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Original Article

Microbial isolates from stroke patients with urinary tract infection, at the University of Benin Teaching Hospital

Francis Ehidiamen Odiase[1,2], Patrick Vincent Lofor[3,4]

Departments of [1]Medicine and [3]Medical Microbiology, College of Medical Sciences, University of Benin, Departments of [2]Medicine and [4]Medical Microbiology, University of Benin Teaching Hospital, Benin City, Nigeria

Abstract

Background: Urinary tract infection (UTI) is a common nosocomial infection amongst stroke patients. It is associated with increased morbidity and mortality. Despite the impact of UTI on stroke, there is a dearth of knowledge regarding the microbial isolates from the urine of stroke patients with UTI in Nigeria.

Aim: The aim of this study was to compile and describe microorganisms causing UTI in stroke patients and it is hoped to provide insight into management.

Methods: This was a retrospective study, which involved review of the laboratory microbiology records of urine specimens of stroke patients with UTI who were on admission from June 2004 to June 2018 at the University of Benin Teaching Hospital.

Results: A total of 2,681 stroke patients had their urine sent for microbiological assessment of which 778 (29%) had UTI. The mean age of the stroke patients with UTI was 65.9 ± 11.4 years, with 53.0% of them being female, while 69.0% had an ischemic stroke. With regard to the urine microbial isolates, *Enterococcus faecalis* accounted for 30.0%, *Escherichia coli* 19.0%, *Enterobacter sakazaki* and *Proteus mirabilis* 16.0% each, while *Citrobacter freundii* (0.8%) and *Klebsiella pneumoniae* (1.1%) were the least isolated microorganism.

Conclusion: Stroke patients are at risk of developing catheter-associated UTI. Catheter-associated UTI predisposes to multidrug-resistant antibiotic isolates, attendant with poor outcome. It is hoped that rational use of antibiotics and appropriate urinary catheter application be ensured in the care of the stroke patients.

Keywords: Microbial isolates, stroke, urinary catheter, urinary tract infection

Address for correspondence: Dr. Francis Ehidiamen Odiase, Department of Medicine, University of Benin Teaching Hospital, Benin City, Nigeria. Department of Medicine, College of Medical Sciences, University of Benin, Benin City, Nigeria. E-mail: francisodiase2000@hotmail.com

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INTRODUCTION

Stroke is a major public health problem globally. It is the second leading cause of death and the third leading cause of disability worldwide. About six million persons die from stroke worldwide every year and many of the survivors are left with permanent disability.[1-3] Each year, worldwide, about 150 million persons have urinary tract infections (UTIs).[4] A growth of $\geq 10^5$ colony-forming units is considered as significant bacteriuria.[5] UTI is a frequent reason for hospital visit, a significant cause of morbidity in the general population and in the hospitalised patient the most common nosocomial infection.[4,6] Stroke sufferers have an increased risk of in-hospital medical complications including infections such as UTI, aspiration pneumonia, infected pressure ulcers or sepsis. Infections following

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stroke are common and these infections are associated with higher mortality and morbidity.[7-9] Thirty per cent of stroke patients would have infections, of which UTI accounts for a third. Post-stroke UTIs have been reported to have a median time from admission of about 2–3 weeks.[7-9]

Factors that are predictive of UTI in stroke patients include use of catheters, severity of the stroke, loss of consciousness, diabetes mellitus prostate disease, neurogenic bladder and obesity.[5-9] Experimental studies have revealed that stroke does induce a systemic immune depression that predisposes to infection.[10] UTI is 3%–10% likely to occur after a day of catheterisation, while a day-30 permanent urinary catheter is a 100% risk for UTI occurring. Gram-negative, Gram-positive bacteria and certain fungi are the causes of UTI.[5-9,11]

Escherichia coli, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus, Enterococcus faecalis*, *Staphylococcus saprophyticus* and *Candida* spp. are the usual pathogens causing UTIs, with earlier studies showing *E. coli* as the most common cause of community- and hospital-acquired UTI. However, in the recent, nosocomial UTI has been characterised by a trend for a higher prevalence of multidrug-resistant Enterococci and coagulase-negative Staphylococci.[12-16]

