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Predictors Patterns Of Bacterial Urinary Tract Infections Among Febrile Children Under-Five Years Of Age At Kampala International University Teaching Hospital

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ABSTRACT

An accurate and reliable diagnosis of UTI in children is critical because they are usually underdiagnosed or over-diagnosed especially in children under five years of age. Antimicrobial susceptibility results are key to effective intervention. This study was done to determine the predictors patterns of bacterial urinary tract infections among febrile children aged less than 5 years presenting at Kampala International University Teaching Hospital. A hospital-based cross-sectional study was conducted in entry points of the pediatric ward of KIU-TH between December 2020 and March 2021. The study enrolled a total of 350 children 2-59 months by consecutive enrolment. Urinalysis and urine culure was done, clinical and demographic data was collected using questionnaires and data analysed using SPSS version 27 with significance at 95% confidence interval. Factors that were independently predictive of a UTI were age less than 24 months (p 0.002), male children (p 0.010), undernutrition (p 0.012), diarrhea (p 0.032), vomiting (p 0.005). Children who were wiped back to front after defecation (p 0.021), diapers use (p *0*.014). Among the laboratory urinalysis predictors, Children with nitrites and those with more than 5 white blood cells at urine microscopy were 17.875(p <0.001) and 6.505(p<0.001) times more likely to suffer from Urinary tract infection respectively.

Keywords: Predictors pattern, bacterial, urinary tract and infections

INTRODUCTION

Urinary Tract Infections (UTIs) have been a health burden throughout the history of mankind. In ancient times the Greeks thought that UTIs resulted from disharmony while the Egyptians and Romans developed different ways to palliatively manage UTIs which included use of herbs, bed rest, diet and use of narcotics [1; 2]. During the ancient days in Babylon, diagnosis of UTIs was made by visual inspection of the colour and cloudiness of urine and in the 20th century diagnosis was transformed by the use of assays for white cell and bacterial counts in urine [3]. Almost 100 years ago, the nitrite test was developed [4] but had a limitation of inability to identify the pathogen because it measures the conversion of dietary nitrate to nitrite by Gram-negative bacteria, currently its used as a screening test where a positive nitrite test makes UTI very likely but the test may be falsely negative if the bladder is emptied frequently or if an organism that does not metabolize nitrate (including all Gram-positive organisms) is the cause of infection. At the beginning of the 20th century, urine culture proved valuable in diagnosis of UTIs [3] and use of antimicrobial agents such as hexamine, pyridium, hexylresorcinol and mercurochrome was recognized [5]. During the first half of the twentieth century, penicillins were introduced but had limited effectiveness in management of UTI [6; 7]. In 1937, sulfanilamide ushered the era of antimicrobial therapy which was effective in management of several types of UTIs such as cystitis and pyelonephritis but poor for different bacterial isolates and in 1953, nitrofurantoin was introduced which was a safe and more effective

antibiotic for UTI and was an antimicrobial agent with good activity against *E. coli*, and a more favourable tolerability and had safety profile than sulphanilamide [8]. Since then different antimicrobial agents such as Cephalosporin and augmented Penicillin have been developed and this has led to great improvement in management of UTIs in children.

AIM OF THE STUDY

The aim of this study was to determine the predictors patterns of bacterial urinary tract infections among febrile children aged less than 5 years presenting at Kampala International University Teaching Hospital.

Specific objective

i. To identify the predictors of urinary tract infections among febrile children aged <5 years presenting at Kampala International University Teaching Hospital.

Research question

i. What are the predictors of urinary tract infections among febrile children aged < 5 years presenting at Kampala International University Teaching Hospital? Teaching Hospital?

METHODOLOGY

Study design

This was a hospital-based cross-sectional descriptive and analytical study to determine the prevalence, describe susceptibility patterns of bacterial isolates and predictors of UTIs among febrile children aged 2 to 59 months presenting at Kampala International University Teaching Hospital. The study was conducted at all entry points of paediatric patients in the hospital; out-patient clinic and A and E, where all eligible children age 2 to 59 months with fever or history of fever were enrolled into the study. Informed consent was sought from the caregiver, then data was collected by use of paper-based investigator-administered questionnaire that was designed in English and translated in Runyankole, based on the problem statement and objectives. Urine samples were collected for urinalysis and culture and bacterial uropathogen susceptibility patterns described as explained in the details below.

Study site

The study was conducted on the Pediatrics outpatient and A and E department/all entry points of KIU-TH which is a university teaching hospital located in Ishaka- Bushenyi municipality approximately 319.7km from Kampala, on Kampala-Mbarara-Kasese highway, 60 km west of Mbarara. KIUTH is private not for profit hospital and one of the general hospitals in western Uganda started in 2008. It is a specialized hospital with the following departments: Pediatrics, Internal medicine, Surgery, Obstetrics and Gynecology, and other specialized clinics with a bed capacity of 700 with a fully functional laboratory (level III) with microbiology, chemistry, hematology and pathology unit departments. The microbiology unit of KIU-TH offers diagnostic bacteriology,mycology,parasistology,virology and mycobacteriology and contains major equipements such as autoclave sterilizers, cell culture incubators, light microscopes, refrigerators, busern burners among others and the chemistry offers both sample preparation and analysis and the major equipments include a centrifuge, spectrometers, dry ovens and other minor apparatuses used. The facility serves as a tertiary point of care for referrals from lower facilities in the districts of Mitooma, Sheema, Rubirizi and Ntungamo. The Paediatric outpatient department receives an average of 350 patients monthly and it is managed by a Pediatrics specialist, a senior house officer, an intern doctor and a nurse on a daily basis.

Target population

Febrile children aged 2 to 59 months attending to KIU-TH.

Study population

All febrile children aged 2 to 59 months attending the paediatric outpatient clinic/all entry points of KIU-TH. Children were considered to be febrile if axillary temperature was ≥37.5^{0}C and this was put into consideration because of easy infection control and axillary temperature

is 0.5 ^{0}C less than rectal temperature which is 38.0^{0}C

Study duration

This study was conducted over a period of three months from December 2020 to March 2021.

