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Profiling of Bacterial and Fungal uropathogens, Antimicrobial susceptibility pattern of bacterial isolates, and associated risk factors among pediatric patients at St Paul Hospital Millennium Medical College.

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This is to certify that the thesis prepared by NUHAMEN ZENA, entitled: "Profiling of bacterial and fungal uropathogens, Antimicrobial susceptibility pattern of bacterial isolates and associated risk factors among pediatric patients at St Paul Hospital Millennium Medical college" and submitted in partial fulfillment of the requirements for Master of Science degree in Clinical Laboratory Sciences (diagnostic and public health microbiology) complies with the regulations of the University and meets the accepted standards concerning originality and quality.

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ABBREVIATIONS

AMR: Antimicrobial resistance

AST: Antimicrobial susceptibility test

BHI: Brain heart infusion medium

CLED: Cysteine lactose electrolyte deficient medium

CLSI: Clinical and laboratory standard institute**.**

CONS: Coagulase negative staphylococcus

ESBL: Extended spectrum beta lacatamase Entrobactreciace

ICU: Intensive care unit

MDR: Multi drug resistance

PBP: Penicillin binding protein

PICU: Pediatrics intensive care unit

SPHMMC: St Paul hospital millennium medical college

SPSS: Statistical package for social science

USIN: Unique survey identification number

UTI : Urinary tract infection

WHO: World health organization

Abstract

Background: Urinary tract infection is an infection caused by uropathogens including bacteria and fungi .Which are the major cause of mortality and morbidity in pediatric patients. Early diagnosis and appropriate treatment is very mandatory. Increasing antimicrobial resistance (AMR) is also becoming a major challenge in the management of pediatric UTI cases.. This study is aimed in profiling of bacterial and fungal uropathogens and antimicrobial susceptibility pattern of bacterial isolates among pediatric UTI patients in SPHMMC.

Methods: A hospital based cross-sectional study was conducted from January 2020-July 2020 among 227 UTI symptomatic pediatric patients. Clean –voided midstream urine was collected and analyzed according to standard microbiological procedures. Pathogenic isolates were identified by gram stain and different biochemical tests. Anti microbial susceptibility test was done by using Kirby - Bauer disk diffusion test following standard procedures. Data was analyzed by SPSS version 23. Result was interpreted by using simple and multivariate logistic regression at 95% confidence interval. P values <0.05 were considered as statistically significant.

Result: The overall prevalence of UTI was 28.63 %(n=65). Gram negative bacteria were the predominant isolates of which E.coli was the most prevalently identified(n= 21; 32.32%) followed by klebsella pneumonia (n=17; 26.15%). Among the total 16 fungal isolates C.albicans(n=6; 9.23%) was the most prevalently identified. All gram negative bacteria showed100% resistance to ampicillin. MDR was seen among 27(55.1%) bacterial isolates. History of catheterization, Admission period, Positive leukocyte esterase and Nitrite had a significant association with UTI (P=<0.05)

Conclusion: The study showed high prevalence of uropathogen and anti microbial resistance pattern(AMR) as compared to recent related studies in Ethiopia. Continuous and sustainable monitoring of antibiotics administration and conducting further studies on AMR and MDR is needed.

Keywords: Symptomatic, Urinary tract infection, Multi drug resistance (MDR)

1. INTRODUCTION

1.1 Background

Urinary tract infection (UTI) is an infection of the bladder (cystitis) or the kidneys (pyelonephritis). It is the second most common type of infection accounting for about 8.1 million visits to health care providers each year [1]. Women are more susceptible to UTI than men. Over 50% of all women will experience at least one UTI during their life-time, with 20–30% experiencing recurrent UTI [2, 3].

Urinary tract infection is a morbid disease in terms of loss of working days and treatment cost [4]. In the United States alone, UTI has been reported to cause > 6 million outpatient visits [5] and 479,000 hospitalizations annually [6]. Furthermore, the annual treatment cost of UTI in this part of the world has been estimated to be greater than 2.47 billion USD [2]. They are also important cause of sepsis resulting in high mortality rates [7].

UTI is also a common and important clinical problem in pediatrics, as recurrent UTIs leads to renal scarring, hypertension, and end-stage renal dysfunction later in life [3]. UTI occurs in 3% to 5% of girls and 1% of boys during childhood, with the first attack occurring in girls by 5 years, peaking during infancy and toilet training. It is also common in boys during the first year of life, especially among those who are uncircumcised [4].

Uncomplicated lower UTI remains one of the most commonly treated infections in primary care. Which is a common source of infection in children and infants and is the most commonly in children < 2 years of age, both in the community and hospital setting. During the first year of life, UTI is more common in boys. In the beginning the outcome is usually benign, but it can progress to renal scarring in early infancy, Renal scarring may lead to complications in adulthood including hypertension, proteinuria, renal damage and even chronic renal failure. [5].

Urinary tract infections can be classified as community acquired or nosocomial based on the place and time of acquiring the infection. Community acquired UTI is an infection which takes place in ones life in environmental setting or within 48 hours of hospital admission. Nosocomial urinary tract infections are the infection of the urinary tract that occurs after 48 hours of hospital admission. Nosocomial urinary tract infections are the infection of the urinary tract that occurs after 48 hours of hospital admission where the patient is not incubating the bacteria within the time of admission. [6]

UTI is caused mainly by bacteria, although viruses, fungi, and parasites can also cause urinary tract infections. Among Gram-negative bacteria organisms isolated from urine samples of children with *Escherichia coli* (*E. coli*) accounting for 70% to 90% of infections [7]. *Klebsiella* species, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Acinetobacter*, and *Serratia* are other Gram-negative bacteria isolated from pediatric patients. However, only 10% of the cases are caused by Gram-positive bacteria and include *Enterococcus*, *Staphylococcus*, and *Streptococcus agalactiae*.All invasive fungi (eg, *Cryptococcus neoformans*, *Aspergillus* spp, *Mucoraceae* spp, *Histoplasma capsulatum*, *Blastomyces*sp, *Coccidioidesimmitis*) may infect the kidneys as part of systemic or disseminated mycotic infection.[8]

In recent years, widespread use of antibiotics has resulted in an increasing incidence of antibiotic resistance among the urinary tract pathogens all over the world. Worldwide, emergence of antibiotic resistance is increasing among the urinary pathogens [9]. More than 80% of bacterial strains causing urinary tract infections in developing countries are now resistant to trimethoprim-sulfamethoxazole [10].

Urinary tract infection (UTI) is one of the most common bacterial infections encountered by clinicians in developing countries and the cause of significant morbidity and mortality [11]. Several studies from the African continent have investigated the profile of common uropathogen and the pattern of their susceptibility to commonly used antimicrobial agents in order to guide the choice of empiric therapy. These studies reported the emergence of antibiotic resistant Gram-negative bacilli with special emphasis on ESBL-producing isolates [12–14]. While morbidity and mortality of UTI in children high, studies carried out in Ethiopia is scanty.

1.2. Statement of the problem

Urinary tract infections can be asymptomatic, acute, chronic, and complicated or uncomplicated, and the clinical manifestations of UTIs depend on the portion of the urinary tract involved, the etiologic organisms, the severity of the infection, and the patient's immune status to mount a response to it. Both asymptomatic and symptomatic UTIs pose a serious threat to public health care, hence reducing the quality of life and resulting economic crisis on the health care system. The symptoms of UTIs such as fever, burning sensations while urinating, itching, formation of blisters and ulcers in the genital area, genital and suprapubic pain, and pyuria generally depend on the age of the person infected and the location of the urinary tract infected [23].