UTI could cause fever, hypotension, hypoxia, immobilisation, kidney damage, pyelonephritis, sepsis, general weakness and activation of pro-inflammatory cytokines and release of free radicles, which could impair neuronal survival in the penumbra. Post-stroke infections have been related to poor recovery, sub-optimal rehabilitation and prolonged hospital admissions and attendant increased expenses. Furthermore, antimicrobial resistance and increased recurrence of UTI worsen the economic burdens of these infections.[8,9,17-19]

Treatment and prevention of UTI is an important component in the management strategy aimed at reducing the impact of stroke on victims. To the best of our knowledge, there is no study that has compiled the urine isolate from stroke patients in the south–south region of Nigeria.

Knowledge of the common microorganism responsible for UTI and the pattern of resistance would influence management and aid the clinician's choice of empiric antibiotics treatment.

METHODS

It was a retrospective study. We reviewed the medical records of stroke patients admitted into the stroke ward at the University of Benin Teaching Hospital with stroke and UTI from June 2004 to June 2018. Ethical approval was obtained from the Ethics and Research Committee of the University of Benin Teaching Hospital. The study population consisted of all stroke patients suspected to have UTI, whose urine samples were sent to the microbiology laboratory for urine microscopy, culture and sensitivity.

The instruction and procedure for the collection of urine samples from the stroke patients and laboratory assessments done were as follows: (1) the conscious and well-oriented stroke patient was told to collect midstream urine of about 20 ml into a provided specimen container, after first voiding of the first part of the urine, while the female stroke patient was to have a normal saline wash of her genitalia assisted by the nurse before collection of the midstream specimen; and (2) the collection of urine specimen from the unconscious or disoriented stroke patient was done by the microbiologists. The patient was catheterised, with about 20 ml of urine specimen collected. The urine collected in both cases was sent immediately to the microbiology laboratory. A standard loop of 1/250 ml was used to culture the urine on blood agar and MacConkey agar, incubated for at most 48 h aerobically. Significant bacteriuria was determined using the urine colony growth counter and all growth that meant the Kass's critical value for significant bacteriuria of $\geq 10^5$ colony-forming unit/ml (CFU/ml) were said to have UTI.[4]

All microbiologic records spanning the period June 2004 to June 2018 were retrieved and reviewed. Data entry and analysis was performed using Statistical analysis was performed using the SPSS Version 21, Inc., Chicago, Illinois, USA. Continuous variables were presented using means, median, standard deviation and range with comparison using Student's *t*-test. Frequency and percentages were used to summarise categorical variables with Chi-square used to assessing the association between the variables. Statistical significance was at the level $P \leq 0.05$.

RESULTS

The urine samples of 2,681 stroke patients were sent to the microbiology laboratory for microscopy, culture and sensitivity. Microbes were isolated from the urine samples of 778 stroke patients accounting for 29% (778/2,681) of the total specimen. The mean age of the patients with UTI was 65.9 ± 11.4 years, with the range of 38–97 years. Sixty-nine per cent had ischemic stroke while 31% had haemorrhagic stroke. There were more female (53%) stroke patients with UTIs than their male (47%) counterparts. Urine microbial isolate was highest within the age range