Sample size determination

To determine the prevalence [9] was used

$$N = \frac{z^2\rho(1-\rho)}{r^2}$$

N= desired sample size

Z= Standard normal deviate (1.96 for a 95% confidence interval)
P= Proportion of children <5 years diagnosed with a UTI. [10], in a cross-sectional study done at Nsambya hospital found a prevalence of 26.8% among children <5 years presenting with fever.
r= the acceptable margin of error (0.05)
Sample size = 302
To estimate the sample size for the predictors of UTIs, the method for calculating sample size for two proportions(Kelsey's formula) was employed and a study by [11] in Tanzania using age as predictive factor for UTIs found a percentage of 45.2%(P1) for children below 2years and Percentage 30.7(P2) for children above 2 years

$$n = \frac{(Z_1 + Z_2)^2 2P(1-P)}{(P_2 - P_1)^2}$$

Where;
Z1 is Z value at 95% level of significance = 1.96,
Z2 is Z value at 80% power = 0.84,
P1 is proportion of patient with UTI among patients below 2 years=45.2%
P2 is proportion of patient with UTI among patients above 2 years=30.7%

$$P = \frac{(P_1 + P_2)}{2}$$

Sample size = 350.

The sample size calculated (350) was more than the sample size for the prevalence so 350 was used, which is the bigger of the two sample sizes.

Selection criteria

Inclusion criteria

All children from 2-59 months presenting with history of fever or axillary temperature of ≥37.5˚C at the paediatric outpatient clinic/all entry points of KIU-TH.

Exclusion criteria

Children with a contraindication to urethral catheterization were also be excluded such as children with hypospadias, evidence of urethral infection, gross hematuria and blood at meatus.

Sampling technique

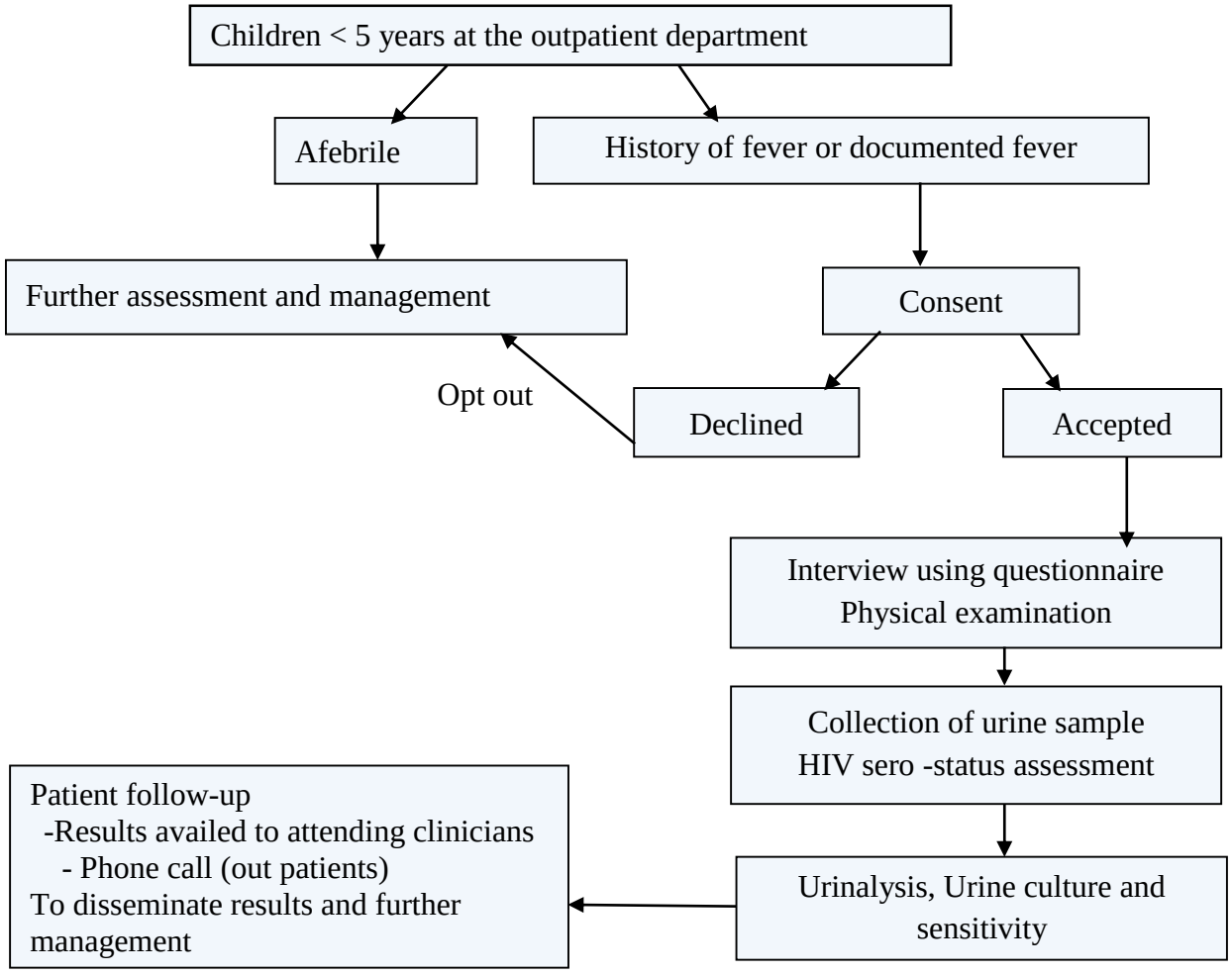
Consecutive enrollment into the study was done for children who met the inclusion criteria until the desired sample size was obtained.

Study procedure

Identification of study participants and screening for eligibility

At the outpatient clinic KIU-TH, all children age 2 to 59 months with history of fever or fever on examination were enrolled into the study.

Figure 1: Patient flow chart



Validity and Reliability of data collection tools

The questionnaires contained both open and close ended questions and was pretested in a similar study population at KIU-TH in Bushenyi. The pretesting was helpful in obtaining data by a pre-determined questionnaire using the Cronbach's coefficient alpha of more than 0.8 which means that the items of the questionnaire were reproducible and consistent. Standard operating procedures for urethral catheterization and mid-stream urine (MSU) sample collection were followed at all times. Urine samples were stored in a cool box at a temperature of 5ºC-7 ºC and then delivered to the laboratory within one hour of collection. Standard operating procedures for urine culture and antibiotic susceptibility testing were followed and a clinical microbiologist was consulted at all levels of the procedure. The antimicrobial susceptibility tests were performed using the Kirby Bauer disk diffusion technique [12] with commercially available disks on Mueller Hinton agar plates. Antibiotics disks validity were controlled using *E. coli (*ATCC 25922). Run control tests for dipsticks on each new batch and weekly.