The diagnosis of UTI in children possesses a big challenge to the clinicians. Nonspecific clinical presentation and difficulty in getting urine sample for laboratory investigations are among the many reasons that are responsible for the challenge [24]. A delay in the diagnosis of UTI may lead to significant morbidity and mortality in pediatric patients. Fever is the most common nonspecific symptom of UTI in infants that can loss originate from different sources such as otitis media or other viral symptoms. Urine culture must be done in order to differentiate UTI from any other infections. [25]

Development of antimicrobial resistance by uropathogens is another global serious problem caused by different reasons such as empirically treating patients without urine culture result ,not requesting urine culture and sensitivity test for using and identifying antibiogram of different uropathogens, improper use of antibiotics or taking antibiotics without physician prescription .Development of MDR in uropathogens increases morbidity, mortality, health-care cost, and hospitalization demanding choice of antibiotic based on AMR profiles[26].

Although the mortality and morbidity of pediatrics is high in our country but studies are scanty .This study is aimed to determine both burden or magnitude and anti-microbial resistance pattern of uropathogens isolated from pediatric patients. Documenting bacterial and fungal uropathogens and determining their drug profile is one of an active field of research. Specially documenting fungal pathogens that causes UTI play a great role and a unique contribution in profiling fungal uropathogen.

1.3. Significance of the study

This study Produces information on the spectrum and magnitude of bacterial and fungal pathogens implicated in causing UTI in children. Which bacteria or fungal pathogen are prone to cause UTI and suggests antimicrobial susceptibility pattern of bacterial isolates.

This study also helps to characterize and isolate the most prevalently identified bacterial and fungal causative agent. Different literatures showed that E.coli and klebsella spp were among the most prevalently identified. Although antimicrobial susceptibility result also needed. This study also identified uropathogens including fungal pathogens.

Antibiotic resistant pathogens are changing and increasing due to the abuse of antibiotics and inappropriate selection, it is necessary to select proper antibiotics in the early phase of treatment. Thus, regular antibiotic sensitivity results from the evaluation of UTI are important to improve the effectiveness of treatment.

In order to decrease the alarming rate of MDR many studies and investigations should be done. Hence this study could help different physicians and health care workers to choose appropriate antibiotic drug. It helps physicians to choose in appropriate drug selection which can decrease MDR.

Many studies merit the health care system in decreasing MDR. It helps to develop prevention mechanisms and create awareness about MDR for the health care workers and for the community. It helps to understand the overall prevalence of UTI among children and antibiotic classes which are becoming resistant. Inline this study can also used for additional data to conduct further study.

2. Literatures Review

A Study conducted in Alka Hospital, Nepal targeting in determining of etiological agents of urinary tract infection in pediatric patients and the antimicrobial resistance pattern plus biofilm producing profile of the isolates in 2014-2015 shows that the overall prevalence of UTI was 18.13% E. coli, was the predominant organism followed by Klebsiella spp. Most E. coli were sensitive to amikacin followed by nitrofurantoin and highly resistant to ampicillin Of the positive isolates, were found to be multidrug- resistant strains.[15]

A Research done in Nepal Pokohara on the Occurrence of urinary tract infection and their antimicrobial susceptibility pattern among children from 2005-2006 shows prevalence of 21.3 % of the sample size, with significant bacterial growth.E. coliwas the most frequently occurring pathogen (39.40%), followed by Proteus spp., Citrobacter spp. and StreptococcusfaecalisKlebsiella spp. and Staphylococcus aureus and Enterobacter. E.coli were susceptible to Gentamycin and Amikacin, to Norfloxacin, to Nalidixic acid and Norfloxacin.[17]

A retrospective chart review was conducted on pediatric patients 0-15years of children with UTI in tertiary care center in Riyadh, Saudi Arabia from 2006-2012G.C. The results showed that E. coli was the predominant uropathogen causing UTIs in children followed by Klebsiella pneumonia , Pseudomonas aeruginosa and Enterococcus species. All uropathogens, 68% were resistant to ampicillin, 54% resistant to co-trimoxazole, and 30% resistant/intermediate sensitivity to amoxicillin/clavulinic acid[18].

A study conducted in ahvaz Iran on Candiduria in children and susceptibility patterns of recovered Candida species to antifungal drugs showed that 5.2 % 0f UTI is caused by candida species . C. albicans was identified predominantly as the most common yeast followed by C. glabrata and C. krusei. Antifungal susceptibility testing revealed that only one isolate of C. glabrata and seven isolates of C.albican were resistant to nystatin and ketoconazole, respectively. However, all tested isolates were resistance to fluconazole.[19]

A research conducted in Tehran Iran on Candiduria in children a first report from an Iranian referral pediatric hospital showed that candiduria was diagnosed in 4.3% of the patients with UTI. It has been reported that 11 to 52% of nosocomial urinary tract infections (UTIs) are caused by Candida spp. Increased age, female sex, antibiotic use, urinary drainage devices and prior surgical procedures were considered as risk factors for candiduria.[20]

A study conducted in southern Iran in shiraz on the determining the antimicrobial resistance pattern of childrens with UTI in 2014 showed that UTI was significantly higher in girls than in boys. The most commonly discovered pathogens were Escherichia coli followed by Klebsiellaspp. And Enterococcus spp. Overall susceptibility test showed the highest resistance to ampicillin and cotrimoxazole and the highest sensitivity to imipenem and Gentamicin .[25]

A Research conduct in India Mizoram State referral hospital in 2018 on antimicrobial resistance pattern of childrens with UTI showed that Urinary tract infections were more prevalent in girls than boys. Uropathogens isolated were Escherichia coli ,followed by Klebsiella spp., enterococcus spp., Proteus spp. ,Staphylococcus spp and Pseudomonas spp. .High level of resistance was found to amoxycillin/ampicillin by all the organisms isolated [26].

A Research done in Tanzania at bugando medical center on the total prevalence and antimicrobial susceptibility pattern uropathogens of febrile children from 2010-2011 shows that the overall prevalence of UTI confirmed by urine culture was 39.7%. Escherichia coli and Klebsiella pneumonia were the most common isolates. It showed there was high antimicrobial resistance rates in klebisella pnuemoniae than Escherichia coli [27].

A study conducted in north western Tanzania, Muwanza city, makongore hospital showed that there was 20.1% total prevalence of UTI among febrile symptomatic children. Escherichia coli was the most prevalently identified organism showing high level of anti microbial resistance to ampicillin , cotrimoxazole and gentamycin respectively. E.coli was also highly susceptible to meropenem, ciprofloxacin and ceftriaxone in descending order [28].

A study conducted in western Africa, Nigeria revealed that there was 39.69% overall prevalence of urinary tract infection among the rural community. Female's had high risk of acquiring UTI than males. *Escherichia coli* was the most prevalent isolate in females as well in general,

while *Staphylococcus aureus* was the predominant isolate causing urinary tract infection in males. The flouroquinnolones were the most effective antibacterial agents [29].

A research done in Uganda mulago hospital on the Prevalence and antibiotic susceptibility of urinary tract infections in febrile children below ten years revealed that 18.1% of total prevalence of UTI. Where E.coli and Klebsella spp were the predominant isolates. Where as 82.8% of from the total isolates show multi drug resistance pattern [30].

A Research conducted in Ethiopia,Gondar in determining the overall prevalence and antimicrobial resistance pattern of children with UTI in 2015 showed 26.45% prevalence. E.coli was the predominant uropathogen followed by S. aureus and P.aeruginosa, P. vulgaris, and Enterococcus species. All K. pneumoniae, P. mirabilis, and K. ozanaestraines were 100% resistance to ampicillin, followed by P. aeruginosa and E. coli. While all Gram- positive bacterial isolates were 100% sensitive to ciprofloxacin [31].

