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Incidence, risk factors and microbiological aetiology of urinary tract infections in admitted stroke patients at a teaching hospital in Zimbabwe: A prospective cohort study

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SUMMARY

Background and purpose: The occurrence of urinary tract infections (UTIs) after stroke is a well recognised complication. The aim of this study was to determine the incidence of UTIs in stroke patients admitted at a teaching hospital in Zimbabwe.

Methods: A prospective cohort study was conducted in stroke patients admitted within 7 days from onset of stroke. Patients were followed up throughout the admission period and those with symptomatic UTI were identified. Urine samples for analysis were collected and causative bacterial organisms were identified with their antibiotic susceptibility patterns analysed.

Results: A total of 145 stroke patients were followed up during their in-patient care. 28 patients (19.3%) developed a urinary tract infection, 45 patients (31%) had asymptomatic bacteriuria and 72 patients (49.7%) had no bacteriuria. The median time from admission to UTI occurrence post stroke was 5 (IQR 4—7) days. Severe stroke (NIHSS score 16—42) was an independent risk factor for UTI development with an odds ratio (OR) 5.15 (1.68—15.75) $p<0.001$. The commonest bacterial causative organisms cultured were *Escherichia coli* (27.6%) ; *Klebsiella* species (21.1%) and *Enterococcus faecalis* (19.7%). Twenty nine percent of the cultured Gram negative bacteria were extended-spectrum beta-lactamase (ESBL) producers.

Conclusions: UTIs are common in admitted stroke patients and a significant percentage of causative organisms are multi-drug resistant. UTI occurrence is more common in patients with severe stroke and is associated with increased hospital stay. These observations

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highlight the need for robust infection prevention and control strategies to curb this common post-stroke complication.

Introduction

Stroke is one of the leading causes of major long-term disability and mortality worldwide. [1,2] In Africa the burden of stroke is high and is still increasing with the increase attributable to population growth and ageing. [3,4] In Zimbabwe stroke is ranked fifth in the causes of death and the in-hospital mortality after stroke is more than 20%. [5,6].

Complications after stroke are common and they contribute significantly to mortality. [7—9] Infections, mostly urinary tract infections (UTIs) complicate stroke especially in the acute phase post-stroke. [10—13] From previous studies, UTIs were shown to complicate stroke in 10—30 % of patients. Studies have also shown that UTIs adversely affect stroke outcome. [14,15].

To understand the burden of UTIs in admitted stroke patients at one of the teaching hospitals in Zimbabwe we carried out a prospective cohort study on admitted stroke patients to determine the in-patient incidence and associated risk factors of UTI in the acute phase of stroke. The microbiological causative organisms and their antibiotic susceptibility pattern were also assessed.

Research methodology

A prospective cohort study was carried out on adult (aged 18 yrs or older) stroke patients admitted into the stroke unit at a teaching hospital in Zimbabwe from April to September 2018. Consecutive sampling was used to recruit participants for this study until the calculated sample size was attained. Stroke patients with stroke duration less than 7 days admitted into the stroke unit for at least 48hrs and consenting to participate in the study were included. For patients who were unable to give consent themselves, the consent was sought from their next of kin or caregivers. The study excluded patients admitted into stroke unit seven days after stroke onset, patients who developed UTI in the first 48 hours of admission and patients who had other medical conditions which mimic a stroke. Ethical approval for the study was obtained from the Medical Research Council of Zimbabwe (MRCZ) and the Joint Research Ethics Committee (JREC) of Parirenyatwa hospital and College of Health Sciences, University of Zimbabwe.

Enrolled patients were assessed for UTI occurrence from admission to discharge. Demographic data, stroke severity as determined by National Institute of Health Stroke Scale (NIHSS) [16] and catheterisation history were recorded on admission. Laboratory investigations carried out for the study included urine dipstick, microscopy, culture and sensitivity. Bacterial culture and sensitivity testing utilised conventional methods using the Clinical and Laboratory Standards Institute (CLSI) guidelines. [17] Detection of extended-spectrum beta-lactamase (ESBL) producing organisms was performed on all Enterobacteriaceae using ceftriaxone and amoxycillin/clavulanic discs. Duration of hospital stay and post-stroke disability as defined by the modified Rankin Scale (mRS) were recorded on discharge. [18] Vancomycin resistance was screened for in Gram positive organisms using a disc diffusion method.

