41.2%) |
| poor | 10(5.5%) | 13(7.1%) | 2(1.1%) |
| Discontinued | 1(0.5%) | | |
| The child experience UTI symptom | | | |
| pain or crying during urination | 12(6.5%) | 8(4.3%) | 8(4.3%) |
| fever | 16(8.7%) | 14(7.6%) | 10(5.4%) |
| reddish discoloration of urine | 10(5.4%) | 9(4.9%) | 10(5.4%) |
| poor feeding or irritability | 1(0.5%) | 2(1.1%) | 6(3.2%) |
| urinary frequency or urgency | 22(12%) | 16(8.7%) | 15(8.2%) |
| none | 121(66.4%) | 133(73%) | 133(73%) |
| Sign of the child | | | |
| Fever | 11(6%) | 6(3.2%) | 5(2.7%) |
| suprapubic tenderness | 2(1.1%) | 0 | 0 |
| none | 169(92.8%) | 176(96.7%) | 177(97.2%) |

## 5.4 Laboratory related characteristics of the study participants

The finding of the study showed that 27% (n=49) of the participant had at list one experience of breakthrough UTI as shown in the figure below.

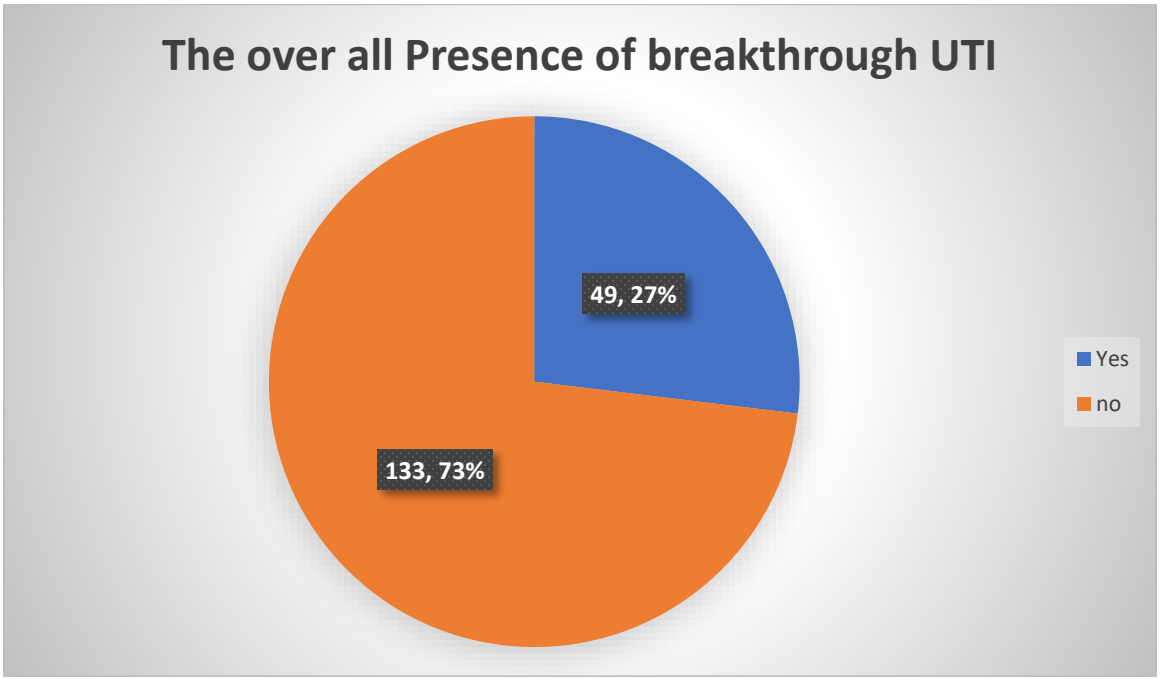


Figure 1. The incidence of breakthrough UTI among patient on prophylactic antibiotics