A study conducted in Ethiopia, Hawassa tertiary center on Pediatric Urinary Tract Infection as a Cause of Outpatient Clinic Visits in Southern Ethiopia showed that there was 27.8 % over all prevalence of UTI among symptomatic pediatric patients. 27.8% of urine samples were positive for urine culture. Among the isolates Escherichia coli and klebsella species were the most prevalent. High antimicrobial resistance was noted against amoxicillin and co-trimoxazole[32].

A study conducted in Ethiopia ,Bahirdar felegehiwot hospital on Bacterial Profile And Antibiotic Susceptibility pattern of urinary tract infection among children showed that there was 15.8% overall prevalence of UTI among symptomatic children. *Escherichia coli* was the predominant pathogen followed by pseudomonas species . Multiple drug resistance (MDR) for Gram-positive and Gram-negative bacteria was 100% and 83.1%, respectively[33].

A Study conducted in Ethiopia, Addis Ababa in Yekatit 12 hospital on bacterial profile and antimicrobial resistance pattern of uropathogens in children with UTI in 2014 showed that the prevalence of UTI was 15.9%.Bacterial species isolated were belonging to six genera genera were Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus , Proteus spp, Acinetobacter spp, and Entrococcus spp. Of the bacterial isolates E. coli was found out to be the most common pathogen followed by Klebsiella pneumoniae. Further more E. coli and Klebsiella pneumoniae were the most common pathogens in female patients.

Regarding susceptibility tests results. Acinetobacter spp had 100% resistance to three antibiotics: gentamicin, trimethoprim-sulfamethoxazole , and augmentin . But they were 100% susceptible to ciprofloxacin , cefuroxime , norfloxacin , and ceftazidime. On the contrary ,Proteus spp. was 100% sensitive to all drugs except to nitrofurantoin. Species of Enterococcus had resistance of to chloramphenicol and to both and erythromycin. S. aureus was 100% susceptible to almost all drugs, while coagulase-negative staphylococci were not as susceptible as S. aureus. Multidrug resistance to two or more drugs was observed in 73.7% of the bacterial isolates[34].

3. Objectives

3.1 General Objective

- To determine the prevalence of UTI, profiling of bacterial and fungal pathogens, antimicrobial susceptibility profile of bacterial isolates and factors associated among pediatric UTI patients at St Paul Hospital Millennium Medical College from January 2020 -July2020.

3.2 Specific Objectives

- To determine the prevalence of UTI.
- To determine the spectrum of bacterial and fungal pathogens.
- To determine the drug susceptibility profile of bacterial isolates.
- To identify major predisposing factors associated with UTI.

4. Materials and Methods

4.1 Study area

This study was conducted in St Paul Hospital Millennium Medical College which is located in Addis Ababa, the capital city of Ethiopia. The hospital was established in 1968 by the late Emperor Haile Selassie. Although the medical school was opened in 2007G.C.The college has more than 2700 clinical, academic, and administrative and support staffs that provide: medical specialty services to patients who are referred from all over the country especially in modern and crucial diagnostic medical treatment (kidney transplantation and infertility). The hospital has 800 beds and gives diagnostic and treatment services for about 370,000-400,000 patients per year. The pediatrics department gives medical service for more than 85,000 patients per year .It have more than 120 beds including neonatal unit. It has more than 250 medical, academic and supportive staff.

4.2. Study design and Period

4.2.1 Study design

A hospital based cross sectional study was conducted at SPHMMC department of Pediatrics

4.2.2. Study Period

The study was conducted from January 2020 to July 2020 at the department of pediatrics..

4.3 Population

4.3.1 Source Population

All pediatric patients who visits SPHMMC Department of pediatrics between January 2020 to July 2020

4.3.2 Study Population

All pediatric patients, with symptomatic UTI, attending at SPHMMC department of pediatrics including outpatient and inpatient unit from January 2020 to July 2020

4.4 Inclusion and Exclusion criteria

4.4.1 Inclusion Criteria

Pediatric patients less than or equal to 15 years of age with feasible symptom of UTI from January 2020 to July 2020 were included in the study.

4.4.2 Exclusion criteria

- Pediatric patients who were taking antibiotics were excluded
- Mothers/guardians of pediatrics who did not volunteer for written consents were excluded.

4.5 Study Variables

4.5.1 Dependent Variables

- Rate of uropathogen isolated from pediatric UTI case.
- Antibiotic susceptibility pattern of the isolated uropathogen.

4.5.2 Independent Variables

- Sex
- Age
- Previous history of UTI
- Catheterization
- Hospitalization time
- Circumcision (for male study participants)
- Location
- HIV status
- Chronic illness
- Temperature

4.6. Sample Size Calculation and Sampling Method

4.6.1. Sample Size Calculation

Sample Size was determined by the following formula: $n = (Z\alpha_{/2})^2 P (1- P)/ d^2$

Where:

- P =is the estimated proportion in the population where the researcher uses p =0.159 which is done in Addis Ababa, Ethiopia [34]
- Z reflects the confidence interval; we have used 95 % confidence interval so the value of zα/2 will be 1.96
- d = is the margin of error &-α =is the level of error one is willing to tolerate

So $n= (1.96)^2 0.159(1-0.159)/ (0.05)^2=206$

Assuming 10% non respondents n =206+206/10 = 227

4.6.2. Sampling Method

Convenient sampling method was used for this study. The data was collected until the required sample size was achieved. And all pediatric patients with feasible symptom of UTI were included in this study..

4.7. Measurement and data collection

4.7.1. Data collection procedure

The data was collected by using a pre-tested structured questionnaire which is developed following through a review of works of literature from different sources .It was employed to collect information about socio-demographic characteristics (age, sex, previous history, circumcision ,catheterization) of study participants after the informed consent is signed. Data was collected by nurses and physicians working in pediatrics department .Information about Temperature, location, hospitalization time, chronic infection and HIV status were taken also by physicians

4.7.2. Sample collection

Sample collection and inoculation

Urine specimens were collected from each pediatric patient with a sterile urine container.Study participants' parents or guardians were given appropriate instructions of clean catch midstream urine sample collection before providing urine samples. Catheterized and suprapubic urine samples were collected by trained nurses and physician. Immediately after collection, the samples were brought to Microbiology laboratory for further process. Part of the sample was inoculated into and Cysteine Lactose Electrolyte Deficient medium (Oxoid, Basingstoke, Hampshire, England) using a calibrated loop with a capacity of 1 µl in safety cabinet. The remaining sample was inoculated onto Brain Heart infusion agar (Oxoid, Basingstoke, Hampshire, England).A part of the sample was inspected for leucucyte esterase and nitrite by using urine dipstick. All inoculated plates were incubated at 37 °C for 18–24 hr aerobically and inspected for the growth of bacteria and/or yeasts. Colony counts yielding bacterial growth of >105/ ml of urine (≥100,000 colonies) were regarded as significant for bacteriuria. Urine samples yielded three and more bacterial species were not considered for further investigation.

Bacterial Identification:

Pure isolates of bacterial pathogen were preliminary characterized by colony morphology, Gram-stain, and catalase and DNASe tests. Gram positive and Gram-negative bacteria were identified to the species level by conductive convention biochemical tests like (Urease, Indole, Citrate ,TSI, H2S,LIA,Motility)

Yeast identification

Yeasts were identified by means of conventional routine diagnostic methods such as Gram stain, Germ tube test , chromogenic medium, CHROMagar Candida (bioM´erieux, France) as per the instruction of the manufacturer.