Data collection instruments

Patient information including socio-demographic details, physical examination findings and past medical history was obtained upon enrollment using a questionnaire that was designed in English and translated in Runyankole. The children were examined for fever by taking the

axillary temperature using a digital thermometer. Cotton swabs, normal saline, urine sample bottles (50ml) and small sized appropriate urine catheters were used to collect urine samples as described in details below and urine samples which were not processed immediately were kept in a cooler box and processed within one hour for urinalysis and urine culture.

Data collection

Based on the problem statement and objectives. Patients were given information about the study, and then a written consent sought and signed. Predictors including age, sex, place of residence and education level of the caregiver were under social demographics while under medical predictors we had factors such as circumcision, HIV status, malnutrition, exclusive breastfeeding and clinical features which may predict UTI in children included; constipation, diarrhea, vomiting, character of fever (fever of ≥ 39°C at the time of recruitment, >24 hours, fever without definite source), sudden onset bedwetting and foul smelling urine in past two weeks. Behavioral predictors included wiping from back to front, toilet training habits, and use of diapers. Laboratory predictors were nitrites, leucocytes and microscopy results. Physical assessment of study participants included taking temperature,checking for oedema and taking anthropometric measurements including MUAC , weight, height, then indices weight for height, height for age and weight for age were compared to the WHO growth standard charts to determine the nutritional status which was classifiesd as moderate or severe malnutrition using under nutrition parameters(wasting,under weight or stunting). The result of MUAC was interpreted as normal, moderately wasted and severely wasted if it is above 12.5cm, between 11.5-12.4 cm, and less than 11.5 cm respectively. Children with bilateral pitting oedema were not assessed for MUAC. The child was regarded as normal if height for age is ≥-2 SD, moderately stunted if is ≥-3SD to <-2SD and severely stunted if is <-3SD. The child was regarded as normal if weight for age is ≥-2 SD, moderately underweight if is ≥-3SD to <-2SD and severely underweight if is <-3SD. The child was considered as normal if the weight-for-length is ≥ -2 SD, moderately wasted if is ≥-3 SD to <-2SD and severely wasted if is <-3SD. All children with bilateral pitting oedema were not assessed for weight-for-length but were considered as malnourished after ruling out other causes of oedema. The subjects' weight in kilograms was taken using a weighing scale manufactured by SECA®. Before the weight was taken, the subject took off his/her shoes and any heavy clothing. The weighing was calibrated every morning according to the manufacturer's manual, for those who cannot stand, a two in one weighing scale will be used and the caregiver carried the participant. The height was recorded to the nearest 0.1 centimeter. The subject's height was measured using a SECA® wall mount station meter and a tape measure for those who cannot stand. The height was recorded as the maximum distance from the floor to the highest point on the head. Sources of other causes of fever were recorded on the questionnaire according to physical examination findings (clinically) done by the principal investigator and this was refined according to the investigations such as CBC,lumbar punctures,malaria tests, thyphoid tests etc requested by the clinician attending to the patient. However it was a limitation in that the research principal investigator couldn't directly be involved in the decision of the investigations requested.

Urine sample collection

One urine sample was collected on the same day of recruitment of study participants. For children older than two years (toilet-trained children) who were able to follow instructions, a mid-stream (clean catch) was collected. For girls, the labia were spread and the perineum cleansed two to three times with non-foaming antiseptic solution or mild soap and for boys, the meatus was cleansed, The foreskin was retracted before cleaning for those who were uncircumcised. For uncircumcised males, the foreskin was reduced to its normal position so that a paraphimosis does not develop. Midway through urination, voided sample of urine was obtained under the observation of the principal investigator [13; 14]. For children aged less than 2 years and those who were

unable to follow instructions, transurethral catheterization was performed; the child was gently restrained in the supine and frog leg position to permit adequate stabilization of the pelvis and complete visualization of the external genitalia, the anterior urethra was cleansed thoroughly with an antiseptic (povidone-iodine solution) and a sterile lubricant jelly was applied to the end of an appropriately sized catheter (5 French for children younger than six months; 8 French for those between 6-59 months, the catheter was passed through the urethra and into the bladder as follows:For boys, the foreskin of the glans was retracted gently to permit complete visualization of the urethral meatus if the boy was uncircumcised, the urethra was straightened by using the non-dominant hand to hold the penis perpendicular to the lower abdomen. Gentle traction was applied; the catheter was inserted with the dominant hand until urine returns. As the catheter was being advanced, it was palpated along the posterior aspect of the penis. If Resistance was encountered near the base of the penis due to contraction of the external bladder sphincter. This was generally overcome by maintaining traction on the penis, while applying gentle pressure with the catheter. For girls, an assistant often was needed to retract the labia majora, having an assistant lift the labia majora anteriorly, laterally, and cephalad to provide better urethral exposure, Swabbing the introitus and the surrounding area from front with the povidone-iodine solution was done, the catheter was inserted into the urethral meatus until urine comes. [15,16]. About 5ml of urine specimen was collected from each patient in a sterile screw-capped, wide-mouth, leak-proof container and labelled with the unique sample number, date and time of collection. Voided sample of urine was obtained under the observation of the principal investigator or research assistants. Urine samples were taken immediately to the laboratory and samples which were not processed immediately were kept in a cooler box for one hour till when urinalysis and urine culture could be done. One drop was utilized for culture and the remaining sample processed for urinalysis.

Diagnosis of UTIs

This was made based entirely on urine culture results and this study considered a threshold of ≥100,000 CFU/ml (10^5) for mid- stream catch urine and ≥10,000 CFU/ml (10^4) for catheter-collected urine sample for a positive culture test for UTI. Rapid techniques were carried out to predict UTI but not making diagnosis and these included urine dipstick tests for leukocyte esterase and nitrites and standard microscopy as described in detail below.