## 5.5 The specific occurrence of breakthrough UTI in the three follow up visit.

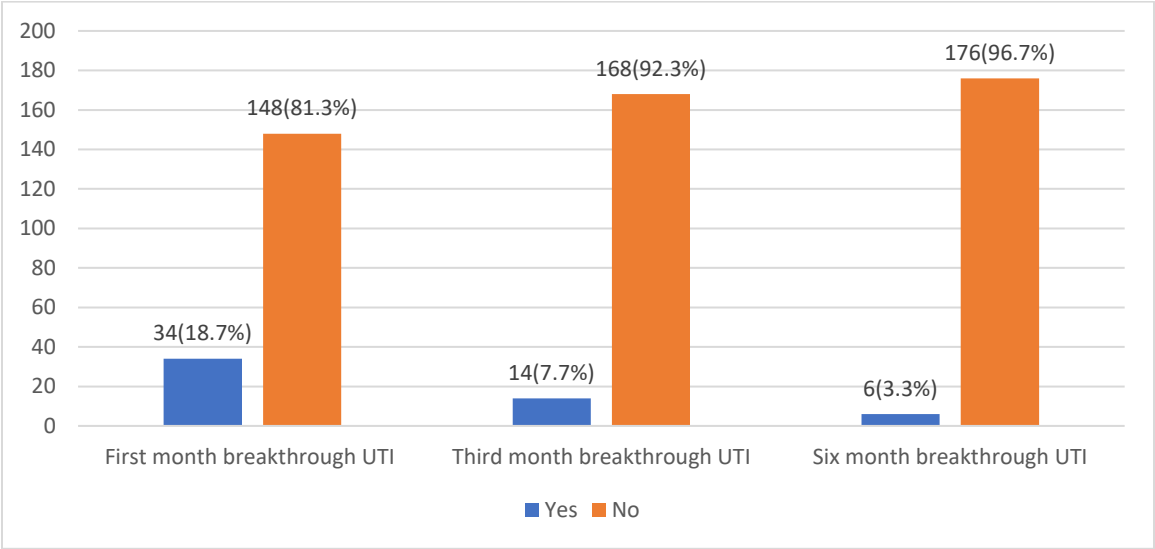


Figure 2. The specific occurrence of breakthrough UTI in the three follow up visit.

The value of urine level of PH <5 was gradually increasing from 32.4% at first follow up to 42.3% at six month and gradually reduced. Urine WBC increased from 59.3% at first follow up to 62.1% at the third month and 65.9% to six month.

The common microorganism in the three visits were E. coli followed by Klebsiella Pneumoniae The resistance pattern for Trimethoprim-sulfamethoxazole were 70.6% at first visit, 71.4% at third month follow up and 81.9% at six month follow up. 85.2%, 80.2% and 81.9% of the participant had a specific gravity of 1-1.015 at first visit, third month visit and sixth month visit respectively and 41.2%, 28.6% and 33.3% of the participant had more than 3 class of drugs resistance pattern during first month, third month and sixth month visit.

Table 4. Laboratory related characteristics of the study participants

| Variable | Base line (%) | Third month (%) | Six months (%) |
|---|---|---|---|
| Urine PH level | | | |
| <5 | 59(32.4%) | 79(43.4%) | 77(42.3%) |
| >5 | 123(67.6%) | 103(56.6%) | 105(%) |
| Urine WBC level | | | |
| <5 | 108(59.3%) | 113(62.1%) | 120(65.9%) |
| >5 | 74(40.7%) | 69(37.9%) | 62(34.1%) |
| Urine RBC level | | | |
| <5 | 142(78%) | 159(87.4%) | 160(87.9%) |
| >5 | 4(22%) | 23(12.6%) | 22(12.1%) |
| Leucocyte esterase result | | | |
| Positive | 75(41.2%) | 60(33%) | 58(31.9%) |
| Negative | 107(58.8%) | 122(67%) | 124(68.1%) |
| Nitrite result | | | |
| Positive | 19(10.4%) | 21(11.5%) | 21(11.5%) |
| negative | 163(89.6%) | 161(88.5%) | 161(88.5%) |
| Urine cast | | | |
| No cast | 181(99.5%) | 181(99.5%) | 152(100%) |
| Cellular or granular | 1(0.5%) | 1(0.5%) | 0 |
| Culture | | | |
| Positive | 34(18.7%) | 14(7.7%) | 6(3.3%) |
| Negative | 117(64.3%) | 133(73.1%) | 105(57.7%) |
| Not sent | 31(17.0%) | 35(19.2%) | 71(39%) |
| Growing Bacteria and blood culture | | | |
| k. Pneumonia | 5(14.7%) | 0 | 2(33.3%) |
| Citrobacter species | 1(2.9%) | 1(7.1%) | 1(16.7%) |
| E. coli | 12(35.3%) | 8(57.1%) | 3(50%) |
| Enterococcus species | 4(11.8%) | 2(14.3%) | 0 |