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of 65–85 years, followed by the age range 35–60 years, while age range 86–100 years had the least urinary isolates [Table 1]. The mean urinary isolate for the 14-year period under review was 56 isolates. The microbial isolates in the first 7years (June 2004 to May 2011) ranged from 31 to 61, while the last 7 years (June 2011 to June 2018) ranged from 36 to 71. Sixty-eight per cent of the urine microbial isolates were aerobic Gram-negative bacilli, while 32% were aerobic Gram-positive cocci. Six-unique genera of aerobic Gram-negative bacilli were isolated, including *P. mirabilis, Proteus vulgaris, Enterobacter sakazaki, Citrobacter freundii, Escherichia coli* and *Klebsiella pneumonia,* while two unique genera of the aerobic Gram-positive cocci were isolated including *Enterococcus faecium* and *Enterococci faecalis*. The predominant urinary microbial isolate was *Enterococcus faecalis (*29.5%*)*, while *E. coli* accounted for 19.0%, *E. sakazaki* (16.0%), *P. mirabilis (*16.0%), *Citrobacter freundii* (0.8%) and *Klebsiella pneumoniae* (1.1%) with 1.6% having mixed growth. The urine from the female stroke patients had more of *E. faecalis* (17.6%), *E. coli* (11.2%), *Proteus vulgaris* (7.4%), while *P. mirabilis* (11.5%) and *E. sakazaki* (8%) were more common in the urine of the male stroke patients [Table 2].

Table 1: Age distribution of the 778 stroke patients with urinary tract infections and number of urine isolates

Age range	Male (%)	Female (%)	Total
35-40	13 (43.3)	17 (56.7)	30
41-45	32 (47.8)	35 (52.2)	67
46-50	33 (47.1)	37 (52.9)	70
51-55	14 (30.4)	32 (69.6)	46
56-60	30 (58.8)	21 (41.2)	51
61-65	62 (48.4)	66 (51.6)	128
66-70	54 (47.4)	60 (52.6)	114
71-75	47 (47.5)	52 (52.5)	99
76-80	35 (47.9)	38 (52.1)	73
81-85	26 (42.6)	35 (57.4)	61
86-90	9 (69.2)	4 (30.8)	13
91-95	8 (47.1)	9 (52.9)	17
96-100	3 (33.3)	6 (66.7)	9

Number of isolates

Table 2: Percentage of urine microbial isolates from 778 stroke patients with urinary tract infections

Isolates	Male (%)	Female (%)	Total (%)
Enterococcus faecalis	12	17.6	29.6
Escherichia coli	7.8	11.2	19
Proteins mirabilis	11.5	4.4	16
Enterobacter sakazaki	8	7.5	15.5
Proteus vulgaris	6.1	7.4	13.5
Enterococcus faecium	0.1	2.8	2.9
Klebsiella pneumonia	0.4	0.7	1.1
Citrobacter freundii	0.5	0.3	0.8
Mixed growth	0.6	1	1.6

DISCUSSION

This study revealed that more female stroke patients had UTI than the male stroke patients, as has been the observation in other studies.[9,20] It is possible that the anatomical difference in the genitourinary system and vaginal flora could be responsible. Our study also revealed that more of the older stroke patients had UTIs compared with the younger stroke patients, ageing has been reported previously as a risk factor for UTI,[18-20] since the elderly have urological and bladder conditions that predispose to infections, including prostatic disease in older males.

Enterococcus spp., a Gram-positive organism, was the predominant isolate in our study (including *E. faecalis* and *E. faecium*), accounting for almost a third of the isolates. In contrast, several studies have shown that *E. coli* is the main cause of UTI, although it was also their observations that *Enterococci* spp. was a prominent isolate in nosocomial UTI.[12-16] In addition, other studies have found that patients with catheter associated UTI (CA-UTI) frequently had polymicrobial infections other than *E. coli*,[13,14,16] which is consistent with findings in our study.

Individuals with stroke are exposed to several antibiotics in the course of admission and their higher likelihood of developing CA-UTI favours the emergence of drug-resistant isolates.[15,17,21]

Enterococci spp. are part of the normal flora of the gastrointestinal tract (*E. faecalis* and *E. faecium* are found in relative abundance in human faeces (10^5–10^7 organisms per gram) and usually cause infections amongst antibiotics hospitalised patients whose intestinal microbiota have been disrupted. *Enterococcus* spp. are about the earliest to inhabit the gut and do have the ability to survive gut host defences. In addition, they are able to withstand and grow in wide temperature and pH ranges.[22-24]