Urine dipstick and microscopy

Immediately after collection of the urine specimen, it was delivered and processed in the microbiology laboratory at KIU-TH. A spot urine dipstick test (Neotest® urine multistix, Neomedic Ltd, Rickmansworth, UK) was performed to detect leucocyte esterase and nitrites then microscopic examination was performed by centrifugation of urine at 3000 rpm for 3 minutes and thereafter the supernatant was discarded aseptically. The sediment was placed on the slide and a cover slip was applied before being examined under the microscope at 40X objective. An average count of white blood cells (WBC) was taken per number of fields examined. The increased number of leucocytes is mostly observed in urinary tract diseases, and thus presence of ≥5 WBCs per hpf (high-power field) was considered positive.

Isolation of bacteria in pure culture

The cysteine lactose electrolyte deficient (CLED) and Chrom Agar were used as selective media for isolation. The media was prepared according to the manufacturer's instructions and 0.001 ml of urine sample was inoculated onto the media using a platinum wire loop. Plates were then incubated for 24 hours at 37°C. Colony counts yielding bacterial growth of 10^4CFU/ml and 10^5 CFU/ml of urine collected by catherisation and mid stream methods were regarded as significant for bacteriuria respectively [16]. Plates with no growth or tiny colonies were returned to the incubator for another 24 hours before discarding the plates since antimicrobial

treatment or other factors may inhibit initial growth [17].

Colony characteristics, morphology and staining

The shape, size, color, elevation and hemolysis of the colony formed on the culture plate was observed after 24 hours of incubation at 37º C. Gram staining was done to determine the microscopic appearance (for-example clusters, rods or cocci) and gram reaction (positive or negative bacteria) of a stained preparation.

Biochemical characteristics

The following biochemical tests were done to determine chemical changes related to different micro-organisms identified including: Methyl red test, Indole test, Catalase test, Urease test, Citrate utilization test and Triple iron agar.

Triple sugar iron test (TSI)

This test was used in Gram negative colonies. TSI agar had glucose with a 0.1 % concentration and lactose and sucrose with a concentration of 1 %. Sterile TSI slants with agar were taken from the refrigerator and wiped using a dry cotton wool. The cap was removed and then the neck was flamed [17]. An inoculating straight loop was sterilized in the blue flame of the Bunsen burner and then allowed to cool. A colony of the suspected organism from CLED agar was picked, stabbed into the medium up to the butt of the TSI tube and then it was streaked back and forth along the surface of the slant. Again the neck of the TSI was flamed, capped and placed in the incubator for 24 hours at a temperature of 37° C. Triple sugar iron agar tube was used to test for the fermentation of only glucose (yellow butt), fermentation of lactose and sucrose (all over yellow), CO_2 formation (crack in agar), or ferrous ammonium sulphate produced (black precipitate) [17].

Catalase test

This test was used to differentiate suspected *Staphylococci spp*. colonies which appeared with a uniform yellow color. Two drops of 3% hydrogen peroxide was put onto a clean glass slide using a dropper; a pure colony of the organism was picked from CLED agar using a wooden applicator stick [17]. Placing the colony on the hydrogen peroxide on the glass slide; emulsification was done. Observation for bubble formation was done within 30 seconds [17].

Mannitol Salt (MSA) Agar

This tests for the bacteria's ability to tolerate 7% salt concentration and ferment mannitol. The media is selective because it selects for salt tolerant bacteria. It was done following results of catalase test for the confirmation of *S. aureus*. A plate of MSA was inoculated with a discrete colony of the test organism using a sterile wire loop by a streak plate method and was incubated at 37^{0}C for 24-48 hours. If the organism was tolerant to salt it grew. If the organism was not tolerant to salt it did not grow. If the tolerant organism fermented mannitol, then there were yellow zones around the colonies indicating *staphylococcus aureus*. If the salt tolerant organism could ferment mannitol, then the media would remain pink.

Indole, Methyl Red, Voges-Proskauer and Citrate test (IMVIC) tests

This test was used in organisms suspected to be *E. coli* and *Klebsiella.* Indole test determines the presence or absence of the tryptophanase, an enzyme which breaks down tryptophan [17]. A 1 % Tryptone broth was used during the test [17]. Kovac's reagent was added to the tryptone broth and if indole was present then a red coloration formed at the top indicating the presence of *E. coli* [17]. A MR-VP broth was used to look for mixed acid and butanediol fermenters in the test organisms. One tube was used for each test. Half of the broth, once incubated, was removed and placed into a different tube. Methyl red was added to one tube to see if the pH was neutral (yellow) indicating negative while the development of red colour after addition of methyl red indicated positive, *E. coli* [17]. Barritt's solution (alpha hapthol and potassium hydroxide) was added to the other tube to test the Butanediol fermenters and if the bacteria were butanediol fermenters then the broth turned red indicating *Klebsiella spp.* Citrate test was used to test for the presence of citrate which was the sole source of carbon for bacteria [17]. An agar slant with synthetic medium containing small amounts of mineral salts (citrate and

ammonium) was used to perform the test (WHO, 2003). Bromothymol blue (pH indicator) was added to the agar slant and if there was growth (presence of citrate) the agar was blue indicating the presence of *Klebsiella spp.* and if there was no growth the agar is green.

Urease test

Urease test was used to determine the bacteria's ability to hydrolyze urea to make ammonia using the enzyme urease. It was conducted by inoculating Urea broth with a sterile inoculating wire loop. ammonia. If ammonia is made, the broth turned a bright pink color, and was positive indicating the presence of *Proteus spp*. If test was negative, broth had no color change and no ammonia was made.

Antimicrobial susceptibility tests

The antimicrobial susceptibility tests were performed using the Kirby Bauer disk diffusion technique [12] with commercially available disks on Mueller Hinton agar plates. Antibiotics disks validity were controlled using *E. coli (*ATCC 25922). This was performed weekly. The agar was poured to a uniform depth of 4 mm and allowed to cool and solidify according to Clinical and Laboratory Standards Institute (CLSI, 2007) and International Guidelines. A 0.5 McFarland turbidity standard was prepared according to the method described by [18]. A solution with 9.95 ml of 1 % chemically pure sulphuric acid was mixed with 0.05 ml of 1.175 % barium chloride to form a barium sulfate precipitate which would cause turbidity. This standard was used to adjust the turbidity of the inoculums for the antimicrobial susceptibility test. Well isolated single colonies were transferred to the tube with sterile saline and suspensions and were compared to 0.5McFarland turbidity. Then the turbidity of the inocula was adjusted, and a sterile cotton swab was dipped into the suspension, and pressed firmly against the inside wall of the tube. The swab was then streaked over the surface of the medium 3 times rotating the plate after each application to ensure an even distribution and was allowed to stand at room temperature for 10 minutes [19].