| | | | |
|---|---|---|---|
| K. Ozaena | 2(5.9%) | 0 | 0 |
| Pseudomonas aeruginosa | 3(8.8%) | 1(7.1%) | 0 |
| Morganella morganii | 2(5.9%) | 1(7.1%) | 0 |
| K. Oxcytoca | 2(5.9%) | 0 | 0 |
| Enterobacter aerogenes or Hafnia | 3(8.8%) | 0 | 0 |
| Acinetobacter species | 0 | 1(7.1%) | 0 |
| Resistance pattern for Cotrimoxazole | | | |
| sensitive | 5(14.7%) | 2(14.3%) | 2(33.3%) |
| resistance | 24(70.6%) | 10(71.4%) | 4(66.7%) |
| not done | 5(14.7%) | 2(14.3%) | 0 |
| Specific gravity | | | |
| 1-1.015 | 155(85.2%) | 146(80.2%) | 149(81.9%) |
| 1.2-1.3 | 27(14.8%) | 36(19.8%) | 33(18.1%) |
| Resistance pattern | | | |
| for 1 class of drug | 5(14.7%) | 6(42.9%) | 0 |
| 2-3 class of drugs | 12(35.3%) | 3(21.4%) | 2(33.3%) |
| for more than 3 class of drugs | 14(41.2%) | 4(28.6%) | 2(33.3% |
| not resistant for any class of drug | 3(8.8%) | 1(7.1%) | 2(33.3%) |

## 5.6 The associated Factor of breakthrough UTI among children in antibiotic prophylactic

The strength of association was measured using odd ratio and 95% confidence interval. Accordingly uncircumcised male, indication of prophylactic Antibiotic use, urine WBC and urine RBC had an association with breakthrough UTI by bivariate logistic regression. The multivariate logistic regression revealed that study male participant who were not circumcised were 3.6 folds increase its chance of developing breakthrough UTI compared to its opposite compartment (AOR=3.6, 95%CI=1.05, 12.00) and study participant whose prophylactic antibiotic indication of neurologic bladder were 2.3 folds increase its breakthrough UTI compare those of indication CAKUT (AOR=2.3, 95%CI=1.05, 12.00). The study participants whose urine WBC >5 were 9.4 folds increase its breakthrough UTI compared to its urine WBC <5 (AOR=9.4, 95%CI=3.35, 26.11).

Table 5. The bivariate and multivariate association between independent variable and breakthrough UTI among children on prophylactic antibiotic at TASH, 2023/4

| Variable | Breakthrough UTI | | p-value | COR with 95%CI | P-Value | AOR with 95%CI |
|---|---|---|---|---|---|---|
| | yes | No | | | | |
| Age of the study participants | | | | | | |
| <1 | 6 | 17 | 1 | | 1 | |
| 1-4 | 22 | 57 | 0.868 | 1.1(0.38, 3.13) | 0.722 | 1.3(0.30, 5.64) |
| 5-10 | 9 | 34 | 0.934 | 0.75(0.23, 2.45) | 0.999 | 1.0(0.13, 7.85) |
| >10 | 12 | 25 | 0.103 | 1.4(0.43, 4.33) | 0.459 | 2.2(0.28, 16.63) |
| Circumcise status of male children | | | | | | |
| Yes | 14 | 74 | 1 | | 1 | |
| No | 20 | 28 | 0.001 | 3.8(1.68, 8.48) | 0.041 | **3.6(1.05, 12.00)** |
| Indication for prophylactic antibiotic | | | | | | |
| CAKUT | 20 | 65 | 1 | | 1 | |
| VUR | 7 | 34 | 0.410 | 0.67(0.26, 1.74) | 0.754 | 1.2(0.33, 4.54) |
| Neurologic bladder | 20 | 25 | 0.015 | 2.6(1.20, 5.63) | 0.046 | **2.3(1.54, 9.50)** |
| others | 2 | 9 | 0.692 | 0.72(0.14, 3.62) | 0.239 | 0.22(0.02, 2.78) |
| Prophylactic adherence | | | | | | |
| Good | 20 | 44 | 1 | | 1 | |
| Fair | 22 | 74 | 0.960 | 0.97(0.34, 2.76) | 0.802 | 0.87(0.29, 2.59) |
| poor | 7 | 15 | 0.384 | 0.64(0.23, 1.76) | 0.513 | 0.59(0.13, 2.78) |
| Hospitalized by UTI | | | | | | |
| no | 16 | 32 | 0.245 | 1.5(0.75, 3.14) | 0.621 | 0.71(0.19, 2.72) |
| yes | 33 | 101 | 1 | | 1 | |
| Urine WBC | | | | | | |
| <5 | 10 | 98 | 1 | | I | |
| ≥5 | 39 | 35 | 0.000 | 10.9(4.88, 23.94) | 0.000 | **9.4(3.35, 26.11)** |
| Urine RBC | | | | | | |
| <5 | 31 | 111 | 1 | | 1 | |
| ≥5 | 18 | 22 | 0.004 | 2.9(1.39, 6.14) | 0.806 | 1.2(0.37, 3.54) |

