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Implicated Aetiological Agents of Neonatal Urinary Tract Infection and Their Antimicrobial Sensitivity Pattern in a Tertiary Health Care Centre, Uyo, South-South Nigeria

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Abstract **Background**: Timely and effective antimicrobial therapy is important in the management of urinary tract infection in the new born. An accurately tailored empirical therapy, informed by periodic documentation of the aetiological agents through urine culture and antimicrobial sensitivity pattern determination is imperative in achieving this goal. This will reduce potential morbidities of delay, and ensure effective therapy before the arrival of urine culture results. The organisms causing neonatal UTI in the University of Uyo Teaching Hospital Uyo, Nigeria and their antimicrobial sensitivity pattern have not been documented in research. **Objective:** To determine the implicated aetiological agents of Neonatal Urinary tract infection(UTI) in the University of Uyo Teaching Hospital and their antimicrobial sensitivity pattern. **Methods:** A cross-sectional study on all neonates diagnosed as `suspected sepsis` who underwent sepsis evaluation between December 2013 and September 2015. Urine specimens were collected by clean catch urine collection method for culture. **Results:** *Escherichia coli* was the commonest organism isolated. Others were *Klebsiella pneumonia*, *Morganella species* and *Staphylococcus aureus.* **Conclusions** *Escherichia coli* was the commonest organism which was sensitive to some of the third generation Cephalosporins such as Ceftazidime and Cefotaxime.Sensitivities to Ceftriaxone, Cefuroxime and Gentamicin which initially were routine in the management of neonatal infections in the facility was comparably low.

Keywords: *neonatal, neonate, urinary tract infection*

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1. Introduction

Urinary tract infection (UTI) is common in all children including neonates and a major cause of morbidity and hospital admissions. [1,2] It has a reported incidence rate of 6.6% for girls and 1.8% for boys in the first six years of life. [3] About 6 to 15% of neonates admitted and evaluated for neonatal sepsis had confirmed UTI. [4,5,6,7] An association between positive urine cultures and development of necrotizing enterocolitis has been shown in preterms, so also has an increased incidence of allergic rhinitis been observed in older children who had documented UTI in the newborn period. [8,9] The importance of UTI in neonates and children is however related both to its frequency of occurrence and its possible long-term consequences of hypertension, [1,2] reduced renal growth [10] and chronic kidney disease. [1,2,9,10] Occurrence of neonatal UTI many times also signal the presence of congenital anomalies of the urinary tract which predisposes to recurrent infections and scarring. [1,2,9,10]

The common aetiological agents of UTI which are those of the faecoperineal bacterial flora, are virulent. They include: Escherichia coli, Klebsiella, Proteus, Morganella, Enterobacter sp, Serratia, and Procidentia. [1,2,10] In most studies including neonates, Escherichia coli is the most common agent accounting for more than 90% of infections. [1,2,3,6] These bacteria enter the urinary tract by ascending up the urethra to cause infection [1,11] Haematogeneous route of infection has also been suggested to also occur in neonates in view of the concurrent culture of the same organism in the blood stream and urine of septic neonates in about 30% of cases. [2,12,13] Other common bacteria are Staphylococcus aureus, Staphylococcus saprophyticus, Staphylococcus epidermidis and Citrobacter specie.

There are no currently available data that unequivocally lay out the optimal approach to treating UTI in the neonate. The drug is chosen on the basis of the resistance pattern of uropathogens in the area. Unfortunately many practitioners

do not routinely obtain urine samples from sick neonates as this is most times difficult. Consequently, there are not many neonatal studies to fill this gap in Nigeria. Some earlier studies in oth the neworn and older children recorded adequate sensitivities to gentamicin and ampicillin. [6,14] More recent studies however suggest increasing resistance to these agents necessitating a paradigm shift. [5,15,16] A study in Maiduguri, Northern Nigeria showed very poor sensitivities to Ampicillin and some other commonly used antibiotics such as, Cotrimoxazole, Nalidixic acid and Erythromycin, with better Sensitivities to Ceftriaxone and the Quinolones; Ciprofloxacin, Ofloxacin, and Peflacine (86.2%, 83.1%, and 73.8%, respectively). [15] In Abakaliki, eastern Nigeria equally poor sensitivities were obtained to Gentamicin and even to Ceftriaxone and Ciprofloxacin underscoring the need for more local surveillance data. [16]