The diagnosis of UTI was made by the attending stroke unit team if a patient satisfied the Centers for Disease Control and Prevention (CDC) guidelines criteria for UTI diagnosis. [19] In those patients who did not develop urinary tract infection during admission period urine samples were collected on discharge to determine patients with asymptomatic bacteriuria.

Data was captured and analysed using Epi-info 7.2.2.2. Dichotomous variables were described using frequencies while continuous variables were summarised using mean, median, range and standard deviation as appropriate. Continuous data was compared using t-test and the association between categorical variables was determined using a chi-square test. A logistic regression analysis model was used to assess factors associated with UTI occurrence in stroke patients and level of significance was assessed by odds ratios, p-values and confidence intervals. For multivariate analysis, factors with p-value <0.25 in the univariate analysis were considered for inclusion in the multivariate analysis. Highly correlated variables had some of the variables not included in multivariate analysis to cater for multicollinearity.

Results

Figure 1 summarises the study recruitment process. The study recruited a total of 145 stroke patients as per calculated sample size and symptomatic UTIs were diagnosed on 28 study participants giving a UTI incidence proportion of **19.3%**. The median time from admission into stroke unit to UTI diagnosis was 5 days (IQR 4—7days). Asymptomatic bacteriuria was noted in 31 % (n=45) of study participants on discharge from stroke unit.

Demographic and clinical characteristics of study participants are summarized in Table 1. The mean (standard deviation) age of study participants was 62.9 (+/- 15.9) years. Average duration of hospital stay in study patients was a median of 5 days (IQR 4—6 days). The proportion of study participants who were catheterised during the in-patient period was 78.6% (n=114) with the majority of catheters inserted in the stroke unit and the median days with catheter in situ being 4 days (IQR 3—5 days). The proportion of study participants who received antibiotics, within seven days prior to admission or during the inpatient care for any other reason besides UTI, was 24% (n=35). The majority of these patients given antibiotics, before a UTI diagnosis, received them for aspiration pneumonia.

As inferred from the logistic regression analysis, severe stroke as demonstrated by NHISS score greater than 16 was independently associated with increased risk of developing UTI by an odds ratio (OR) of 5.15 ((1.68—15.75) $p<0.001$). Prolonged hospital stay and high discharge mRS score were also significantly associated with UTI development (Table 2). Hospital stay was longer in patients with UTI with a median

