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Prevalent Bacterial Etiologies of Urinary Tract Infections in Febrile Children Under Five Years of at Federal Medical Centre, Owerri, Imo State, Nigeria

[1]Nwigwe U. M., [2]Esezobor C. I., [1]Iregbu F. U. and [3]Ushie S. N.

[1]Federal University Teaching Hospital Owerri
[2]Lagos University Teaching Hospital Lagos State
[3]Nnamdi Azikiwe University Teaching Hospital Nnewi

ABSTRACT

Urinary Tract Infections (UTIs) in children under five years old pose a significant health concern, influenced by various factors like bacterial agents, anatomy, immunity, and genetics. The study aimed to identify prevalent bacterial causes of UTIs in febrile children under five at a medical center in Nigeria. Among 170 participants, E. coli was the most frequently isolated bacteria (37.5%), followed by Klebsiella spp (18.8%) and Staphylococcus aureus (15.6%). The research underscores E. coli as the primary uropathogen, aligning with global trends, while acknowledging local variations in UTI causative agents.

Keywords: Urinary Tract Infections, Febrile Children, Bacterial Etiologies and Pediatric UTI

INTRODUCTION

The pathophysiology of UTI is complex and involves many factors such as aetiologic agents, anatomical, immunological, urodynamic and genetic which may influence its location, course and prognosis [1],[2-8]. The majority of urinary tract infections are ascending infections and the bacteria usually arise from faecal flora [8]. These pathogens usually colonize the periurethral area and there is an upward migration towards the bladder [1,8]. The short urethra in the female child means the bacteria is more likely to reach the bladder faster than in the male child [9-10]. The ability of microorganisms to achieve adherence to the uroepithelial cells is the major cause of the initial colonization of the bladder mucosa and subsequent ascent of the bacteria to the upper urinary tract [2,8]. The adherence to the uroepithelial cells is normally achieved by means of specialized filamentous structures called pili or fimbriae located on the bacterial capsule [2,8]. These fimbriae are of two types; type I and type II. Type I fimbriae are found on most strains of *Escherichia. coli* (*E. coli*) and are responsible for mostly cystitis and asymptomatic bacteriuria and rarely cause pyelonephritis [2,8]. Their attachment to target cells can be blocked by mannose hence they are referred to as mannose-sensitive [8]. However, type II fimbriae are the main cause of pyelonephritis, their attachment is not inhibited by mannose hence they are known as mannose –resistant and are usually expressed by only certain strains of E. coli [2,8]. Other virulence factors of uropathogenic *E.coli* include capsule and lipopolysaccharide. The capsule is predominantly a polysaccharide covering that protects the bacteria from the host immune system. The capsule also provides protection against phagocytic engulfment and complement –mediated bactericidal effect in the host. Certain types of capsule example K1 and K5, show molecular mimicry to tissue components, preventing a proper humoral immune response of the infected host [9-12]. Other secretory virulence factors include some toxins ; alpha hemolysin (HlyA), cytoxic necrotizing factor 1 and secreted autotransporter toxin(SAT) which have all been implicated in the pathogenesis of UTI [13-15]. In the bladder, regular and complete emptying of the bladder urine ensures that the bacteria count is significantly depopulated [2,3,8]. However, when

this regular emptying of the bladder is impaired as seen in children with posterior urethral valve, constipation , neuropathic bladder or dysfunctional voiding, this important defence mechanism is lost predisposing the children to repeated UTI [2,8]. As soon as sufficient colonization occurs, bacteria may ascend to the ureters towards the kidneys [2,3,8]. Infection of the renal parenchyma gives rise to an inflammatory response called pyelonephritis [2,3,8]. Most infections of the renal parenchyma are as a result of bacterial ascension although, haematogenous spread can occur [3,8]. Progression of the inflammatory cascade can cause tubular obstruction and damage leading to interstitial oedema which may manifest as acute kidney injury [3]. Urinary tract infection (UTI) is a common cause of fever in under-five children, however it is grossly under-diagnosed and untreated. Unrecognised UTI increases the likelihood of adverse short and long-term outcomes such as renal scarring, hypertension and chronic kidney disease (CKD).Furthermore, antibiotic sensitivity (or resistance) profile of UTI-causing organisms is a dynamic event, with global and regional data indicating reducing sensitivity to commonly used antibiotics; this creates a need for each practice environment to routinely assess the antibiotic sensitivity profile of common organisms.