Antimicrobial disks containing specified concentrations in micrograms were placed on the agar plates after 10 minutes (to allow the agar to dry) using a pair of sterile forceps and then gently pressed down on the agar to ensure contact. The plates were inverted, and incubated at a temperature of 37°C for 24 hours. After incubation the zone diameters with complete inhibition, including the diameter of the disk were measured using a ruler and were recorded in millimeter on the under surface of the plate without opening the lid. The diameter of the zone of inhibition for each antibiotic was measured and interpreted as resistant, intermediate and sensitive according to Clinical Laboratory Standards Institute criteria (2007) and commercially available discs containing commonly prescribed antibiotics were used and the results were recorded as per the manufacturer's instructions. The criteria used to select the antimicrobial agents was based on both their availability for the management of UTIs and their recommendation for use by the World Health Organisation and Clinical Laboratory Standard Institute (CLSI) guideline.

Safety of the environment

All cultured microorganisms were autoclaved, packed and incinerated and the ash was buried to prevent spread of the cultured bacteria.

Data quality control

Pre-testing was done at KIU-TH located in Bushenyi district in western Uganda, using ten (10) questionnaires. This checked if the questions were accurate and easily understandable by the caregivers. The pre-test questionnaires were not included in the data analysis. All research assistants who were involved in data collection during the study period were trained on how to collect a non-contaminated urine sample. Each filled questionnaire was cross-checked for inconsistencies and incompleteness before the interview was terminated.

Data management

Data from completed questionnaires was arranged, summarized and entered using the statistical computer software package, Microsoft Excel 2019. The data was cleaned, checked for errors and corrected, then imported to SPSS for analysis.

Data analysis

Data was analyzed using IBM SPSS 27.0 statistics for windows (Armonk. NY: IBM Corp).

Objective 1: The prevalence of urinary tract Infections was determined as a proportion using frequencies, percentages. This was presented using a pie chart.

Ethical considerations

For the study to be ethical, the following were considered;

Institutional consent

Ethical approval of the research protocol was obtained from the Research Ethics Committee (REC) of Kampala International University, Western Campus (Nr.UG-REC-023/202017). Permission to conduct the study was obtained from the director of KIU-TH as shown in appendices X and XI.

Privacy, confidentiality and non-maleficence

All questionnaires did not have provisions for participant's names, and the interviews were carried out in the side room in the pediatric clinic, to ensure privacy and confidentiality. Collection of urine samples was done from the procedure room near the out-patient clinic. Completed questionnaires were kept under lock and key, only accessible by the Principal Investigator and authorized individuals. Data was kept in password-protected files, where it remained until dissemination and didn't include patient identifiers. There was sensitization and training of research assistants about the study, specifically on urine sample collection procedure to minimize the risks.

Informed consent

Written informed consent was sought from each caregiver and the purpose of the study was well explained to the participants in a language they understood before they started answering the questions. In order to participate in the study, the caregiver was requested to sign a written informed consent document or use a thumb print for those who could not write. A copy of the signed consent form was given to the participant and another copy kept by the Principal Investigator. The consent forms were written both in English and Runyankole, and the participants had a right to decline to participate or withdraw from the study at any time without any penalty.

Respect of individual persons

Participants who declined to participate in the study at whatever stage of the interview were respected and this did not interfere with the quality of medical care that was provided to them.

Benefits and risks

Some participants experienced some pain and discomfort during urethral catheterization, to minimize that, an appropriate size of urethral catheters and a lubricant was used to minimize patient discomfort, pain and urethral trauma which might have occurred during urine sample collection. Least harm was expected during urine sample collection and less invasive procedures were considered; mid-stream urine sample collection method was used for children above to two years and in and out catheterisation for those below 2 years and the smallest appropriate catheters were used to avoid the complications which may have risen if suprapubic catheterisation is used. The results of urine culture and sensitivity were immediately availed and discussed with the clinician and caregiver of each study participant. Those who were found with a UTI were started on effective antimicrobial therapy as per urine culture results. A courtesy call was made to inform patient who had left the hospital premises without their results especially OPD patients.

Dissemination of results

The research findings are to be disseminated to the office of the director of KIU- TH, department of Pediatrics and child health at KIU-TH, and KIU western campus library. The results of this study will also be disseminated to a peer-review journal and presented at scientific conferences

RESULTS

Study participants

A total of 927 children presented to Kampala International University Teaching Hospital from 1st December 2020 to 31th March 2021. Of these, 152 did not fit in the age group (were either below 2 months or

above 59 months) and 419 had no fever or history of fever. Six participants were excluded because four failed produce urine, one had hypospadias, one had local urethral infection 350 participants met the inclusion criteria and were consecutively enrolled into the study. Out of 350, 97 had positive urine culture of a single uropathogen, 250 had no growth on urine culture and 3 had mixed growth on culture.