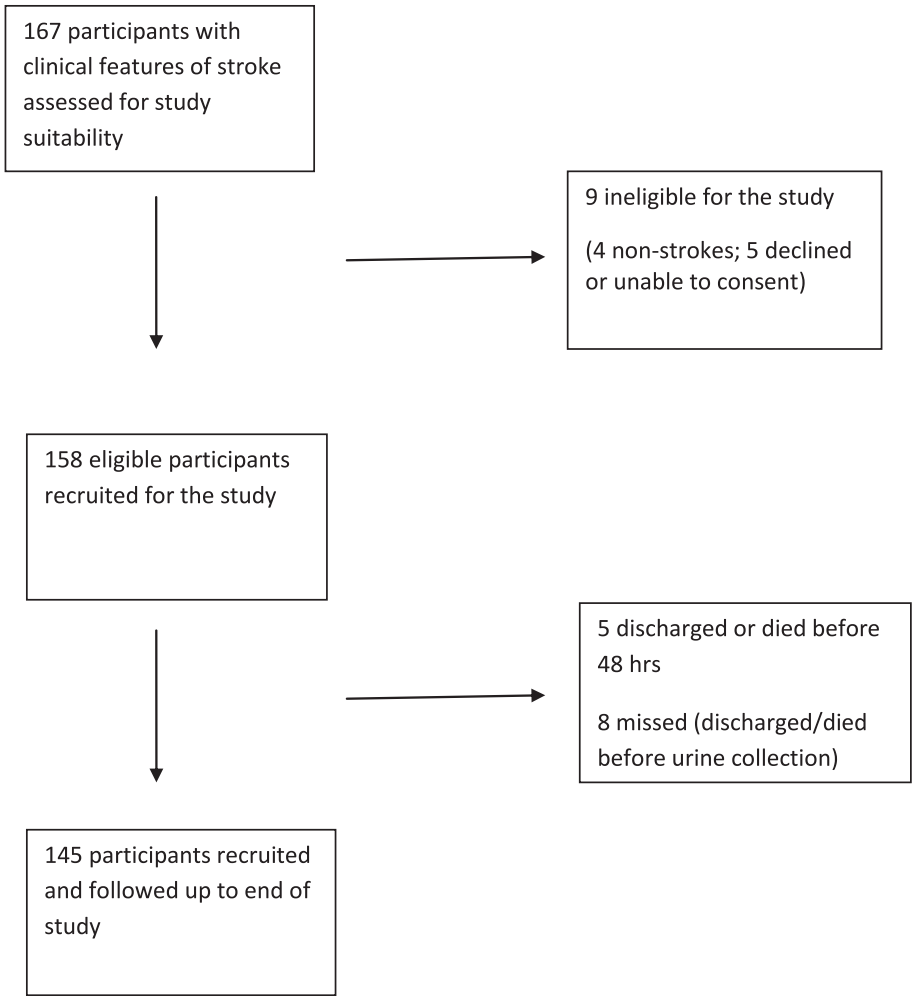

Figure 1. Flow diagram showing study recruitment.

duration of 9 days (IQR 8—11days) compared to a median of 4 days (IQR 4—5 days) in participants who did not develop a UTI during their inpatient stay.

Bacteria were identified in **73** (50.3%) samples submitted for urine culture and a total of 76 bacterial organisms were identified, with three samples having grown two different organisms. The different types of organisms grown and their frequencies are shown in Table 3. Of the 76 bacterial isolates identified, 27 (36%) were Gram positive and 49 (64%) were Gram negative organisms. Differentiation of pathogenic organisms from commensals was based on colony count combined with urine dipstick and microscopy findings. Presence of leucocyturia, nitrites and urine culture showing colony count $\geq$ 10 colony forming units per millilitre was suggestive of pathogenic organism.

In study patients who developed symptomatic UTIs, *E.coli*, *Klebsiella pneumoniae* and *Enterococcoccus faecalis* were the commonest causative organisms (Figure 2). In patients who had asymptomatic bacteriuria the frequency of common causative organisms was similar, with a small percentage being contributed by Salmonella and Streptococcus species (Figure 3).

The antibiotic susceptibility pattern of common UTI causative organisms was assessed. Of the 49 Gram negative organisms cultured 14 (28.5%) organisms were ESBL positive and 1 (2%) organism was a carbapenamase producing enterobacteriaceae (CPE) (Figure 4). Gram negative organisms showed a similar susceptibility pattern with good sensitivity to aminoglycosides and carbapenems. They showed increased resistance to co-trimoxazole and ampicillin. About 20—25% of the Gram negative organisms were resistant to fluoroquinolones, 2nd and 3rd generation cephalosporins and amoxicillin/clavulanic acid.

E.faecalis demonstrated good sensitivity to penicillin G and ampicillin. Graphs summarising the antibiotic susceptibility of E.*coli* and *E.faecalis*, the two commonest Gram negative and Gram positive UTI causative organisms respectively are shown on Figures 5 and 6 below.

Stroke outcome in this study was assessed using the modified Rankin Score (**mRS**) which is a well established and validated tool for assessing functional disability post-stroke. The stroke outcome in the study participants and their corresponding UTI diagnosis during the study period is summarized in Table 4. The majority of patients (93%) in the group that developed symptomatic UTI had a mRS score $\geq$4; 43% of patients with asymptomatic bacteriuria had a mRS score $\geq$4 and 42% of patients who did not have bacteriuria had an mRS score $\geq$4.