Antimicrobial susceptibility testing

Antimicrobial susceptibility test was carried out by Kirby Bauer disc diffusion method as per Clinical Laboratory Standards Institute (CLSI) guidelines on Muller Hinton agar (Oxoid, Basingstoke, England) [18]. The growth suspension was prepared in 0.5 ml of the same broth medium and the turbidity will be adjusted to match that of 0.5 McFarland standards to obtain approximately the organism number of 1 × 106 colony forming units (CFU) per ml. A sterile swab was dipped into the suspension and the excess of inoculum was removed by pressing it against the sides of the tube. Then the swab was applied to the center of Muller Hinton agar plat and evenly spread on the medium. Antibiotic discs were placed after 15 min of inoculation to Muller Hinton agar seeded with each isolate and was incubated for 24 h at 35–37 °C .For gram negative isolates we used antibiotic discs AUG: augmentin (30µg); CIP: ciprofloxacin (5µg); F: nitrofurantoin (300µg);AMP :ampicillin(10 µg); AMK :amikacin(30µg); MRP: meropenem(10µg); TZP:piperacillin tazobactam(100/10 µg)CZ: cefazolin (30µg); SXT: trimethoprim-sulfamethoxazole (1.25/23.75µg) .

Anti microbial disks used for gram positive isolates were P: penicillin (10 U); CLN: clindamycin (30µg); (10µg); AZM: azitromycin (30µg); FOX: cefoxtin (30µg); NIT: nitrofurantoin (300µg); VAN:vancomycin(30µg) ;SXT: trimethoprim-sulfamethoxazole (1.25/23.75 µg) .

The diameter of the zone of inhibition around the disc was measured using sliding metal caliper break points were interpreted according to Clinical Laboratory Standards Institute (CLSI 30th edition) guidelines [18].

4.8. Quality Assurance

The prepared culture media were checked for sterility by incubating the prepared media for 24 hour and observed for the presence of any contamination or growth. The saline was also checked for sterility by inoculating on Blood agar. The sample tube was labeled with the same unique survey identification number (USIN) that is indicated in the questionnaire.

Control strain organisms such as S. aureus (ATCC 25923), E. coli (ATCC 25922) and P. aeruginosa (ATCC 27853) were used as quality control strains to check the efficacy of the antibiotics agents.

4.9. Data analysis and interpretation

All data were encoded , cleared and analyzed using Statistical Package for Social Sciences (SPSS) version 23 software. Simple and multivariate logistic regression was used to calculate the association of every independent variable with UTI.For every independent variable P value less than 0.05 were considered as statistically significant.

4.10. Operational definition

- **UTI** - is colonization of a pathogen occurring anywhere along the urinary tract: kidney, urether, bladder, and urethra.
- **Pediatrics-** is branch of medical science which mainly deals with medical care of infants and children.
- **Multi drug resistance –** is a pattern exhibited by a pathogenic microbe which show resistant to three or more antimicrobial agents of different antibiotic classes.
- **Previous history of UTI –** is a case of UTI within the past 1 year.
- **Chronic Illness** – disease that is persistent or otherwise long-lasting in its effects that comes with time. Which include cardiovascular diseases, cancers, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes.
- **HIV status-** a status of a study participant having of human immuno deficiency virus or not.

- **Catheterization** – being on a catheteher for the past one year.
- **Beta-lactam resistance**- Pathogenic bacteria that are resistant to beta-lactam antibiotics. i.e amoxicillin, ampicillin.

4.11. Ethical consideration

Ethical clearance was obtained from Department of Research and Ethical Review Committee of Medical laboratory Science, College of Health Science, Addis Ababa University and from institution review board of SPHMMC research directorate. The purpose of the study was clearly explained for each study participant and written signed informed ascent was obtained from study participants prior to sampling. Participant‘s confidentiality was strictly maintained during the interview process, during data processing and report writing.

4.12. Dissemination of the results

The result is submitted to Addis Ababa University, College of Health Science, Department of Medical Laboratory Science and SPHMMC. the result of the study finding may be used as baseline information for further studies. The findings will be presented at national and international scientific conferences. The findings were also be sent/ submitted to different peer reviewed journals for publication.

5 . RESULTS

5.1 Socio-demographic characteristics of study participants

A total of 227 symptomatic pediatric patients were enrolled in this study. Majority of study participants were less than 3 years age 119(52.42%). The study population was consisted of 138(60.79%) male and 89(39.21%) female sub groups of which 35(25.36%) of male and 35 (33.71%) of female have a significant uropathogen isolated. Most of the study participants are urban residents 160(70.48%). 61(26.1%) of study participants had previous history of UTI and 16.7% of them had been catheterized.(Table 1).

Table 1 Socio demographic characteristics of pediatric patients in SPHMMC from Jan2020-July 2020

Variables	**Frequency (%)**	
Sex	Male	138 (60.8)
	Female	89 (39.2)
Age	<3yr	119 (52.4)
	3-6yr	31(13.7)
	6-9yr	19(8.4)
	9-12yr	21(9.3)
	12-15yr	37(16.3)
Area	Urban	160(70.5)
	Rural	67(29.5)
Circumcision	Yes	104 (75.9)
	No	33 (24.1)
Previous History of UTI	Yes	61(26.1)
	No	166(73.9)
Catheterization	Yes	38(16.7)
	No	189(83.3)

A total of 65 urine samples were positive for urine culture. Males show slightly higher prevalence (n= 35: N=65) than Female (n= 30: N=65).

5.2 Prevalence of urinary tract infection

The over all prevalence of UTI in our study is 28.63%. A total of 65 isolates were identified which is consisted of 49 (75.38%) bacterial and 16 (24.62%) fungal isolates. Among the pathogenic bacteria gram negative bacteria accounts for (n=44 ; 90.0%) and gram positive bacteria (n=5;10.0%). From the fungal uropathgen the genera Candida accounts for (n=10;62.5%) and non candida albican yeasts (n= 6; 37.5%). From the candida family C.albican have high prevalence (n =6; 60.0%) followed by C.tropicalis (n=2 ; 20.0%) and C. kruzai(n=2 ; 20.0%).

Gram negative bacterias were the predominant isolates of which E.coli was the most prevalently identified. which is followed by kllebsella pneumoniae, C.albicans ,non candida albican , Acitinobacter spp, Entrococcus spp, C. tropicalis, C.krusei ,Providencia spp, Entrobacter spp, S.aureus and CONS respectively as shown in Table 2.