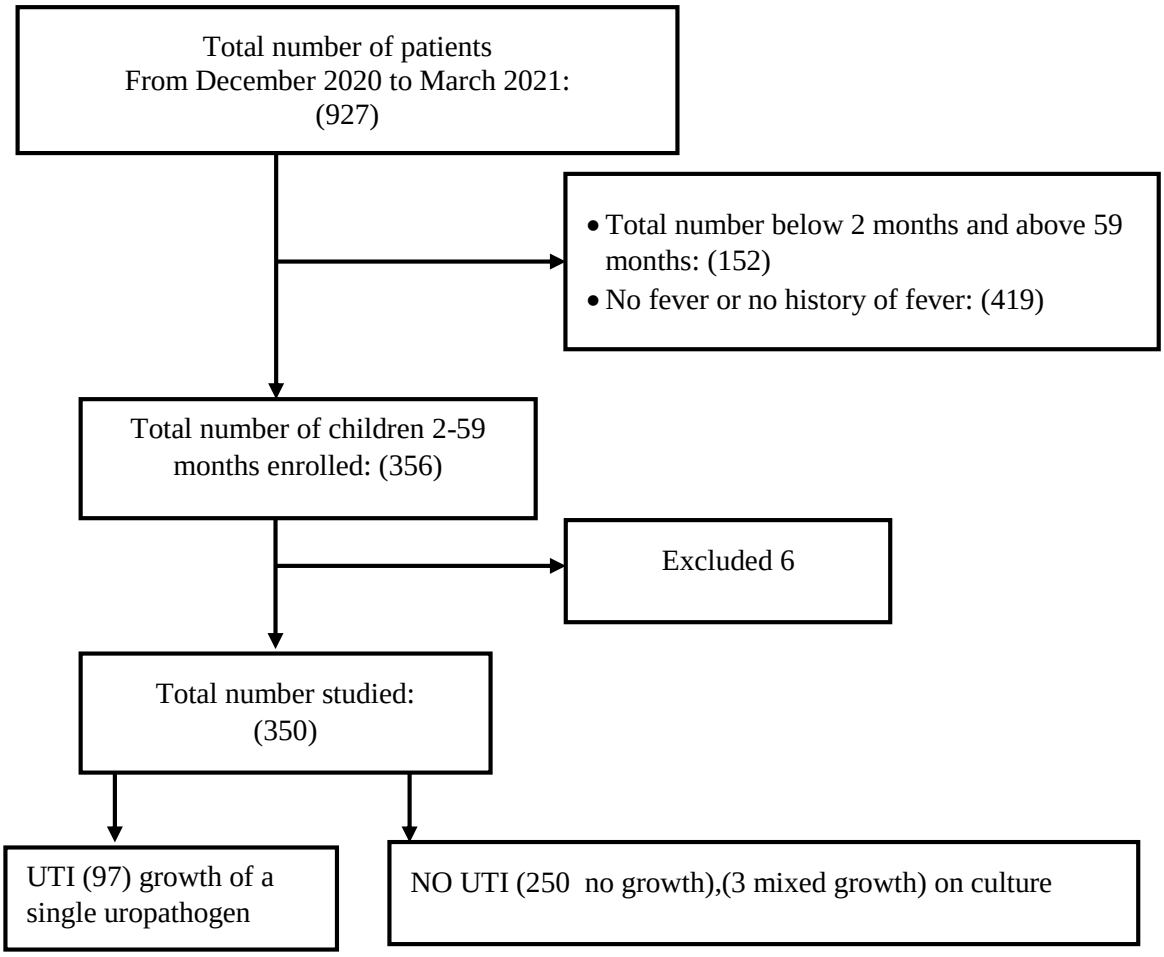


Figure 2. Study profile.

Baseline characteristics of study participants

Socio-demographic characteristics

Out of 350 children, more than half of study participants were aged less than 24 months of age, 208(59.4%). Study participants were aged 2 to 59 months with the overall mean age of 10.13 ± 1.44 months, that for children with no UTI was 14.10 ± 1.26 months while that of children with UTI was 8.21 ± 1.63 months, majority of the study participants were males 224(64%). and other socio-demographic characteristics of the participants were distributed as shown in table 1 below.

Table 1. Baseline socio-demographic characteristics of study participants

Variable	Frequency	Percentage
Age		
< 24 months	208	59.4
≥ 24 months	142	40.6
Sex		
Female	126	36.0
Male	224	64.0
Residence		
Urban	153	43.7
Peri-urban	86	24.6
Rural	111	31.7
Education level of care giver		
Utmost primary	156	44.4
Secondary	98	28.2
Tertiary	96	27.4

Medical characteristics,clinical presentation and behavioural characteristics of participants

Most of the study participants had a known source of fever 262 (74.9%) and of the 350 participants, 230(65.7%) had fever for less than 24 hours. Almost one third of the study participants were undernourished 105(30.0%). More than two thirds of the study participants were using diapers 257(73.4%). Other baseline clinical presentation, bevavioural and medical characteristics of study participants are detailed in Tables 2 and 3 below.

Table 2. Baseline medical characteristics and clinical presentation of study participants

Variable	**Frequency**	**Percentage**
Circumcision		
No	185	82.6
Yes	39	17.4
Undernutrition		
No	245	70.0
Yes	105	30.0
Exclusive breastfeeding		
No	196	56.0
Yes	154	44.0
Constipation		
No	326	93.1
Yes	24	6.9
Diarrhoea		
No	205	58.6

Yes	145	41.4
Vomiting		
No	169	48.3
Yes	181	51.7
Foul smelling urine		
No	243	69.4
Yes	107	30.6
Duration of fever		
< 24 hours	120	34.3
≥24 hours	230	65.7
Intensity of fever		
< 39°C	232	66.3
≥39°C	118	33.7
Source of fever		
Unknown	88	25.1
Known	262	74.9
Sudden bed wetting		
Yes	258	73.7
No	92	26.3
HIV		
Negative	346	98.9
Positive	4	1.1

Table 3. Baseline Behavioural characteristics of study participants

Variables	**Frequency**	**Percentage**
Wiping from back to front		
No	136	38.9
Yes	214	61.1
Toilet training		
No	218	62.3
Yes	132	37.7
Use of diapers		
No	93	26.6
Yes	257	73.4

Urinalysis laboratory predictors of the participants

The urinalysis predictive parameters were distributed as shown in table 4 below.

Table 4. Baseline urinalysis laboratory predictors of study participants

Variable	Frequency	Percentage
Leucocyte esterase		
Absent	278	79.4
Present	72	20.6
Nitrites		
Absent	295	84.3
Present	55	15.7
Microscopy		
< 5 WBC/hpf	256	73.1
≥ 5 WBC/hpf	94	26.9

Bivariate analysis for predictors of UTIs among febrile children < 5 years of age at KIU-TH

Children who were less than 24 months had a 2.160 increased likelihood of having bacterial UTI (*p* 0.009). Males were 1.458 times more likely to suffer from bacterial UTI compared to the female children with a p value of 0.119 and those not circumcised had increased odds of having a UTI (p 0.158). Among the medical and clinical presentation, under nourished children, Children presenting with diarrhea and vomiting were more likely to suffer from UTI with p value of < 0.001. Other results of bivariate analysis for predictors of UTIs are presented in Table 5, 6, 7 and 8 below.