Table I
Demographic and clinical characteristics of study participants

Characteristic	Frequency or mean (SD) n (%)
Age mean*(SD)*	62.9 (+/- 15.9) years
<45 years	19 (13.1)
45—65 years	62 (42.8)
>65 years	64 (44.1)
Gender	
Male	48 (33.1)
Female	97 (66.9)
Time to presentation	
<24 hours	65 (44.8)
24—48 hours	38 (26.2)
>48 hours	42 (29.0)
Stroke severity NIHSS	
1-4	8 (5.5)
5-15	69 (47.6)
16-20	36 (24.8)
21-42	32 (22.1)
Stroke type	
Ischaemic	97 (66.9)
Haemorrhagic	29 (20.0)
Unknown	19 (13.1)
Catheterisation	
No	31 (21.4)
Yes	114 (78.6)
Antibiotic exposure	
Yes	36 (24.8)
No	109 (75.2)
Discharge mRS	
≤3	71 (49.0)
≥4	74 (51.0)

SD: standard Deviation; NIHSS: National Institute of Health Stroke Scale; mRS: modified Rankin Score.

Discussion

UTIs are common after stroke and have been reported to have an impact on stroke outcome. [13] Previous studies have shown UTIs to be associated with a decline in neurological status, increased hospital stay and increased risk of disability or death. [20—22] In an effort to better understand how UTIs affect stroke patients in our unit, a prospective cohort study looking at the incidence of UTIs in the acute phase post-stroke was carried out. Risk factors associated with UTI occurrence, bacterial aetiological agents and their antibiotic susceptibility pattern were also assessed. This study showed that the incidence of symptomatic UTI in the acute phase post-stroke was 19.3%. This is consistent with previous studies which showed incidence rates of 6—27%. [10—12,22,23]The main reason for the varied incidence rates in these studies was difference in study designs, definition of UTIs and duration of follow up. In a meta-analysis of 87 studies by Westerndorp *et al.*, the pooled incidence rate of UTI in stroke patients was 10%. [14] In another recently performed meta-analysis by Tianyuan Yan *et al.*, which looked at 16 studies; the pooled prevalence of UTI in stroke patients was 19.0%. [15] Our study showed an incidence rate of 19.3% which was almost similar to the incidence rate of this meta-analysis. Of note is that all studies included in these meta-analyses were done in developed countries so the lack of robust infection control programs in developing countries might explain why our incidence rate was higher.

Asymptomatic bacteriuria was common in our study with 31% of study participants found to have it at discharge. This is consistent with other studies which showed similar trends in their study cohorts. [24] In a study by Aizen *et al.*, patients who had asymptomatic bacteriuria at baseline had an increased risk of developing a UTI compared to those without. [25] Therefore it might be prudent to follow up these patients with monitoring for possible development of a symptomatic UTI.

In our analysis, stroke severity was found to be an independent predictor of UTI occurrence with an NIHSS ≥ 16 associated with an increased risk of a UTI diagnosis on a multivariate analysis [OR 5.15 (1.68—15.76) p<0.01]. This is consistent with findings from other studies which showed a similar association. [11,12] This association is possibly due to the increased rate of bladder dysfunction and rate of catheterisation in patients with severe stroke. Severe stroke is also associated with an impairment of the immune system, due to stroke induced immune-suppression, which will predispose stroke patients to bacterial infections. [26—28].

Catheterisation, female gender and increased age showed a trend towards high odds of UTI occurrence but were statistically insignificant on a multivariate analysis. Other studies of acute stroke have found these factors to be independent predictors of UTI occurrence after stroke. A meta-analysis by Tianyan Yan *et al.* found similar associations. [15] A small sample size, the unequal proportion of catheterised and uncatheterised patients, and an unequal proportion of females and male patients in our study cohort could explain why these factors were not statistically significant.

Another important finding in our analysis was the increased hospital stay [median 9(IQR 8—11) days] in patients who developed UTIs compared to those who did not develop UTI in the inpatient period [median 4(IQR 4—5) days]. UTI occurrence was associated with increased hospital stay which means increased economic burden to patients and to the hospital. Patients who developed UTIs were noted to have increased disability on discharge as measured by the mRS which is a well validated rating scale for assessing functional disability post-stroke. [29] However it should be noted that these two observations could result in a controversial assertion that UTI occurrence is associated with poor stroke outcome. The increased hospital stay can be a risk factor for UTI development or it can be a result of urinary tract infection development. Increased disability (high mRS) on discharge could be because these patients had a severe stroke on admission, which predisposed them to UTI development; hence their poor outcome is due to a severe stroke rather than UTI occurrence. As a result, we cannot confidently conclude that UTI occurrence is a relevant independent predictor of poor stroke outcome as measured by discharge mRS or hospital stay because of the confounding effect.