Table 2 Uropathogen isolated from pediatric patients in SPHMMC from Jan 2020-July2020

Uropathogen	**Frequency (%)**
E.coli	21 (32.32)
Klebsella pneumonia	17 (26.15)
Acitinobacter spp	4 (6.16)
CONS	1 (1.54)
S.aureus	1(1.54)
Providencia Spp	1 (1.54)
Entrobacter spp	1 (1.54
C.albican	6 (9.23)
C.tropicalis	2 (3.07)
C.kruzai	2 (3.07)
Non candida albican	6 (9.23)
Entrococcus spp	3 (4.62)
Total	65 (100)

Among the uncircumcised boys 25.53% of them showed significant isolation of a uropathogen. Previous episodes of UTI is shown among 61(26.87%) children of which 37.7% of them showed significant isolation of uropathogen. Pediatric patients which have chronic infection(Diabetus milletus, Maligancy,..) showed 34.62% Urine culture positivity. Pediatrics which are HIV positive showed 62.5% UTI positivity. In our study History of catheterization(COR=3.56:P=0.001) admission period(COR=2.12:P=0.002 ,positive leukocyte esterase (COR=88.66:P=0.001) and nitrite(COR=225.88 : P=0.000) have significant association with UTI (P=<0.05 : 95%CI) as shown in Table 3

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Table3 Association of risk factors with UTI in SPHMMC pediatrics unit from Jan- July2020

Characteristics		**Positive no(%)**	**Negative no (%)**	**COR**	**95%CI**	**P value**	**AOR**	**95%CI**	**P Value**
Sex	Male(ref)	35(25.36)	103(74.64)	-	-	-	-	-	-
	Female	30(33.71)	59(66.29)	1.49	0.84 - 2.68	0.176			
Age in years	<3(ref)	35(29.41)	84(70.59)	-	-	-	-	-	-
	3-6	9(29.03)	22(70.97)	0.49	0.23-1.04	0.06			
	6-9	2(10.53)	17(89.47)	0.48	0.17-1.32	0.15			
	9-12	2(9.52)	19(90.48)	1.06	0.88-1.28	0.517			
	12-15	17(45.95)	20(54.05)	1.02	0.89-2.89	0.69			
Area	Urban	41(25.63)	119(74.37)	1.62	0.88 - 2.99	0.12	-	-	-
	Rural(ref)	24(35.82)	43(64.18)	-	-				
Circumcision	Yes(ref)	27(25.96)	77(74.04)				-	-	-
	No	8(23.53)	26(76.47)	1.14	0.46 – 2.82	0.77			
Hospitalization time	<3 day(ref)	25(19.38)	104(80.62)						
	3-30 day	37(42.05)	51(57.95)	2.12	1.31 – 3.43	0.002	6.06	1.99-18.4	0.01
	1-2 month	2(22.22)	7(77.78)	0.86	0.02-26.2	0.83	-	-	-
	2-3month	1(100)	0(0)	1.18	0.57-2.96	0.9	-	-	-
Location	OPD(ref)	25(20.83)	95(79.17)	-	-	-	-	-	-
	Ward	25(36.76)	43(63.24)	0.78	0.26-2.381	0.67			
	ICU	10(52.63)	9(47.37)	1.33	0.99 – 1.79	0.055			
	Emergency	5(25)	15(75)	3.34	0.86-12.91	0.08			
Previous History	Yes	23(37.70)	38(62.30)	1.79	0.96 – 3.34	0.069			
	No(ref)	42(25.30)	124(74.7)	-	-	-			
Catheterization	Yes	20(52.63)	18(47.37)	3.56	1.73 – 7.3	0.001	0.28	0.13-0.57	0.04
	No(ref)	45(23.8)	144(76.2)						
HIV status	Positive	5(62.5)	3(37.5)	0.66	0.15 – 2.84	0.575	-	-	-
	Negative(ref)	62(28.31)	157(71.69)	-	-	-			
Temperature	<37.5(ref)	44(28.2)	112(71.8)	-	-	-	-	-	-
	>37.5	21(29.58)	50(70.42)	1.07	0.58 – 1.98	0.83			
Leukocytes esterase test	Positive	48(90.57)	5(9.43)	88.7	31.08-252	0.001	0.01	0.004-0.03	<0.01
	Negative(ref)	17(9.77)	157(90.23)						
Nitrite test	Positive	46(100)	0	225.88	50.38-1012.58	0.001	0.004	0.001-0.02	<0.01
	Negative(ref)	19(10.5)	162(89.5)						
Chronic infection	Yes	27(34.62)	51(65.38)	1.55	0.85 – 2.80	0.15	-	-	-
	No(ref)	38(25.5)	111(74.5)						

5.3 Antimicrobial susceptibility patterns of bacterial uropathogens

The overall gram negative bacteria were sensitive to augementin(n=8; 18.18%) , Amikacin(n=41; 93.18%) , cefazolin(n=3; 6.82%), Ciprofloxacin (n=24;54.55%) ,Nitrofurantoin (n=20;45.45%),Meropenem (n=40;90.9%) , PiperacillinTazobactam(n=29;65.91%), trimetoprim sulphamethoxazole(n=7;15.91%).

Antimicrobial resistance pattern was observed in gram negative isolates ranging from 4.55% to 100%.All gram negative bacteria were 100% resistant to ampicillin. Eschercia coli shows resistance to ampicillin(100%) ,augmentin (66.67%), cefazolin (90.48%), ciprofloxacin(38.09%),Nitrofurantoin(23.81%),Meropenem(0%),PiperacillinTazobactam(28.57 %),Trimetoprimsulphamethoxazole(80.95%) respectively followed by klebsella pneumonia showing antimicrobial resistance to ampicillin(100%) ,augmentin(64.71%), cefazolin(94.11%),ciprofloxacin(35.29%), Nitrofurantoin (64.71%), Meropenem(11.76%) ,Piperacillin Tazobactam(23.53%), trimetoprim-sulphamethoxazole(88.24%) as shown in table 4

Table 4: Antimicrobial Susceptibility Pattern of Gram-Negative Bacteria Isolated From Children With UTI Attending in St Paul Hospital Millennium Medical College (January To July 2020)

ISOLATE	TOTAL		**ANTI-MICROBIAL AGENT (%)**								
			AMP	**AUG**	**AMK**	**CZ**	**CIP**	**NIT**	**MRP**	**TZP**	**SXT**
E.coli	21	S	0(0)	5(23.81)	20(95.24)	2(9.52)	12(57.14)	15(71.43)	21	13(61.9)	4(19.05)
		I	0(0)	2(9.52)	1(4.76)	0(0)	1(4.76)	1(4.76)	0(0)	2(9.52)	0(0)
		R	21(100)	14(66.67)	0(0)	19(90.48)	8(38.09)	5(23.81)	0(0)	6(28.57)	17(80.95)
Klebsella pneumoniae	17	S	0(0)	3(17.65)	15(88.23)	1(5.88)	10(58.82)	5(29.41)	15(88.23)	11(64.71)	2(11.77)
		I	0(0)	3(17.65)	0(0)	0(0)	1(5.88)	1(5.88)	0(0)	2(11.77)	0(0)
		R	17(100)	11(64.71)	2(11.77)	16(94.12)	6(35.29)	11(64.71)	2(11.77)	4(23.53)	15(88.23)
Acitinobacter spp	4	S	0(0)	0(0)	4(100)	0(0)	1(25)	0(0)	2(50)	3(75)	1(25)
		I	0(0)	0(0)	0(0)	0(0)	1(25)	1(25)	0(0)	0(0)	0(0)
		R	4(100)	4(100)	0(0)	4(100)	2(50)	3(75)	2(50)	1(25)	3(75)
Entrobacter spp	1	S	0(0)	0(0)	1(100)	0(0)	0(0)	0(0)	1(100)	1(100)	0(0)
		I	0(0)	1(100)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
		R	1(100)	0(0)	0(0)	1(100)	1(100)	1(100)	0(0)	0(0)	1(100)
Providencia spp	1	S	0(0)	0(0)	1(100)	0(0)	1(100)	0(0)	1(100)	1(100)	0(0)
		I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
		R	1(100)	1(100)	0(0)	1(100)	0(0)	1(100)	0(0)	0(0)	1(100)
Total	44	S	0(0)	8(18.18)	41(93.18)	3(6.82)	24(54.55)	20(45.45)	40(90.9)	29(65.91)	7(15.91)
		I	0(0)	6(13.64)	1(2.27)	0(0)	3(6.82)	3(6.82)	0(0)	4(9.09)	0(0)
		R	44(100)	30(68.18)	2(4.55)	41(93.18)	17(38.64)	21(47.73)	4(9.09)	11(25)	37(84.09)