The aim of the study was to determine the implicated aetiological agents of neonatal urinary tract infections in University of Uyo Teaching Hospital, Uyo, South-South Nigeria and the antimicrobial sensitivity pattern of the isolates.

2. Materials and Methods

A prospective descriptive cross sectional study of neonates admitted into the new-born unit of the University of Uyo Teaching Hospital, Uyo, Nigeria, for sepsis evaluation between December 2013 and September 2015 was conducted. Consecutively admitted neonates aged between 1-28 days who met the inclusion criteria were studied. Information on duration of pregnancy including gestational age assessment by date calculated from the last menstrual period (LMP) was obtained from mothers or caregivers of the neonates who gave consent for the study. Ethical approval for the conduct of the study was obtained from the University of Uyo Teaching Hospital Ethical committee prior to commencement of the study.

2.2. Sample Collection

Urine samples for culture were obtained by the clean catch method as described by Fernandez *ET al*. [19,20] The procedure was carried out about 20 - 30 minutes after a feed. The Investigator after wearing a pair of sterile surgical gloves, washed the genitalia of the subjects with soap and water, and dried them with sterile gauze. The neonate was then carried by the underarms by a trained assistant with the legs dangling freely in air. The suprapubic area was percussed several times by the Investigator at a frequency of about 100 taps per minute for about 30 seconds. This was usually followed by voiding in a majority of cases. A sterile universal bottle was then placed in the flowing stream of urine to collect some of the flowing urine. The paravertebral area was also sometimes massaged to help stimulate the voiding process when there was a delay in voiding.

2.3. Urine Culture and Identification of Organisms

Urine culture was done using the Leigh and Williams method [21]. Inoculation of the urine sample on the culture plates was done before microscopy to avoid contamination. About two to ten millilitres of the urine sample was centrifuged for five minutes at a rate of 1500 revolutions per minute, the supernatant was discarded and a wet preparation made from the sediment for examination under the 10X and 40X objective of a microscope. Presence or absence of pus cells and bacteria were noted. A portion of the urine sample was again mixed and inoculated into Cysteine Lactose Electrolyte Deficient (CLED) and blood agar plates and incubated at 37°C for 24 hours. More than 25 colonies on the plate were considered equivalent to $\geq 10^5$ colony forming units (CFU)/ ml of urine. [22,23] Identification of the isolates was carried out as described by Gowan and Steels [24] and appropriate bacterial tests were done for characterisation of the organisms. Antibiotic sensitivity following the Clinical and Laboratory standards institute guidelines 2012 with the disc diffusion method of Stokes using Oxoids multidisc (Oxoid Ltd, Basingstoke, Hampshire, England). [25] The tested antimicrobials include: Gentamicin (10mcg), Ceftazidime (30 mcg), Cefuroxime (30 mcg). Ceftriaxone (30mcg), Cefotaxime (30mcg), Amoxicillin-Clavulanate(30mcg), Imipenem(10mcg) and Ciprofloxacin (5mcg). The Sensitivity testing was done using Mueller Hinton Agar (BIOTEC Lab, Ipswich, Suffolk, IP57RG, United Kingdom) at a pH of 7.2-7.6. *Escherichia coli* NCTC 10481 and *Staphylococcus aureus* Oxford strain NCTC 6571 were employed as the control strains in the antibiotic sensitivity testing. [24] Data processing was done using the Statistical Package for Social Sciences (SPSS) version 18.