In this study the distribution and antibiotic susceptibility patterns of UTI microbial causative organisms was described. *Enterobacteriacae* were the commonest UTI causative organisms, which might be due to their inherent ability to attach to uro-epithelium. The high frequency of *E.coli* was comparable with other studies done in Africa which showed a similar trend. [24,30] For the Gram positive organisms, *Enterococcus faecalis* and coagulase negative *Staphylococcus* were the commonest isolated organisms. This pattern of distribution and frequency

Table II
Risk factors associated with UTI occurrence: univariate and multivariate binary logistic regression analysis

Factor	UTI		Univariate analysis	Multivariate analysis
	Yes	No	OR (95% CI)	OR (95% CI)
Gender				
Male	5	43	Ref	Ref
Female	23	74	2.67 (0.95—7.54)	1.46 (0.43—4.99)
Catheterisation				
No	2	29	Ref	Ref
Yes	26	88	4.28 (0.96—19.17)	2.10 (0.36—12.21)
Stroke severity				
1-15	8	69	Ref	Ref
16-42	20	48	3.59 (1.46—8.82)***	5.15 (1.68—15.76)**
Stroke type				
Ischaemic	18	79	Ref	Ref
Haemorrhagic	6	23	1.14 (0.41—3.22)	0.75 (0.22—2.62)
Unknown	4	15	1.17 (0.35—3.95)	1.14 (0.24—5.48)
Antibiotic exposure				
Yes	6	30	Ref	Ref
No	22	87	1.26 (0.47—3.41)	3.53 (0.99—12.59)
Catheter + antibiotics (n=114)				
Yes	6	29	Ref	
No	20	59	1.64 (0.59—4.52)	
Age				
<45 years	3	16	Ref	Ref
45—65 years	11	51	1.15 (0.29—4.64)	1.31 (0.21—8.27)
>65 years	14	50	1.49 (0.38—5.87)	1.32 (0.21—8.07)
Time to presentation				
<24 hours	16	49	Ref	Ref
24—48 hours	5	33	0.46 (0.15—1.39)	0.39 (0.11—1.39)
>48 hours	7	35	0.61 (0.23—1.65)	0.43 (0.12—1.51)
Duration with catheter, median (IQR) (days)	8 (6—10)	3 (3—4)	1.07 (0.95—1.19)	
Hospital stay duration	9 (8—11)	4 (4—5)	8.74 (3.30—23.14)***	
Discharge mRS				
≤3	2	69	Ref	Ref
≥4	26	48	18.69 (4.23—82.48)***	15.84 (3.15—79.66)**
Diabetes mellitus				
No	22	102	Ref	
Yes	6	15	1.85 (0.65—5.32)	
HIV status				
Negative	27	109	Ref	
Positive	1	8	0.50 (0.06—4.21)	

*Significant at α=0.05, **Significant at α=0.01, ***Significant at α=0.001.
UTI: Urinary tract infection; OR**:** odds ratio; IQR**:** interquartile range; mRS**:** modified Rankin Score; **HIV:** Human Immunodeficiency Virus.

Table III
Frequencies of bacterial isolates from urine samples of stroke patients

Bacterial organisms	Frequency n=76	Percentage of total
Escherichia coli	21	27.6%
Klebsiella pneumoniae	16	21.1%
Proteus mirabilis	10	13.2%
Salmonella species	2	2.6%
Enterococcus faecalis	15	19.7%
Coagulase negative Staphylococcus	10	13.2%
Streptococcus spp	2	2.6%
Total	**76**	**100%**

is consistent with what is described in the literature where these organisms are among the most reported nosocomial organisms. [31] Staphylococci are an increasingly recognized causative agent of UTIs particularly in catheterised patients. They are also implicated in promoting resistance among other gram positive UTI causative species because of its wide variety of multidrug resistant genes on its plasmids. [32] One of the commonest group of organisms described in the literature to cause nosocomial UTIs are *Pseudomonas species*. In our study cohort, *Pseudomonas* was not identified in any of the urine samples submitted for culture.