AUG: augmentin (30µg); CIP:ciprofloxacin (5µg); NIT: nitrofurantoin(300µg); AMP :ampicillin(10µg); AMK:amikacin(30µg); MRP:meropenem(10µg); TZP:piperacillin tazobactam(100/10µg) ;CZ:cefazolin (30µg); SXT:trimethoprim-sulfamethoxazole (1.25/23.75µg)

Table 5: Antimicrobial Susceptibility Pattern of Gram-Positive Bacteria Isolated From Children With UTI Attending in St Paul Hospital Millennium Medical College (January 2020 To July 2020)

ISOLATE	**TOTAL**		**Antimicrobial Agent (%)**								
			PEN	**VAN**	**FOX**	**AZM**	**CIP**	**CLN**	**NIT**	**SXT**	**DOXY**
S.aureus	1	S	0(0)	0(0)	1(100)	1(100)	1(100)	1(100)	1(100)	0(0)	0(0)
		I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
		R	1(100)	1(100)	0(0)	0(0)	0(0)	0(0)	0(0)	1(100)	1(100)
CONS	1	S	0(0)	1(100)	1(100)	1(100)	1(100)	0(0)	0(0)	0(0)	0(0)
		I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
		R	1(100)	0(0)	0(0)	0(0)	0(0)	1(100)	1(100)	1(100)	1(100)
Entrococcus spp	3	S	2(66.67)	2(66.67)	3(100)	NT	1(33.33)	NT	0(0)	0(0)	NT
		I	0(0)	0(0)	0(0)	NT	0(0)	NT	0(0)	0(0)	NT
		R	1(33.33)	1(33.33)	0(0)	NT	2(66.67)	NT	3(100)	3(100)	NT
Total```	5	S	2(40)	3(60)	5(100)	2(100)	3(60)	1(50)	1(20)	0(0)	0(0)
		I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
		R	3(60)	2(40)	0(0)	0(0)	2(40)	1(50)	4(80)	5(100)	2(100)

CONS: coagulase-negative staphylococci; P: penicillin (10 U); CLN: clindamycin (30µg); (10µg); AZM: azitromycin (30µg); FOX: cefoxtin (30µg); NIT: nitrofurantoin (300µg); CHL: chloramphenicol (30µg);VAN:vancomycin(30µg) ;SXT: trimethoprim-sulfamethoxazole (1.25/23.75 µg) ; CIP:ciprofloxacin (5µg); NT: Not done

5.4 Multidrug resistance patterns of bacterial isolates

Among the total bacterial isolates multi drug resistance is shown in 10(20.41%) isolates from the total of 49(100%) bacterial pathogens of which gram negative bacteria consists of 9(90%) and gram positive bacteria 1(10%) respectively as shown in table 6.

Table 6: Multidrug resistance pattern of gram-negative and gram positive bacteria isolated from pediatric patients at SPHMMC Hospital Medical College. (January 2020 - July 2020)

Bacterial isolate	***Anti-microbial resistance*** (%)					
	Total	R0	R1	R2	R3	R4
Gram Negative	**44(89.8)**	0(0)	15(34.09)	20(45.45)	5(11.36)	4(9.09)
E.coli	21(47.73)	0(0)	9(42.85)	10(47.62)	1(4.76)	1(4.76)
K.pneumonia	17(38.64)	0(0)	5(29.41)	6(35.29)	4(23.53)	2(11.76)
Acitinobacter spp	4(9.1)	0(0)	1(25)	2(50)	0(0)	1(25)
Entrobacter spp	1(2.27)	0(0)	0(0)	1(100	0(0)	0(0)
Providencia spp	1(2.27)	0(0)	0(0)	1(100)	0(0)	0(0)
Gram Positive	**5(10.2)**	0(0)	1(20)	3(60)	1(20)	0(0)
S. aureus	1	0(0)	0(0)	0(0)	1(100)	0(0)
CONS	1	0(0)	0(0)	1(100)	0(0)	0(0)
Entrococcus spp	3	0(0)	1(33.33)	2(66.67	0(0)	0(0)
Total	**49(100)**	0(0)	16(32.65)	23(46.94)	6(12.24)	4(8.16)

R0- No antibiotic resistance, R1- Resistance to one, R2-Resistance to two, R3-Resistance to three, R4- ≥Resistance to four

6. Discussion

UTI is an infection caused by microbial agent which causes infection, to the kidney , bladder and urethra. The overall prevalence of UTI in the present study is 28.63% of which prevalence of UTI caused by bacteria and fungal isolates is 21.59% and7.05% respectively .which agree with studies done in Gondar[31], Hawassa[24] and high prevalence of UTI is seen in Cameron[27],Nepal[28],China[21] as well as low prevalence rate is shown in Turkey[35],India[36],Nepal[44] Bahirdar[38], Addisababa[39]. The difference may arise from total sample size and different geographical location.

This study showed that prevalence of urinary tract of infection caused by fungal pathogen is 7.05% which is comparable with the study done in Ahvaz, Iran[19]which showed a total prevalence of UTI caused by fungal agents is 5.3%.

In our study females (33.7%) are more susceptible than male(25.36%) which is in line with Addis ababa[34],Gondar[16], Iran[30]. The major cause of female UTI is proximity of their reproductive organ to the anus the shorter and wider urethra through which the bacteria, from fecal flora may readily enter into the bladder and kidney and cause UTI [43]. UTI is also common in boys during the first year of life, especially among those who are uncircumcised because during this time of age, they get exposed to pathogens easily with weak immune system. [45].

Our study showed gram negative bacteria accounts for 89.5% followed by 10.2% gram positive bacteria from the over all isolates. which agree with studies done in Mekelle[40],Gondar[16], Southafrica[41]. Gram negative bacteria is more prone to cause UTI than Gram positive bacteria due to presence of unique structure in Gram- negative bacteria which facilitates attachment to the uroepithelial cell, with resultant high prevalence in the gastrointestinal tract. This unique structural characteristics prevent elimination of bacteria with urinary lavage, and allow its multiplication and tissue invasion ensuing in invasive infection and pyelonephritis.[16]

In this study among all bacterial isolates E.coli accounts the dominant prevalence (42.85%) which agrees with studies done in addisababa45.9%[34],Hawassa45.9%[24], bahirdar34.9%[38]. The second most leading isolate in our study was klebsella pneumoniae followed by

acitinobacter , entrococcus spp, entrobacter spp, Providencia spp ,S.aureus and CONS.which is in line with studies done in Addisababa[34] and Uganda[29]. But it isn't the same as researches done in Iran(45) where S.saprophyticus was the second most leading bacteria as well as in Bahidar [42] and in Gondar [16] Pseudomonas spp was the second isolate with high prevalence rate.

In our study the first leading isolate from gram positive bacteria is Entrococcus spp(60%).which is the same as in Germany[33]. And our study disagrees with research done in Gondar[16]where S.aureus and S.saprophyticus were the dominant from all gram positive isolates.

In our study high carbapenem group antibiotic (meropenem) sensitivity is seen 90.9% among gram negative isolates which agrees with study done in Iran [35]. As well as high level of amikacin (93.3%)sensitivity is also observed among gram negative isolates .Mean while high level of resistance is observed for ampicillin ,cefazolin and trimetoprim-sulphamethoxazole (100%), (93.18%) and (84.09%) respectively. Which is comparable with study done in Uganda (45) which showed (96.6%) and (82.2%) resistance for ampicilin and trimetoprim-sulphamethoxazole respectively.