Aim and Objectives

The aim of this research was to determine the Prevalent Bacterial Etiologies of Urinary Tract Infections in Febrile Children Under Five Years of at Federal Medical Centre, Owerri, Imo State, Nigeria.

RESEARCH QUESTION

What are the common bacterial causes of UTI among febrile under-5 children?

Specific Objective

To identify the common bacterial aetiologic agents of UTI in febrile under-five children.

METHODOLOGY

Study Area

The study was carried out at the Paediatric Outpatient Clinics and Emergency Paediatric Unit of the Federal Medical Centre Owerri, Imo state. The State is one of the five states of South-Eastern Nigeria and it is made up of 27 local government areas. Owerri is the capital of Imo State and it is made up of three local government areas namely: Owerri Municipal, Owerri North and Owerri West. The estimated population of Owerri is about 400,000. The projected population for 2020 is about 872,604. The Federal Medical Centre is a tertiary health facility located centrally in Owerri. It has two outreach centres located at Umunama-Mbaise and Izombe-Oguta and serves as a referral centre for hospitals from all over the state and the neighbouring states of Rivers and Anambra. The Paediatric Outpatient Clinics run from Mondays through Fridays between 8am and 4pm. An average of 70 patients are seen daily with an annual average of 13,000 patients. It is the first point of care for all sick children visiting the hospital except for emergencies and children who come to the hospital during the weekend who are managed in the emergency paediatric unit. Sick children presenting after 4pm are also seen at the emergency unit. The emergency paediatric unit runs a 24-hour service and an average of 300 patients seen monthly with an average of 4000 patients seen per annum.

Study Design

This was a hospital-based descriptive cross-sectional study.

Ethical Considerations

Ethical clearance and permission to carry out the study was obtained from the Research and Ethics Committee of the Federal Medical Centre Owerri. Also, parents and care givers of eligible children provided a written informed consent. The study was conducted in a manner that ensured that participation in the study did not result in undue delay of commencement of standard treatment or management. In addition, the results of children with positive urine culture were passed on to the team responsible for the care of the child as soon as it became available.

Study Population

The study population consisted of all febrile (axillary temperature > 37.5°C) children between the ages of 0 and 59 months attending the Paediatric Outpatient Clinics and Emergency Paediatric Unit that met the inclusion criteria.

Inclusion Criteria

1. Children between the ages of 0 and 59 months presenting with fever (axillary temperature > 37.5°C).
2. Children whose parents or caregivers provided written informed consent.

Exclusion Criteria

1. Very ill children requiring immediate resuscitation and commencement of antibiotics which would have delayed by participation in the study.
2. Children who received systemic (oral or parenteral) antibiotics within the previous 72 hours.

Sample Size Calculation

The minimum sample size was estimated using the Cochran formula for prevalence studies.[115]

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Sample size, $n = \frac{Z^2 pq}{d^2}$

Where n= sample size

Z= Standard normal deviation at 95% confidence level= 1.96

P= Prevalence of UTI in febrile under 5 children in Enugu[9] *= 11%*

Q= (1-p)

d =level of precision= 0.05

$$n = \frac{Z^2 pq}{d^2}$$

$= [(1.96)^2 \times 0.11 \times 0.89] / (0.05)^2$

Therefore, the minimum calculated sample size=152

A further 10% (16) was added to the minimum sample calculated to factor in risk of attrition.
Therefore 170 children were recruited for the study.

Sampling Technique

Eligible children were recruited consecutively.

Study Procedure

Each recruited subject had a detailed history and physical examination. The findings were documented in the data entry form. The variables entered into the form included demographic data (research number, age, and gender), history of fever, presence of symptoms suggestive of urinary tract infections and treatment received prior to enrolment in the study. Other information recorded in the form included the temperature reading, the presence of bladder mass, ballotable kidneys, uncircumcised penile shaft, neural tube defects and the presence of other focus of infections.

Temperature

Body temperature was measured by using mercury in glass clinical thermometer. This was placed in contact with the skin on the subjects' axilla for four minutes after which reading was recorded. A subject was considered febrile when the temperature was above 37.5^{0}C.