## 6. Discussion

This study was a  hospital based cross-sectional study, conducted at Pediatric wards, Renal, Pediatric surgical, Pediatric Neurology and neurosurgical follow up clinic, Tikur Anbessa Specialized Hospital, Addis Abeba, Ethiopia, done from August 2023 to February 2024 on 12 patient through  month follow up.

In this study, the majority of the children were in the age group of 1-4 years and 74.2% of the children were male. The age group was similar to the other studies done in Iran, USA and sub-Saharan Africa. The male predominance was similar to the study done at USA and sub-Saharan Africa.

In our study the prevalence of Breakthrough UTI was found to be 27% and 2.7% had more than one episode of UTI. When we compare it to the studies done in China, Indonesia and Sub-Saharan Africa, our prevalence of breakthrough UTI was lower. But when we compare it to the one done in USA which could be due to the age group difference because they used age less than 1 year.

The most common indication for prophylactic antibiotic was found to be CAKUT which is similar to the other studies except the one done in Iran which showed that Vesicoureteral reflux was the most common reason. The most common antibiotic used that was found in our research was Trimethoprim-Sulfamethoxazole which could be explained by the wide availability and lower cost than the other antibiotic option.

The duration of prophylactic antibiotic was more than 12 month for 69% of the participant which is significantly higher than seen in the other studies, likely due to early diagnosis and intervention unlike us which takes months to do definitive treatment. And the adherence pattern showed that only 33% of the caretakers responded as good on the first visit which showed improvement on the subsequent follow up.

Our study also showed that only 20-30% of the children complained any symptom or sign of UTI and out of those fever and urinary frequency was the most common complaints.

The study also showed that there was increased risk factor for breakthrough UTI for those who are not circumcised, neurogenic bladder and those whose Urine analysis showed WBC>5 cell per high power field.

The most common organism identified was E.coli (42%) which was followed by K.pneumoniae and Enterococcus species. Which is similar finding compared to the other studies done in USA, Iran, Indonesia, Sub-Saharan Africa and in our country too.

The resistance pattern seen in our study was that 36% of the organism that grew were resistant to more than class of drugs and 70% of them were resistant to trimethoprim-Sulfamethoxazole, which was significant compared to the studies done in USA and Iran but compared to the study done in our country, the resistance to trimethoprim was lower in our study.

## 7. Strength

This is the first research to be done in our country, which will hopefully open door for further studies to be done. It included all the children from different clinic in Tikur Anbessa Hospital. During the follow up there was low number of drop outs.

## 8. Limitation

The sample size was not adequate despite including all the clinics. Out of the 202 that was initially enrolled 20(1%) patient discontinued there follow up. For 12% of the patient resistance pattern of Trimethoprim-sulfamethoxazole was not done majorly for those that grew enterococcus and when the medication wasn't available. Some urine culture results were not done because sample wasn't given.

## 9. Conclusion

This study showed that there is high burden of breakthrough UTI more affecting the males. There is also significant delay in the definitive repair of the underlying disease which puts the children for risk of repeated infection and kidney injury, also for prolonged exposure to antibiotic. There is also high rate of uncircumcision which reflect cultural and religious view on top of poor health education on the benefit on circumcision. There is high resistance pattern for commonly used antibiotic which reflects a prolonged use and irrational use of antibiotics.

## 10. Recommendation

From the finding we got from this study, we recommend to have a wider and longer study that could include other hospitals and we recommend to do nationwide health education on the benefit of circumcision. To work strongly on the adherence of the prophylactic antibiotic and to avoid using of prophylactic antibiotic for more than 6 month period. We also recommend to consider alternative antibiotic as prophylaxis which may include the second generation cephalosporin and nitrofurantoin. We also recommended to have national guideline for prophylaxis antibiotic for recurrent UTI.