Gram positive isolates were Penicillin(40%),Ciprofloxacin(50%),vancomycin(60%), Cefoxitin(100%),Azitromycin(60%),Clindamycin(60%), Nitofurantoin(20%),and Doxycyline (20%) sensitive respectively.

The over all gram positive bacterias showed 100%,80%,80% and 60% resistance to trimetoprim-sulphamethoxazole, Doxycycline , Nitrofurantoin and Penicillin respectively. Which is in line with research done in hawassa[27] showing 100% and 97.1% resistance to penicillin and trimetoprim-sulphamethoxazole respectively.

Multi drug resistance (MDR) is seen among (20.41%) of all total isolates. From all Gram negative isolates 20.45% and from gram positive isolates 20% shows multi drug resistance pattern(MDR) .Mean while research done in Gondar[16] showed high MDR pattern (58.53%) as compared to current study.Although high prevalence of MDR is seen in bahirdar[42](90.3%) and Uganda (82.8%)[30] among both group bacterial isolates. This high prevalence of MDR arises from inappropriate antibiotic agent misuse, Empirical treatment by physicians, increase in the production of enzymes producing enzymes such as Beta lactamase by bacterias such as E.coli

and klebsella spp. Showing 100% resistance including the current study to ampicillin(Beta lactam antibiotic) [16].High prevalence of Urine culture positivity is seen among pediatric ICU patients (52.63%). This might arise from ICU patients are prone to use cathether which favors major route of entry to the pathogen to cause bladder infection and pyleonephritis and also they are highly susceptible to hospital acquired infection with their impaired immune status which is comparable with research done in Tehran Iran[46].

In our study history of catheterization ,admission period ,positive leukocyte esterase and nitrite test have significant association with UTI which is supported by research done in hawassa[24].

7. Strength and Limitation of the study

7.1 Strength of the study

- ✓ Includes study participants from all wards including neonatal unit.
- ✓ Identification for fungal pathogens was done.
- ✓ Antimicrobial susceptibility for bacterial isolate was done from different antibiotic classes.

7.2 Limitation of the study

- ✓ Anti microbial susceptibility pattern for fungal isolates is not done.
- ✓ Inappropriate sample collection was seen from neonatal patients in resulting contamination and repeating the sample.
- ✓ All Anti microbial drugs recommended by CLSI were not used .
- ✓ Few isolates were not identified to the species level.

8 .Conclusion and Recommendation

8.1 Conclusion

In our study the overall prevalence of UTI is 28.63% . From the overall prevalence UTI caused by bacteria comprises the largest percentage and followed by fungal pathogens accounts for the remaining.

Our study result showed that high prevalence of UTI among pediatric patients where E.coli and klebsella pneumoniae were predominantly isolated. Where all gram negative and gram positive bacteria exhibited high level of antibiotic resistance. Gram negative isolates showed a high level of resistance to ampicillin ,cefazolin and cotrimoxazole. Gram positive isolates also show a high level of resistance to cotrimoxazole, doxycycline and penicillin.

High level of multi drug resistance pattern was shown in our study. Antibiotic misuse by patients, empirical treatment by physicians and health care workers,taking inappropriate dosage of antibiotic by patients may contribute for the increment of MDR.

8.2 Recommendation

This study suggests that bacterial culture only is not enough to diagnose urinary tract infection although fungal culture test should be a requested for UTI case. According to this study meropenem, amikacin ,cefoxitin and ciprofloxacin are the best antibiotic treatment against Gram negative and Gram-positive bacterial uropathogens respectively.

Investigations mainly focused on urinary tract infection caused by fungal pathogens,Fungal culture and susceptibility pattern should be conducted all over the country to see the level of resistance to anti fungal agents and prevalence of UTI caused by fungal pathogens.

Antimicrobial drug administration guideline has to be revised regularly based on results of different investigations. Mean while the current MDR prevalence shows that we are in alarming time to do more to reduce MDR including continuous monitoring in antibiotic administration and conducting further more studies on MDR incorporating with molecular techniques in different areas of our country.

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10. Annex

I. Participant information sheet

Participants' Information sheet in English Version

Title of the Research Project: Profiling of bacterial uropathogen and fungal pathogen , anti microbial susceptibility pattern of bacterial isolates and associated risk factors among. pediatric patients at St Paul Hospital Millennium Medical college.

Principal Investigator: Nuhamen Zena (BSc, MSc candidate)

Name of the Organization: Addis Ababa University, College of Health Sciences School of Medical laboratory.

Introduction

You are invited to participate as a study subject in a research conducted by MSc candidate, from Addis Ababa University. Your participation is voluntarily. The research teams will include principal investigator and advisor from Addis Ababa University School of Medical laboratory Sciences. Please take time as you need to read or listen in the information sheet.

Purpose of the Research Project

The purpose of the study is to determine the prevalence and antimicrobial resistance pattern of uropathogens isolated from pediatric patients at St Paul hospital millennium medical college..

Duration

The study will be conducted among pediatric patients complaining urinary tract infection cases at St Paul Hospital Millennium Medical College from Nov 2019 – Jun 2020

Procedures and the expected participation

If you are willing to participate, you need to understand the purpose of the study and give your consent. Not only this but also specimen collected from you will be used for the research purpose, and the results of your sample will be exposed to some concerned professional staffs as it is needed. You are requested to give your consent to the sample collector. After consent, a

sample will be taken from the volunteer. Moreover, there will be structured questioner for additional information.

Confidentiality

We respect your privacy and confidentiality. Any information that identifies you will not be shared with anyone else outside the study team. The information we will collect from you as part of the study will be protected by a password on the computer only accessible to personnel involved in the study. There is no sensitive issue that you will be asked related with your social interest but any information that is obtained in connection with this study will remain confidential.

Potential benefits to subjects and the society

You will not receive any payment for your participation in this research. However, based on the diagnosis result . In addition, the result of the study will be beneficial for management of urinary tract infection. Therefore, you are indirectly benefiting other patients and the society in this respect.

Participation and Withdrawal from the Study

The participation is voluntary and you have the right not to participate in this study. You may withdraw at any time and prevent your child's participation in the study. This decision will not affect you and your child's current or future medical care in the health facility free. The information you give us is important to prevent and control the scope of the problem, we respectfully ask you to answer directly to the question.

If you agree to participate in the study, you are required to sign or put written signature on the consent form.

Contact information

If you have any questions about this study you can contact the following principal investigators and advisor for further information.

Nuhamen Zena Phone: 0910371994 E-mail: nuhamenzf@gmail.com
Dr. Adane Bitew E-mail: adane.bitew@aau.edu.et

II. Informed consent form for parents/guardians in English version

Participant code:_____

I had been informed that the objective of this study is to determine the prevalence of urinary tract infections and antimicrobial susceptibility profile. I have been informed there is no harm related to giving specimen. I have been informed that other people will not know my child results as it coded with number rather than writing name. It is therefore with full understanding of the condition I agreed to give the informed consent voluntarily to the researcher that my child gives sample for the study. I understand that there may be no benefit to me personally apart from clinical service I get from these results. I have been encouraged to ask questions and have had my questions answered. I have been told that participation in this study is voluntary and I may refuse to be part of the study. I know my participation will also be approved by my child. By signing below I agree to let my child to participate in this research study.

Signature: _____ Date_____

For those who can't read the information

Advisor name……..

Signature …… Date ……..