3. Results

Table 1. Bacterial Isolates among Neonates with Urinary Tract Infection in subjects (n=5)

Isolates	Frequency	Percent
Escherichia.coli	2	40.0
Morganella species	1	20.0
Klebsiella species	1	20.0
Staphylococcus aureus	1	20.0
Total	5	100

Table 2. Sensitivity Patterns of Organisms to the Selected Antimicrobial Agents

Organisms	Pharmaceutical Agents							
	Amoxicilin-Clavulanate	Ceftriaxone	Ceftazidime	Cefuroxime	Ciprofloxacin	Gentamicin	Imipenem	Cefotaxime
E. coli	S	S	S	S	S	S	S	S
E.coli	R	R	S	R	R	R	S	S
Morganella	R	S	S	R	S	S	S	S
Klebsiella	R	R	R	R	S	R	R	R
Staph aureus	S	S	S	S	S	S	S	S
Percentage Sensitivity	2(40.0)	3(60.0%)	4(80.0)	2(40.0%)	4(80.0%)	3(60.0%)	4(80.0)	4(80.0)

One hundred and nine (109) patients were recruited into the study. There were 65 males and 43 females giving a M: F ratio of 1.5:1 The bacterial isolates found among the neonates with UTI are as shown below in Table 1.

3.1. Sensitivity Pattern among the Isolates

Analysis of the sensitivity pattern showed that the isolated organisms were most sensitive to Cefotaxime, Ceftazidime, Imipenem and Ciprofloxacin and least to Cefuroxime, Amoxicillin-Clavulanate and Gentamicin as shown in Table 2.

4. Discussion

This study provides the first documented local evidence of the aetiology of neonatal urinary tract infection in the University of Uyo Teaching Hospital in South-south Nigeria and the antimicrobial susceptibility patterns. Gram negative organisms were the predominant agents isolated. This is consistent with most reports. [1,2] *E coli*, usually the commonest cause of UTI in children,was the commonest isolate among those with positive urine cultures. This is in contrast with the study in Benin [5] also in South south Nigeria, where *Klebsiella* was commonest. *E coli* have anatomic and physiologic adaptations that favour this pre-eminence position. [2] *Morganella* species, an uncommonly reported aetiological agent of neonatal UTI was found in this study.It has however been reported in some studies as a cause of maternal chorioamnionitis and neonatal sepsis. [27,28,29] Sensitivities of the common etiological agents of UTI *(E coli and Klebsiella*) to the third generation Cephalosporinssuch as Ceftazidime and Cefotaxime is worthy of note. So also are the sensitivities to Imipenem and Ciprofloxacin. This may be due to the relatively infrequent use of these agents in our neonatal unit as against Cefuroxime, Ceftriaxone andGentamycin which had been the more regularly used agents and to which lower sensitivities were recorded. This however differs from that seen in the Benin [5] study where poor sensitivity of the isolated *E coli* to Ceftazidime was recorded. This may have resulted from an overuse of this very trusted antimicrobial in the centre.The study has highlighted a need for review and possible change in the choice of empirical therapy for neonates admitted with sepsis from the more commonly used antimicrobial agents in the neonatal unit of UUTH such as Cefuroxime and Gentamicin, to other more potent agents like Ceftazidime and Cefotaxime.

5. Conclusion

Periodic evaluation of bacterial epidemiology and antibiotic sensitivity of uropathogens is crucial for paediatricians in their choice of appropriate empirical commencement of antibiotic treatment of UTI before obtaining the microbiologic results. This will help in reducing any long term renal damage that may have resulted from delayed or inappropriate treatment.

The urinary isolates in neonates with UTI in UUTH, Uyo are: *Escherichia coli*, *Klebsiella specie*, *Morganella morgagni and Staphylococcus aureus.* Until further periodic review of antibiogram,Ceftazidime, Cefotaxime and Imipenem should be used in the initial treatment of neonates with UTI in this environment while awaiting results of urine microscopy, culture and sensitivity.

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