## 11.Reference


1. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: a meta-analysis. Pediatr Infect Dis J. 2008 Apr;27(4):302-8. doi: 10.1097/INF.0b013e31815e4122. PMID: 18316994.
2. Shabani Y, Sadeghi H, Yousefichaijan P, Shabani D, Rafiee F. Prevalence of Risk Factors of Urinary Tract Infections in Infants and Children in Arak, Iran: A Cross-sectional Study. Nephro-Urol Mon. 2023;15(1):e131333. https://doi.org/10.5812/numonthly-131333
3. Larcombe J. Urinary tract infection in children: recurrent infections. BMJ Clin Evid. 2015 Jun 12;2015:0306. PMID: 26067232; PMCID: PMC4463760.
4. O R Ramayani et al 2018 IOP Conf. Ser.: Earth Environ. Sci. 125 012112
5. Lloyd JC, Hornik CP, Benjamin DK, Clark RH, Routh JC, Smith PB. Incidence of Breakthrough Urinary Tract Infection in Hospitalized Infants Receiving Antibiotic Prophylaxis. Clin Pediatr (Phila). 2017 Jan;56(1):65-70. doi: 10.1177/0009922816638664. Epub 2016 Jul 19. PMID: 27006413; PMCID: PMC5031513
6. Su D, Shen Q, Zhai Y, Chen J, Rao J, Miao Q, Tang X, Zhang Z, Liu J, Liu J, Xu H, Fang X. Risk factors for breakthrough urinary tract infection in children with vesicoureteral reflux receiving continuous antibiotic prophylaxis. Transl Pediatr. 2022 Jan;11(1):1-9. doi: 10.21037/tp-21-398. PMID: 35242647; PMCID: PMC8825939
7. Mwang'onde BJ, Mchami JI. The aetiology and prevalence of urinary tract infections in Sub-Saharan Africa: a Systematic Review. J Health Biol Sci. 2022; 10(1):1-7
8. Mitiku E, Amsalu A, Tadesse BT. Pediatric Urinary Tract Infection as a Cause of Outpatient Clinic Visits in Southern Ethiopia: A Cross Sectional Study. Ethiop J Health Sci. 2018 Mar;28(2):187-196. doi: 10.4314/ejhs.v28i2.10. PMID: 29983516; PMCID: PMC6016340

**9.** Nickavar A, Sotoudeh K. Treatment and prophylaxis in pediatric urinary tract infection. Int J Prev Med. 2011 Jan;2(1):4-9. PMID: 21448397; PMCID: PMC3063462.

**10.** Tewary K, Narchi H. Recurrent urinary tract infections in children: Preventive interventions other than prophylactic antibiotics. World J Methodol. 2015 Jun 26;5(2):13-9. doi: 10.5662/wjm.v5.i2.13. PMID: 26140267; PMCID: PMC4482817

**11.** Karpman E, Kurzrock EA. Adverse reactions of nitrofurantoin, trimethoprim and sulfamethoxazole in children. J Urol. 2004 Aug;172(2):448-53. doi: 10.1097/01.ju.0000130653.74548.d6. PMID: 15247700

**12.** Coulthard MG, Lambert HJ, Vernon SJ, Hunter EW, Keir MJ, Matthews JN. Does prompt treatment of urinary tract infection in preschool children prevent renal scarring: mixed retrospective and prospective audits. Arch Dis Child. 2014 Apr;99(4):342-7. doi: 10.1136/archdischild-2013-304428. Epub 2013 Dec 18. PMID: 24351607; PMCID: PMC3963540.

**13.** Ali Reza Nateghian, Joan L. Robinson, Shahab Mohandessi, Nakysa Hooman, Resistance pattern of breakthrough urinary tract infections in children on antibiotic prophylaxis, Journal of Infection and Public Health, Volume 2, Issue 3, 2009, Pages 147-152

**14.** Robinson JL, Finlay JC, Lang ME, Bortolussi R; Canadian Paediatric Society, Community Paediatrics Committee, Infectious Diseases and Immunization Committee. Prophylactic antibiotics for children with recurrent urinary tract infections. Paediatr Child Health. 2015 Jan-Feb;20(1):45-51. doi: 10.1093/pch/20.1.45. PMID: 25722643; PMCID: PMC4333755

**15.** Robinson JL, Finlay JC, Lang ME, Bortolussi R; Canadian Paediatric Society, Community Paediatrics Committee, Infectious Diseases and Immunization Committee. Prophylactic antibiotics for children with recurrent urinary tract infections. Paediatr Child Health. 2015 Jan-Feb;20(1):45-51. doi: 10.1093/pch/20.1.45. PMID: 25722643; PMCID: PMC4333755.