Informed consent form for parents/guardians in Amharic version

የጥናቱ ስላማ ከ ሽንት ናሙ ናዎች ላይ በሽታየሚያመጡጀርሞችንመጠንማወቅ፣የፀረ-ተህዋሲያን የመቋቋም ዘይቤ እና ህመሙን የሚያባብሱ ተዛማጅነት ያሳቸውን ነገሮች ማወቅ እንደሆነ በቂ ገለጻ ተደርጎልኛል።ናሙና መስጠት ምንም ስይነት ጉዳት ልጄ ላይ እንደሌለዉ ተነግሮኛል።በጥናቱ ወቅትም የልጄ መረጃዎች በሚስጥር ስለሚያዝ በሌላ ሰዉ ዘንድ እንደማይታወቅ ተረድቻለሁ።በሙጤቱ ከሚገኝዉ የህክምና አገልግሎት በቀር ሌላ ልጄ በግሉ የሚያገኝዉ ጥቅም እንደሌለ ተረድቻለሁ ። ጥያቄ እንድጠይቅ ሰድል ተሰጥቶኝ ለጥያቄዎቼም በቂ ምላሽ አግኝቻለሁ።የልጄ በጥናቱ መሳተፍ በእኔ ፍላጎት ብቻ እንደሆነ እና በጥናቱም ስለመሳተፍ ምንም ስይነት ተፅዕኖ በልጄ ላይ እንደማያስከትል ተረድቻለሁ።በከዚህ ባሻገር የልጄ በጥናቱ ውስጥ ስመካተት የእኔ የወላጄ አሳዳጊ ፈቃድ እንደሚያስፈልግ ተረድቻለሁ።በእኔፍቃደኝነት ልጄ በጥናቱ እንደሚሳተፍ ከዚህ በታች በፈርማዬአረጋግጣለሁ።

የአሳዳጊው ፈርማ----------

ቀን ----/---/----------

የስምምነት ቅጹን ማንበብ ስማይችሉ ተሳታፊዎች

የአማካሪስም ----------

ፈርማ .....

ቀን----------

Informed Assent form for children in English version

It has been read to me that the objective of this study is to determine the prevalence of urinary tract infections and antimicrobial susceptibility profile . I have been informed there is no harm related to giving specimen. I have been informed that other people will not know my result since it coded with number rather than writing name. I voluntarily assent that I would participate in this study provided if my parents/guardians give their consent.

Signature: _____ Date_____

For those who can't read the information

Advisor name……..

Signature …… Date ……..

Informed Assent form for children in Amharic version

የጥናቱ አላማ ከሽንት ናሙናዎች ላይ በሽታ የሚያመጡ ጀርሞችን መጠን ማወቅ፣የፀረ-ተህዋሲያን የመ ቋቋም ዘዴዉ እና ህመሙን የሚያባብሱ ተዛማጅነት ያላቸውን ነገሮች ማወቅ እንደሆ ነበቂ ገለጻ ተደርጎልኛል፡፡ ናሙና መስጠት ምንም አደነት ጉዳት እንደሌለዉ ተነግሮኛል፡፡ በጥናቱ ወቅትም ከኔ የሚወሰዱ መረጃዎች በሚስጥር ስለሚያዙ በሌላ ሰዉ ዘንድ እንደማይታወቅ ተረድቻለሁ ::ወላጆቼ / አሳዳጊዎቼ ፈቃደኝነት ከሰጡ በዚህ ጥናት ዉስጥ ለመሳተፍ ፈቃደኝቴን አረጋግጣለሁ፡፡

የአሳዳጊው ፊርማ----------

ቀን ----/---/----------

የስምምነት ቅጹን ማንበብ ለማይችሉ ተሳታፊዎች

የአማካሪስም ----------

ፊርማ ……

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III. Laboratory procedure

- Clean-catch midstream urine will be collected from patients complaining of UTI patients with sterile wide-mouthed urine cup
- Part of the sample will be inoculated onto Blood Agar base and Cysteine Lactose Electrolyte Deficient medium, and Brain Heart infusion agar by using calibrated loop with a capacity of 1 µl in safety cabinet.
- Pure isolates of bacterial pathogen were preliminary characterized by colony morphology and Gram-stain.
- Further identification of the isolate is selected and performed accordingly by gram reaction result.i.e
  - i.e Gram positive isolate : catalase test, coagulase test, bile esculine test, bacitracin and optochin disc test
  - Gram negative isolate : triple sugar iron test (TSI), urease test, citrate utilization test, indole test, motility test
  - Yeast isolate: germ tube test(for c.albicans), chromogenic medium agar colony characterstics
- Antimicrobial susceptibility test was done by Kirby Bauer disc diffusion method.
- The growth suspension was prepared in 0.5 ml of the same broth medium and the turbidity was adjusted to match that of 0.5 McFarland
- Sterile cotton swab applied to the center of Muller Hinton agar plat and evenly spread on the medium.
- Antibiotic discs were placed after 15 min of inoculation to Muller Hinton agar seeded with each isolate and incubated for 24 h at 35–37 °C.
- The diameter of the zone of inhibition around the disc was measured using sliding metal caliper
- Break points interpreted according to Clinical Laboratory Standards Institute (CLSI) guidelines.

IV. Questionnaire

Sample ID----------

Socio demographic characteristics of participants

1 . Sex

☐ Male ☐ Female

2. Age

☐ < 3 yrs

☐ 3-6 yrs

☐ 6-9 yrs

☐ 9-12 yrs

☐ 12-15 yrs

3. Patient location

☐ OPD ☐ ICU

☐ Ward ☐ Emergency

4. Area of living

☐ Urban

☐ Rural

5. Are you circumcised (only for male patients)?

☐ Yes

☐ No

6. How long have you stayed in this hospital after admission?

☐ <3 days ☐ 2-3 months

☐ 3-30 days ☐ 3-4 months

☐ 1-2 months ☐ > 4 months

7. Previous illness with UTI

☐ Yes

☐ No

8. Have you ever take an antibiotics for urinary tract infection case?

☐ Yes

☐ No

9. If yes the drug is prescribed by physician?

☐ Yes

☐ No

10. Temperature during the time of diagnosis?

☐ <37.5 ☐ >37.5

11, Have you been on catheter?

☐ Yes

☐ No

12. HIV status

☐ Negative ☐ Positive

13. Any other chronic infection ?

☐ Yes ☐ No

14. If yes for the question in the above specify----------?

V. Declaration

Declaration I, the undersigned agree to accept responsibility for the scientific ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research publications office.

M.Sc. candidate: **Nuhamen Zena (B.Sc.)**

Signature: _____

Date of submission: _____

This thesis has been submitted with our approval as advisors.

Advisor: **Adane Bitew (PhD)**

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.

መ ግ ለ ጫ

ይ ህ ሀሳብ የዩኒቨርሲቲ ው ን ህጎች የሚ ያከብ ር እና ከኦፊያ ናል እና ጥራት ስንጣር ተቀባይነት ያላቸ ውን መመዘኛዎች የሚያሟላ መ ሆ ኑን ም ልክት የተደረገበት ሰነድ ስለደ ታ ል።ዋና ተመራማሪ በተጨማሪም ለምርምር ፕሮጀክቱ ሳይንሳዊ ሥነ ምግባር እና ቴክኒካዊ ምግባር ኃላፊችን ለመ ቀበል እና ስሚያስፈልጉ የእድገት ሪፖርቶችን ለማቅረብ ተስማምቷል።

ኬ ም ኬ ስሲ እጩ: ኑላሚን ዝና (ቢ ኬ ስሲ)

ፊርማ _____

ቀን _____

ይህ ሳሳብ ስማካሪ በመሆን በእኛ ማረጋገጫ ገብቷል።

ስማካሪ

ስዳነ ቢተው (ፒ ኤ ች ዲ)

ፊርማ _____

ቀን _____

ስዲስ ስበባ፣ኢ ትዮጵያ።