This study showed that Gram negative organisms were resistant to co-trimoxazole and ampicillin which are some of the cheaper and more readily available antibiotics in Zimbabwe.

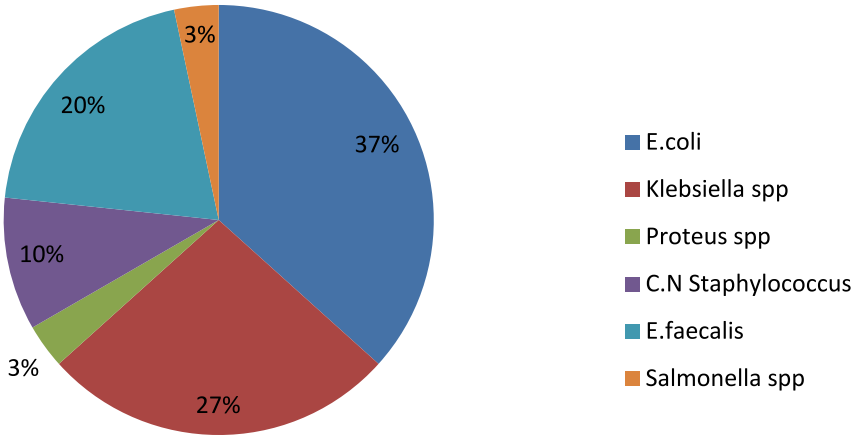

Figure 2. Pie chart showing causative organisms in patients who developed symptomatic UTI.

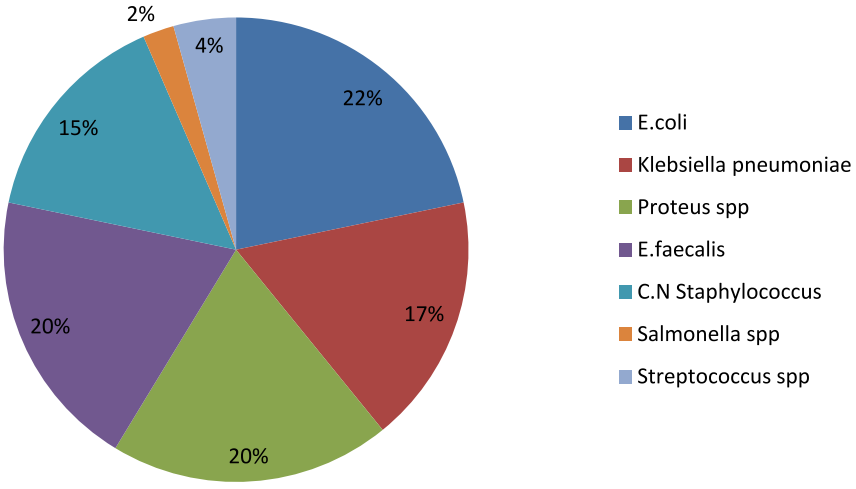

Figure 3. Pie chart showing frequency of bacterial isolates in participants with asymptomatic bacteriuria.