Specimen Collection

After recruitment into the study, the investigator labelled the sample bottles appropriately and midstream urine was collected by the researcher or the caregivers under supervision. This was done by voiding the initial part of the urine stream into the toilet or another container and at approximately the middle of the urine flow the specimen bottle was positioned to capture urine. However, in children not yet toilet trained, spot urethral catheterization was carried out under aseptic conditions. In collecting the sample by urethral catheter, the researcher or the assistant wore sterile gloves then the child was placed in supine position and the labia or penis was cleaned with antiseptic swab. In females, the labia was parted to expose the urethral opening, the catheter was lubricated with sterile anaesthetic gel (KY jelly) before insertion into the urethral opening upward until urine begins to flow out. For the male child, the penis was lifted and the foreskin retracted in the uncircumcised. The urethral opening was cleaned with antiseptic swabs in a circular motion from the urethral opening to the base of the penis and a sterile lubricant was applied to the catheter before insertion. The penis was held with slight upward tension and perpendicular to the child's body and the catheter was inserted. The size of the catheter to be used was French gauge (Fr) 6 for children under one year of age while French gauge (Fr) 8 was used in subjects older than one year. Urine specimen was collected into two sterile wide necked leak proof universal bottles. One sample was used for dipstick urinalysis and the other for microscopy, culture and sensitivity in the laboratory. Specimens for culture were sent to the laboratory within 15-20 minutes of collection. In cases where a delay was anticipated before processing, specimens were stored in the refrigerator for no longer than six hours.

Specimen Processing

A macroscopic examination was done for every urine sample to record the colour and nature (to assess whether the urine was clear or turbid). Urinalysis was also carried out qualitatively using chemstrip-10 dipsticks (Roche Diagnostics Montreal, Quebec Canada) to detect the presence of protein, blood, nitrite and leucocyte esterase. The strip was dipped for no longer than one second into the specimen and excess urine was removed by drawing the edge of the strip along the rim of the container, the test strip was turned on its side and placed on a piece of absorbent paper to prevent mixing of chemicals. A timer was set for two minutes. After one minute, the strip was held close to the colour blocks printed on the reagent vial and read for protein, blood and nitrite while the leucocyte esterase was

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read at two minutes. Each test pad was carefully matched to its reference. All results were read and recorded between one and two minutes. Results were subsequently recorded in the questionnaire.

Urine Microscopy

Urine microscopy was carried out at the laboratory by the microbiologist with active participation of the investigator using a wet preparation. This was done using about 5 ml of well mixed urine which was aseptically transferred to a labelled conical tube and centrifuged at 2000 revolutions per minute (rpm) for five minutes. The supernatant was decanted into a second container. A drop of the well mixed sediment was transferred to a slide and covered with a cover glass. The preparation was viewed under a light microscope using 40x objective. Presence of pyuria (>5WBC/HPF) was regarded as significant and suggestive of UTI.

Urine Culture

A sterile calibrated wire loop that takes 0.001 ml of urine was used to inoculate a loopful of urine on blood agar and Cysteine Lactose Electrolyte Deficient (CLED) agar. Then the plate was incubated aerobically at 35^0C- 37^0C for18 - 24 hours, after which those with significant growth (colony count $\geq 10^5$ CFU/ml for MSU or ≥ 50,000 CFU/ml for catheter specimen) were identified by standard bacteriological methods, colonial morphology and *Microbact*® 12 A[116]. Urinary tract infection was defined as the presence of compatible clinical features and significant bacteriuria taking into consideration the mode of urine collection[8]. Urinary tract infection was defined as a growth of at least 50,000CFU/ml of a single organism in catheter specimen urine and at least 100,000 CFU/ml in midstream urine samples. The results of subjects with confirmed UTI was communicated to the managing team for treatment according to standard protocol and the subsequently referred to Nephrology clinic for follow-up.

Data Analysis

Data was coded and entered into a computer. It was analysed using IBM Statistical Package for Social Sciences (SPSS) version 20.0. Frequency tables, charts and figures were used to summarize variables as appropriately required. Mean and standard deviation were used to summarize quantitative variables that were normally distributed. Chi square (χ^2) and where necessary Fisher's exact test and likelihood ratio were used to test for association between categorical variables. A p-value of < 0.05 was considered statistically significant. Security of data was ensured as information on the data entry form was made anonymous by excluding names and phone numbers. The proforma were also kept safe and made available only to the researcher, supervisors and research assistants.

RESULTS

Demographic characteristics of study subjects

One hundred and seventy children aged 0-59 months were recruited for this study. One hundred and fourteen (67.1%) of the 170 subjects were males while 56 (32.9%) were females with a male-female ratio of 2:1. Fifty (29.4%) of the subjects were aged 0-11 months. The mean age was 24.0±16.1 months (Table 1).