Table 5. Results of bivariate analysis of socio-demographic predictors of UTIs among febrile children < 5 years of age at KIU-TH

Variable	Presence of bacterial isolates		cOR (80% C.I).	P-value
	No (%)	Yes (%)		
Age				
< 24 months	138(66.3)	70(33.7)	2.160(1.033-3.188)	**0.009**
≥ 24 months	115(81.0)	27(19.0)	-1-	
Sex				
Female	97(77.0)	29(23.0)	-1-	
Male	156(69.6)	68(30.4)	1.458(0.901-2.461)	**0.119**
Residence				
Urban	102(66.7)	51(33.3)	-1-	
Peri-urban	69(77.5)	17(22.5)	0.472(0.179-0.671)	**0.002**
Rural	82(73.9)	29(26.1)	0.630(0.368-1.078)	**0.092**
Education level of caregiver				
Utmost primary	105(67.3)	51(32.7)	-1-	
Secondary	72(73.5)	26(26.5)	0.756(0.546-1.306)	0.216
Tertiary	76(79.2)	20(20.8)	0.497(0.216-1.760)	0.644

cOR; crude odds ratio, CI; confidence interval

Table 6. Results of bivariate analysis of medical predictors and clinical features of UTIs

Variable	Presence of bacterial isolates		cOR(80% C.I)	P-value
	No (%)	Yes (%)		
Circumcision				
Yes	17 (43.6)	22 (56.4)	-1-	
No	139 (75.1)	46 (24.9)	1.211 (0.744-2.129)	**0.158**
Undernutrition				
No	201(82.0)	44(18.0)	-1-	
Yes	52(49.5)	53(50.5)	4.656(1.458-12.988)	**<0.001**
Exclusive breastfeeding≥6				
No	145(74.0)	51(26.0)	-1-	
Yes	108(70.1)	46(29.9)	0.256(0.079-1.3999)	0.250
Constipation				
No	232(71.2)	94(28.8)	-1-	
Yes	21(87.5)	3(12.5)	0.353(0.101-1.192)	**0.080**
Diarrhoea				
No	175(85.4)	30(14.6)	-1-	
Yes	78(53.8)	67(46.2)	5.011(3.462-9.554)	**<0.001**
Vomiting				
No	141(83.4)	28(16.6)	-1-	
Yes	112(61.9)	69(38.1)	3.103(1.718-7.057)	**<0.001**
Foul smelling urine				
No	174(71.6)	69(28.4)	-1-	
Yes	79(73.8)	28(26.2)	0.894(0.525-1.349)	0.257
Duration of fever				
< 24 hours	81(67.5)	39(32.5)	-1-	
≥24 hours	172(74.8)	58(25.2)	0.673(0.487-1.263)	**0.176**
Intensity of fever				
< 39°C	164(70.7)	68(29.3)	-1-	
≥39°C	89(75.4)	29(24.6)	0.786(0.428-1.174)	0.309

Table 6 continued

Source of fever				
Unknown	41(46.6)	47(53.4)	-1-	
Known	212(80.9)	50(19.1)	1.206(0.760-2.289)	0.469
Sudden Bed wetting				
No	175(67.8)	83(32.2)	-1-	
Yes	78(84.8)	14(15.2)	0.378(0.186-0.648)	**0.001**
HIV				
Negative	250(72.3)	96(27.7)	-1-	
Positive	3(75.0)	1(25.0)	0.868(0.082 -7.869)	0.893

cOR; crude odds ratio, CI; confidence interval

Table 7. Results of bivariate analysis of behavioural predictors of UTIs among febrile children < 5 years of age at KIU-TH

Variables	**Presence of bacterial isolates**		**cOR (80% C.I)**	**p- value**
	No (%)	**Yes (%)**		
Wiping from back to front				
No	106(74.3)	30(22.1)	-1-	
Yes	147(68.7)	67(31.3)	1.610(0.814-2.125)	**0.084**
Toilet training				
No	153(70.2)	65(29.8)	-1-	
Yes	100(75.8)	32(24.2)	0.753(0.060-2.911)	**0.028**
Use of diapers				
No	70(75.3)	23(24.7)	-1-	
Yes	183(71.2)	74(28.8)	1.231(0.787-2.318)	**0.058**

cOR; crude odds ratio, CI; confidence interval

Table 8. Results of bivariate analysis of urinalysis laboratory predictors of UTIs among febrile children < 5 years of age at KIU-TH

Variable	Presence of bacterial isolates		cOR (80% C.I)	P-value
	No	Yes		
Leucocyte esterase				
Absent	230(82.7)	48(17.2)	-1-	
Present	23(31.9)	49(68.1)	9.044(1.782-16.133)	**0.114**
Nitrites				
Absent	244(81.7)	51(18.3)	-1-	
Present	9(16.4)	46(83.6)	24.453(13.130-71.323)	**<0.001**
Microscopy				
< 5 WBC/hpf	217(84.8)	39(15.2)	-1-	
≥ 5 WBC/hpf	36(38.3)	58(61.7)	8.964(4.578-13.156)	**0.191**

cOR; crude odds ratio, CI; confidence interval

Multivariate analysis for independent predictors of UTI among febrile children < 5 years of age at KIU-TH

Predictors of UTIs were multifactorial and diverse. Urinalysis results were strongly predictive of UTI, where children with nitrites on urinalysis and those with more than 5 white blood cells at urine microscopy were 17.875 times and 6.505 times more likely to suffer from Urinary tract infection respectively with a p value of < 0.001. Other predictors are shown below in table 9.