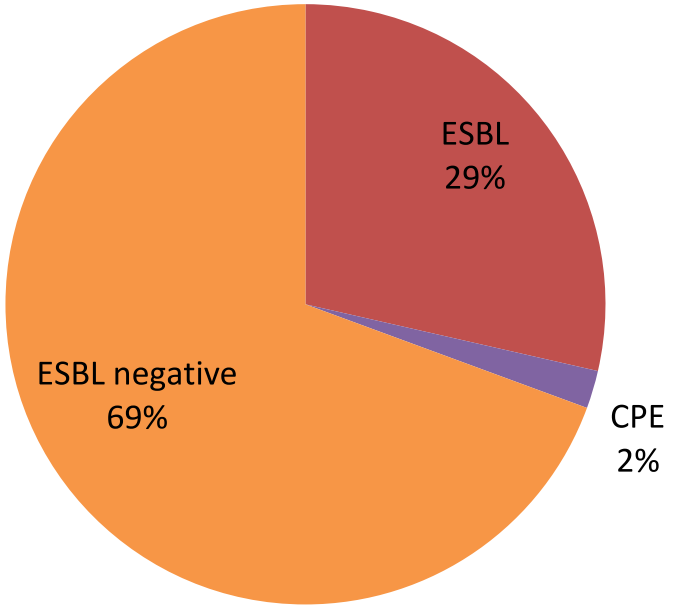

Figure 4. Pie chart showing resistance pattern of cultured Gram negative organisms.

20—25% of Gram negative organisms were resistant to fluoroquinolones, cephalosporins and amoxicillin/clavulanic acid. More than 90% of Gram negative organisms were susceptible to aminoglycocides, carbapenems and fosfomycin, hence they might be the antibiotics of choice in cases of UTI not responding to first line antibiotics.

About a third (29%) of Gram-negative isolates were ESBL-producing organisms. This is consistent with other studies which estimated the prevalence of ESBL producing Enterobacteriacae in Zimbabwe to be between 20 and 40 %. [33—35] Proteus species showed increased levels of resistance with half of the isolated Proteus species being ESBL positive and one [1] isolate being resistant to carbapenems (a CPE). A third of E.*coli* isolates and 18% of Klebsiella species isolates were ESBL producing organisms. This observation is quite alarming and it highlights the need for policy makers and infection control teams to formulate strict infection prevention and control measures as well as antibiotic stewardship policies in our institution and the country at large.

From the findings of this study certain recommendations can be made. Since UTI is a common occurrence in acute stroke care, there is a need to establish effective and robust infection control measures such as hand hygiene and good catheter care

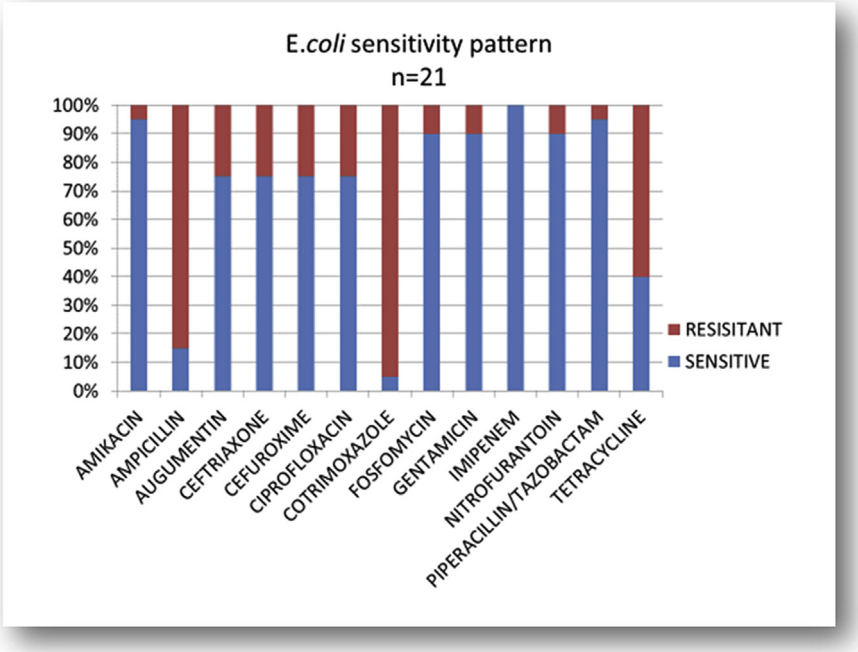

Figure 5. Graph showing antibiotic susceptibility pattern of *Escherichia coli*.

in the stroke units to curb the high frequency of hospital acquired infections. There is also a need to reduce the rate of catheterisation in stroke patients by using alternative methods of urine collection in very sick patients.

We recommend strict monitoring for UTI occurrence and early management of infections in admitted stroke patients, especially those with severe stroke so as to improve stroke outcome. Most importantly we recommend establishment of antibiotic stewardship programs to give guidance on antibiotic use so as to curb the increase of antibiotic resistant organisms.