Table 1: Demographic characteristics of study subjects

Variables	Frequency n (%)
Gender	
Male	114 (67.1)
Female	56 (32.9)
Age Groups (months)	
0 – 11	50 (29.4)
12 – 23	39 (22.9)
24 – 35	37 (21.9)
36 – 47	22 (12.9)
48 – 59	22 (12.9)

Presenting complaints of febrile under-five children

Cough (103; 60.6%) and catarrh (93; 57.6%), were the most common symptoms at presentation to the hospital among the study participants. A small proportion of the children had symptoms suggestive of urinary tract infection; Twenty-three (13.5%), 4 (2.4%), and 4 (2.4%) had frequent urination, foul smelling urine and painful urination respectively. Most symptoms were non-specific (Table 2).

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Table 2: Presenting complaints of febrile under-five children

Symptoms	Frequency n (%)
Fever	170 (100)
Cough	103 (60.6)
Catarrh	93 (57.6)
Vomiting	46 (27.1)
Abdominal pain	30 (17.6)
Frequent urination	23 (13.5)
Diarrhoea	14 (8.2)
Convulsions	5 (2.9)
Foul smelling urine	4 (2.4)
Painful urination	4 (2.4)
Jaundice	1 (0.6)

Bacterial agents causing urinary tract infection among the study subjects

E. coli was the most common bacteria isolated in children with UTI with a prevalence of 37.5%. The second and third most common bacteria isolated were *Klebsiella spp* (18.8%) and *Staphylococcus aureus* (15.6%). *Serratia liquefacien* was the least occurring bacterial agent (3.1%). (Figure 1).

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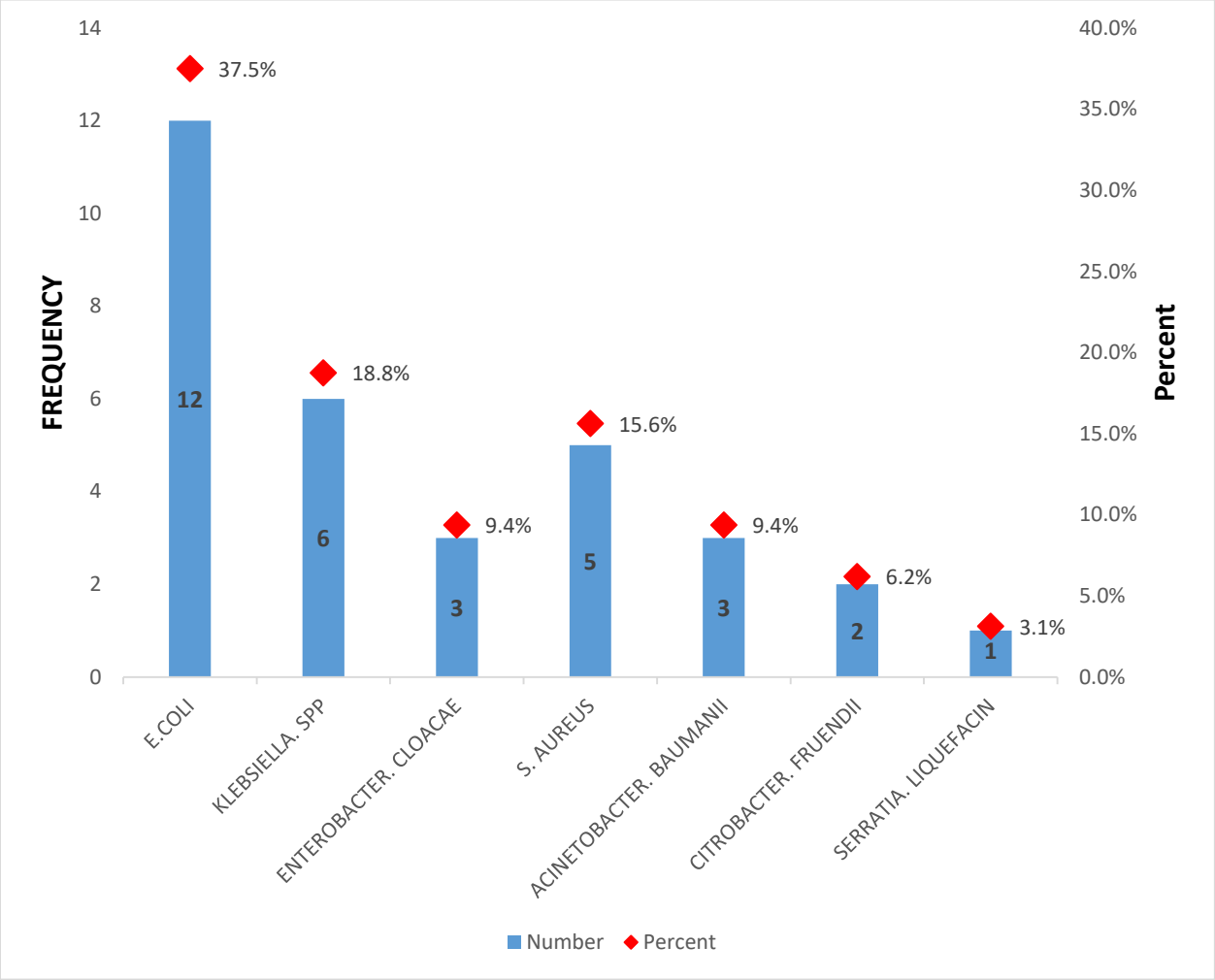