## 12.Annex:

Data collecting Questionnaire

TITLE: PREVALENCE OF BREAKTHROUGH URINARY TRACT INFECTION AMONG PATIENT ON PROPHYLACTIC ANTIBIOTICS FOR RECURRENT UTI ON FOLLOW UP AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

Code number _____ Date ____/___/___ IC_____

### 12.1. Consent Form-

My name is Dr Gelassa Merga, a third year pediatric and child health resident, am doing my research on prevalence of breakthrough UTI among patient on prophylactic Antibiotic for recurrent UTI. I would like to include your child in the research with your permission. Your name and Personal identification will not be asked or included in the interview or study. Any part of the data collected in this study is confidential and will not be used for purpose other than this study. All information will be coded and data collection tools will be locked and will not be accessed by any individual. We kindly ask you to participate in this study by answering the questions listed in the check list.

All the information you give is confidential and you have the right to not participate or withdraw from the study at any point. We are delighted to answer any of your questions.

I have read (was read to me) and clearly understood the purpose of the research, the procedures, the risks and benefits, issues of confidentiality, and the right of participating and withdraw from the study at any time.

I hereby confirm the above statement with my signature.

Participant: Name_____ Signature: _____

Data collector: Name _____ Signature: _____

**Contact address-** Dr gelassa Merga Phone number-0913587378

**Email address-** gelassa13@gmail.com

## 7.2 Questionaries

Part I – Socio-demographic Data

1. Age in years

2. Sex:

a. Male b. Female

3. Address (Region)

a. A/A b. Oromia c. Amhara d. SSNPR e. Tigray f. Afar g. Benishangul-gumuz h. Dire Dawa I. Gambela j. Harari k. Somali

4. Residence

a. Urban b. rural

5. Religion:

a. Orthodox Christian b. Muslim c. Protestant d. Catholic e. Other

6. If male, Circumcised?

a. yes b. no

Part II-Clinical profile

1. Indication for prophylactic antibiotic

a. CAKUT b. VUR C. Neurogenic bladder D. other

2. How long on prophylactic antibiotic

a. Less than 1 month b. less than 3 month c. 3-12 month d. more than 12 month

3. What prophylactic antibiotic are you using?

a. Trimethoprim- sulfamethoxazole b. Amoxicillin c. Nitrofurantoin d. other

4. How is the adherence to the prophylactic antibiotic?

a. Good(<2 dose/30 days) b. fair (2-4 dose/30 days) c. poor(≥5 dose/ 30 days) d. discontinued

5. How many episodes of UTI did he have since he started the prophylactic antibiotic?

a. None b. 1-3 c. 3-5 d. more than 5

6. How many times was the child hospitalized for UTI until now

a. None b. 1-3 c. 3-5 d. more than 5

Part III- follow up visit

1. How is the adherence to the prophylactic antibiotic now?
   a. Good b. fair c. poor d. discontinued
2. Does the child experience any of the following symptoms?
   a. Pain or crying during urination?
   b. Nausea or vomiting
   c. Fever
   d. Reddish discoloration of urine
   e. Poor feeding or irritability
   f. Urinary frequency or urgency
   g. None
3. Does the child have any of the following sign?
   a. Fever
   b. Tachycardia
   c. Suprapubic tenderness
   d. None
   e. Others

Part IV- laboratory finding

1. What is the urine analysis finding?

a. PH 1. Less than 5 2. More than 5

b. WBC- 1. Less than 5 2. More than 5

c. RBC- 1. Less than 5 2. More than 5

d. Leucocyte esterase- 1. Positive 2. Negative

e. Nitrite- 1. Positive 2. Negative

f. Urine cast- 1. No cast 2. Cellular or granular

g. Urine specific gravity 1. 1.0-1.015 2. 1.2-1.30

1. What is the culture result?

a. Positive b. negative

2. If positive, what the microorganism that grew? _____

3. What is the sensitivity and resistance pattern?_____

4. Resistance pattern for Cotrimoxazole?