Enterococcus spp. are known to have intrinsic and acquired resistance to antibiotics and this complicates UTI caused by these isolates. *E. faecalis* and *E. faecium* are known to accumulate to high numbers in patients on prolonged antibiotics exposure and co-infect with other bacteria that are resistant to multiple antibiotics. *E. faecalis* and *E. faecium* are naturally resistant to cephalosporins, aminoglycosides, trimethoprim, clindamycin and penicillin, while *E. faecalis* and *E. faecium* resistance to vancomycin is now world-wide in distribution.[14,25-27]

Studies have shown that *E. faecalis* and *E. faecium* can be transmitted in the hospital from person-to-person including health-care personnel, facilitating its persistence in the hospital environment. *E. faecalis* and *E. faecium* tolerate and resists antiseptics, disinfectants and dryness and detergents and are able to survive

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hygienic protocols in hospital settings meant to control infections.[28-30]

E. coli a Gram-negative bacteria was the second most common isolate in our study, although other studies have found it to be the most common causative organisms in uncomplicated and complicated UT;[31,32] Difference in the method of isolation and identification of this organism could be responsible for the varying observation.

Proteus spp., including *P. mirabilis* and *Proteus vulgaris* put together were a significant isolate in our study. They have been an important urinary isolate in many other studies, especially in individuals with long-term catheterisation.[33-35] *Proteus spp*, is a gut resident that contaminates the urethra. It elaborates urease which breaks down urea to carbon dioxide and ammonia, causing a rise in urine pH, with crystallization of calcium and magnesium salts that forms a film on the urinary catheter. *P. mirabilis* UTI is associated with the development of kidney and bladder stone, and this is said to make eradication difficult since the isolates are imbedded within the stone matrix which shields it from antibiotics action. In addition, *Proteus* spp., produces resistant pilli that are important in catheter-associated biofilm development and adhesion to environmental surfaces, hence promoting spread.[33-35]

E. sakazaki and *C. freundii,* both Gram-negative gut bacteria, were also isolated in this study, but are not common urinary isolates. The uropathogen colonisation or elimination in the urinary tract depends on the host–pathogen interactions. The isolates causing UTI and its antibiotics susceptibility may vary based on geographical location and may even change in the same locality with time *Klebsiella pneumonia* a Gram negative non motile rod was not a significant isolate in this study, though a gut resident that is ubiquitous in nature.. *Klebsiella pneumonia* has been shown to cause nosocomial UTI with a high tendency to developing antibiotics resistance and these have been related to previous and prolonged antibiotics exposure, protracted hospital stay and the use of urinary catheter.[36,37]

This study had shown that UTI was caused by both Gram-positive and Gram-negative isolates and stroke patients diagnosed with UTI and other infections are usually treated with antibiotics. These antibiotic treatments do result in alterations of the normal microbiotas flora of the gastrointestinal tract and vagina in females with emergence of multidrug-resistant microorganisms. The persistent use of antibiotics against Gram-negative bacteria over the years might have caused an antibiotic selection pressure, which has led to the emergence of the Gram-positive bacteria, *E. faecalis* as the predominant cause of UTI in our stroke patients, in contrast to *E. coli* as the main cause of UTI. This is a likely explanation in this study as majority of the stroke patients, are elderly and they could have over the years had antibiotics exposure for other conditions, other than UTI.

Limitations

This study was limited by its retrospective design. In addition, there were no records on antibiotics used prior to doing urine microbiology. In addition, we could not distinguish between stroke patients with hospital-acquired UTI from those with community-acquired UTI.

CONCLUSION

This study has revealed the emergence of *E. faecalis* as the predominant urine microbial isolate in our stroke patients with UTI. *E. faecalis* has been shown to have wide spread natural and acquired resistance to antibiotics and this could increase the morbidity and mortality in these stroke patients. It is hoped that appropriate urinary catheter use be ensured, while judicious antibiotic usage practiced following sensitivity.

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Conflicts of interest

There are no conflicts of interest.

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