Our study had a number of limitations. Firstly, the duration of follow up in our study was short, with a median hospital stay

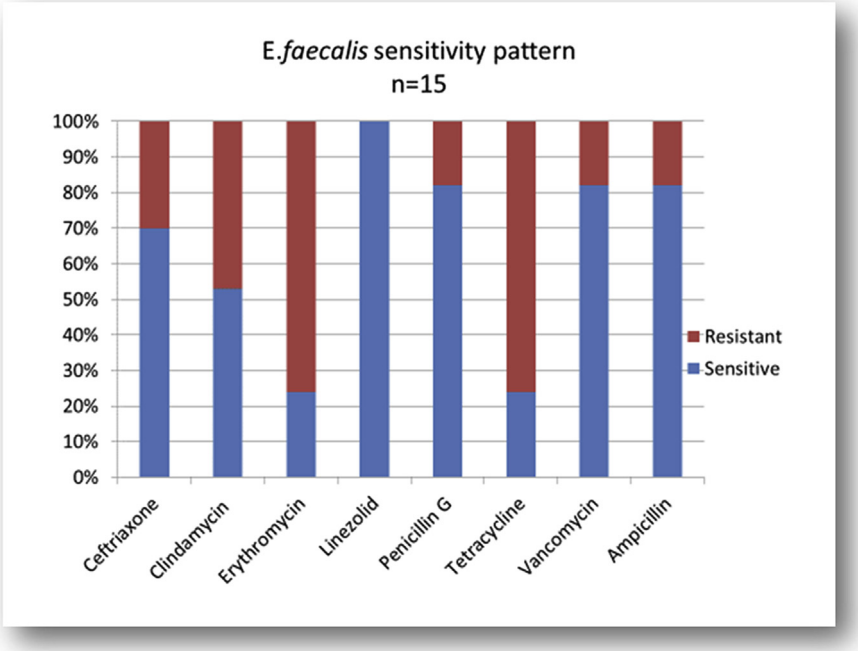

Figure 6. Graph showing antibiotic susceptibility pattern of *Enterococcus faecalis*.

Table IV
Stroke outcome (mRS) in study participants and their corresponding UTI diagnosis

mRS Score	*UTI Diagnosis*			
	Symptomatic UTI	Asymptomatic bacteriuria	No bacteriuria	Total
0	0 (0)	0 (0)	0 (0)	0 (0)
1	0 (0)	2 (1.4%)	2 (1.4%)	4 (2.7%)
2	0 (0)	7 (4.8%)	9 (6.2%)	16 (11%)
3	2 (1.4%)	17 (11.7%)	31 (21.4%)	50 (34.5%)
4	14 (9.7%)	18 (12.4%)	26 (17.9%)	58 (40%)
5	9 (6.2%)	1 (0.7%)	4 (2.7%)	14 (9.7%)
6	3 (2.1%)	0 (0%)	0 (0)	3 (2.1%)
Total	**28 (19.3%)**	**45 (31%)**	**72 (49.7%)**	**145 (100%)**

of 5 days (IQR 4–6 days) which might be too short a period to follow up patients for UTI occurrence. Again, the study lacked statistical power to assess effect of UTI occurrence on stroke outcome. Additionally, our laboratory did not have appropriate clinical and laboratory standards institute minimum inhibitory concentration breakpoints to effectively determine antibiotic susceptibility for certain antibiotics such as vancomycin and the fluoroquinolones.

Conclusions

UTI is a common occurrence in the acute phase post stroke with stroke severity being the main independent risk factor. Multi-drug resistant bacteria are on the rise with increased resistance to the cheaper and more readily available antibiotics. These observations highlight the need for robust infection prevention and control strategies to curb this common post-stroke complication.

Conflict of interest statement

None.

Credit author statement

Nickson Mukapa: Conceptualisation, Methodology, Software, Writing original draft.
Andrew Mataruse: Methodology, Software, Formal analysis.
Gift Ngwende: Writing- review & editing, Supervision.
Valerie Robertson: Investigations, Resources, Reviewing and editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.infpip.2022.100210

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