Table 9. Multivariate analysis results for predictors of UTI among febrile children under five years of age at KIUT-TH

Variable	aOR (95% C.I.for aOR)	P-value
< 24 months	6.324(1.934-20.685)	**0.002**
≥ 24 months	1.0	1
Sex		
Female	1.0	1
Male	2.035(1.703-5.887)	**0.010**
Residence		
Urban	1.0	1
Peri-urban	0.097(0.021-1.045)	0.063
Rural	0.298(0.076-1.177)	0.084
Undernutrition		

No	1.0	1
Yes	8.973(2.714-29.660)	**0.012**
Circumcision		
Yes	1.0	1
No	3.461(1.162-5.313)	**0.026**
Constipation		
No	1.0	1
Yes	0.254(0.036-1.775)	0.167
Diarrhoea		
No	1.0	1
Yes	6.790(4.019-11.474)	**0.032**
Vomiting		
No	1.0	1
Yes	4.178(2.475-7.055)	**0.005**

Table 9 Continued

Duration of fever		
> 24 hours	1.0	1
≤ 24 hours	0.704(0.245-2.026)	0.515
Wiping from back to front		
No	1.0	1
Yes	3.631(1.212-10.874)	**0.021**
Toilet training		
No	1.0	1
Yes	0.792(0.537-0.981)	0.647
Sudden bed wetting		
No	1.0	1
Yes	0.383(0.110-1.334)	0.132
Use of diapers		
No	1.0	1
Yes	5.491(1.407-21.427)	**0.014**
Leucocyte esterase		
Absent	1.0	1
Present	0.972(0.025-2.094)	0.065
Nitrites		
Absent	1.0	1

Present	17.875(8.658-36.808)	**<0.001**
Microscopy		
< 5WBCs/hpf	1.0	1
≥ 5WBCs/hpf	6.505(3.859-10.964)	**<0.001**

aOR; Adjusted odds ratio, C.I; confidence interval.

DISCUSSION

Predictors of UTIs among febrile children < 5 years of age at KIU-TH

The predictors of UTIs among febrile children were multifactorial and diverse. In the current study, children aged less than 24 months were more likely to have UTIs compared to those aged above 24 months which is in line with many studies showing children less than 24 months having increased odds of having a UTI. A study by Festo and his colleagues (2011) showed children less than 24 months to have an increased risk of UTIs which was congruent with the results of the study done by [20] .This is basically attributed to the reduced immunity in the younger age group and lack of toilet traning which increases the Odds of UTI in this age group. In this study, male children were more likely to have a UTI than females. This could be because of bigger number of males who were below one year and were uncircumcised who were enrolled in this study. This increased the chances of picking on a male who is not circumcised than a female to be included in the study and the fact that UTIs are more common in uncircumcised males than females in children below one year could also have been a contributory factor. This finding was comparable to a study in Nigeria by [21] but was at variance with several other studies which have reported greater association of female gender with UTIs. A study by [11] found that female sex was predictive of a UTI among children and this was similar to the study by [22]. Undernutrition was a potent predictor of UTIs. In this study, children who were undernourished were more likely to have a UTI compared to those who were well nourished. Our findings are congruent with those of [23] who reported that 22.4% of the 85 children aged 6-59 months with severe acute malnutrition had a UTI in India. In a meta-analysis by [24], found that the prevalence of UTIs among children with severe acute malnutrition ranged from 6% to 37%. This could be attributed to the fact that undernutrition impairs the body's ability to mount an effective immune response in the face of infection hence making children prone infections of which UTIs is among. As reported by several studies that there is evidence that uncircumcised males are more likely to have UTIs, also in this study, being uncircumcised was significantly predictive of UTI in male participants. A study by [25] showed that the prevalence of UTI in febrile male infants is markedly affected by the circumcision status of the infant. The above is similar to results reported by [26] that uncircumcised febrile male infants have a 20% risk of UTI, compared with a 2.4% risk in circumcised male infants. This is attributed to the fore skin of the glans habouring uropathogens and the hardship concerning hygiene in uncircumcised males.

In this study, children that had diarrhea had increased odds of developing bacterial UTI among the participants. These findings are similar to those reported by [11] among febrile children in Tanzania that among clinical characteristics that predicted positive UTI was diarrhea (OR 2.3, p=0.001),out of the 370 children enrolled,136 had diarrhoea. In keeping with these findings, a cross sectional study by [22] in Mulago, found that diarrhoea was significantly associated with UTIs (p value of 0.014). This difference is most likely attributable to the fact that loose motions increases the exposure of urethral opening to colonic uropathogens. A cross sectional study by [21] in Nigeria found that vomiting was the most common predictive factor for UTIs in febrile under-fives. The findings are similar to this study in that vomiting was statistically significant with a higher likelihood of having a UTI. This could have

been due to the fact that some cases of UTIs proceed to urosepsis or disseminated UTIs which can cause vomiting. However, a study by [27] in Tanzania, found that vomiting was not predictive of a UTI. In Bangladesh, significant behavioral predictors of UTIs in children were; wiping from back to front, diaper use and poor personal hygiene. Diaper use was the major behavioral contributing predictor [28]. This is comparable with results of this study where children who were wiped from back to front had increased risk of having a UTI and those who used diapers were more likely to have a UTI than those who never used diapers. This could be attributed to increased exposure of the urethral opening to the colonic uropathogens. Rapid techniques including urine dipstick tests for leukocyte esterase and nitrites and various forms of urinalysis, including standard microscopy have been utilized to determine possibility of a UTI in children and various studies have shown positive urinalysis results as a quick confirmation of the clinical significance of positive urine culture results in most cases [29]. In an analysis done by [30] showed that nitrites (75%) and microscopy (35%) on urinalysis highly predicted a UTI and results are in agreement with this study showing that children who had nitrites and ≥ 5WBCs on microscopy were more likely to have a UTI than those who presented with normal urinalysis results. Not differing from this study, [11, 31,32] in Tanzania, showed sensitivity of urine WBC microscopy, leukocyte esterase and nitrite test in diagnosing UTI using culture as a gold standard to be 44.2%, 8.8% and 21.7% with specificity of 86.5%, 99.1% and 97% respectively with positive urine culture strongly predicted by positive WBC microscopy (OR 4.9, $p<0.001$), positive nitrite test (OR 11.5, $p<0.001$). This is imputed to the inflammatory component of a UTI and the ability of gram negative uropathogen to convert dietary nitrates to nitrites to yield a positive test.

CONCLUSION

The independent predictors for UTIs were multifactorial and diverse including; age, sex, undernutrition, circumcision, diarrhoea, vomiting, wiping from back to front, use of diapers and urinalysis results. Diarrhoea, under nutrition and urinalysis results (nitrites and >WBCs on microscopy) were strongly associated with UTIs.

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