Figure 1: Bacterial agents causing urinary tract infection among study subjects

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Distribution of the bacterial agents based on age and gender

Escherichia coli was the most common cause of UTI in both infants and older children. Among the infants 66.7% of the *E. coli* were isolated in girls, in contrast to older children where 83.1% of the *E. coli* were isolated in boys. All the three *Acinetobacter* UTI as well as the only *Serratia* occurred in boys aged 12 - 59 months. Also, 83.3% (n = 5) of the *Klebsiella* UTI occurred in children aged 12 - 59 months with fairly equal distribution among both sexes (Table 3). It should be noted that a total of 11/32 =34.4% of all UTI were in infants.

Table 3: Distribution of the bacterial agents based on age and gender

Organisms	Infants, n (%)			Children aged 12-59 months, n (%)		
	Male	Female	Total	Male	Female	Total
E. coli, n = 12	2 (33.3)	4 (66.7)	6 (54.5)	5 (83.1)	1 (16.7)	6 (28.6)
Klebsiella spp, n = 6	1 (100.0)	0 (0)	1 (9.1)	2 (40.0)	3 (60.0)	5 (23.7)
Enterobacter, n = 3	0 (0)	1 (100.0)	1 (9.1)	1 (50.0)	1 (50.0)	2 (9.5)
S. aureus, n = 5	1 (50.0)	1 (50.0)	2 (18.2)	2 (66.7)	1 (33.3)	3 (14.3)
Citrobacter, n = 2	1 (100.0)	0 (0)	1 (9.1)	0 (0)	1 (100.0)	1 (4.8)
Acinetobacter, n = 3	0 (0)	0 (0)	0 (0)	3 (100.0)	0 (0)	3 (14.3)
Serratia liquefacien, n = 1	0 (0)	0 (0)	0 (0)	1 (100.0)	0 (0)	1 (4.8)
Total = 32	5 (45.5)	6 (54.5)	11 (100.0)	14 (66.7)	7 (33.3)	21 (100.0)

DISCUSSION

The predominant uropathogen isolated in this study was *Escherichia coli*. This finding may be explained by the observation that UTI is majorly caused by colonic bacteria translocating from the rectum to the bladder, of which *E.coli* is one of them [8]. *Escherichia coli* was also predominantly cultured by O'Brien *et al* [4] in the UK, as well as [15-20] in India and several Nigerian authors [9], [21-34], [35-40] among febrile under-five children. On the contrary, Muoneke *et al* [15] in Abakaliki Nigeria reported *Proteus* and *Klebsiella spp* respectively as the most common isolates in their studies. The study in Abakaliki was a retrospective type and therefore may have encountered some missed cases within the period or may suggest a change in the aetiology within the study period. Also both Okunola *et al* [10] in Benin – City Nigeria reported *Staphylococcus aureus* as the predominant uropathogen among febrile under-five children in their localities. Both studies were in the same geographic region of Nigeria may suggest some peculiarity with the common uropathogens in their localities.

CONCLUSION

The study reiterates Escherichia coli as the dominant bacteria causing UTIs in febrile children under five in the specified Nigerian medical center. This reaffirms the global trend while acknowledging local variations observed in different geographic regions, emphasizing the importance of understanding regional patterns for effective management and treatment strategies.

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