Article

Antimicrobial resistance patterns of urinary tract infection organisms isolated from pregnant women's urinary samples at lancet clinical laboratories in Zimbabwe, 2021

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ABSTRACT

Worldwide, bacterial infections are a main cause of morbidity and mortality, mainly in low-income countries. The world emergence of antimicrobial resistance negatively impact the management of infectious diseases. Nationwide, there is an increasing concern over antimicrobial resistance (AMR) recently evaluated to contribute for more than 700,000 deaths per year across the globe. The key objective of this present study is to characterise the antimicrobial resistance patterns of urinary tract organisms isolated from pregnant women's urinary samples analysed at Lancet Clinical Laboratories in Zimbabwe from January to December 2021. This was a laboratory based, cross sectional study conducted among pregnant women's samples analysed at the laboratory. Microbiology results logbook and patients' clinical data were used to evaluate basic descriptive statistics (proportions and mean) of participants engaged in this study. We describe the characteristics of variables of respondents where categorical variables were portrayed in the form of numbers and percentages in table, figures format. The prevalence of UTI was 60% with the main isolated bacteria being Escherichia coli (28.10%), Staphylococcus aureus (9.18%) and Kleibseilla pneumoniae (10.27%). There was association between gestational ages with UTI. The prevalence of AMR was 54%. The highest resistant drugs being Ampicillin (60%), Vancomycin (45%) and Penicillin (40%), the least resistant were chloramphenicol (15%), ciprofloxacin (23%) and nitrofurantoin (25%). The prevalence of AMR was high with regards to AMR prevalence rates in a study conducted in Zimbabwe Bulawayo. This is mainly due to the misuse of drugs therefore re-enforcement of prescription-only policies is crucial.

I. INTRODUCTION

There are several etiologic agents (fungi, protozoa, bacteria and viruses) that can initiate UTIs generally in pregnant women. Escherichia Coli as main pathogen contribute for 75%-90% of UTI isolates followed by Staphylococcus saprophyticus and aureus, Klebsiella Pneumoniae, enterobacter species, coagulase negative staphylococci (CNS), and Proteus mirabilis. Age, sex, catheterization, and hospitalization leads to variation of the relative frequency of the pathogens1. Resistance to Antimicrobial can provide a clinical difficulty in treating (UTI) in pregnant women. Pregnant women are highly vulnerable to urinary tract and therapeutically is challenging as the risk of dangerous complications is highly significant to both the mother and her child. Previous report revealed that 20% of women will end up having UTI and pregnant women showed four times higher rate of developing UTI compared to non-pregnant women (Prestinaci et al, 2015). There is an increase in antimicrobial resistance among causative agents of UTI in pregnant women (Belete e t al, 2020). The aim of the study is to characterise the (AMR) patterns of urinary tract organisms isolated from pregnant women's urinary samples analysed at Lancet Clinical Laboratories in Zimbabwe in 2021.

Antimicrobial agents having safety in pregnancy are nitrofurantoin, β lactam antibiotics including, penicillin and cephalosporin and fosfomycin trometamol. However, the emergence of antimicrobial resistance particularly the Extended–Spectrum Beta–Lactamases (ESBL) production among bacterial uropathogens is increasing and limits the choice of antimicrobials and becoming principal cause of treatment failure. ESBL production hydrolyses the β-lactam ring of antimicrobials, which provide bacterial resistance to regularly prescribed antibiotics including penicillin, first second and third –generation cephalosporin, aztreonams. AMR includes resistance to all antimicrobial agents. AMR accounts for 700,000 deaths per year internationally AMR will cost the world around 10 million lives and approximately $100 trillion per year by 2050 if serious actions are not taken to stop its alarming increases4. Africa and Asia were identified as continents without established AMR surveillance systems (WHO 2014). UTIs are widely found diseases in developing countries, with an approximate annual global incidence of about 250 million1.Without treatment UTI in pregnancy both asymptomatic or symptomatic corroborate with a 50% rise in the risk of low birth weight and a high risk of premature delivery, renal scarring, pre-eclampsia, hypertension, anaemia, renal failure and postpartum endometritis.

Pregnancy associated with untreated UTI could lead to maternal-foetal complications leading to significant rise in perinatal morbidity and mortality (Belete e t al, 2020). Developing countries like Zimbabwe have greater burden of infectious diseases (Foreman et al, 2018). Sad to relate, emerging antimicrobial resistance in bacteria threatens to undermine the management and curing of bacterial infections. In Zimbabwe, similarly to several countries, there is accumulating evidence of antimicrobial resistance in several UTI pathogens and researchers like J. Mbanga, and N. Zakazaka, have ventured into studying this peril to try and combat it early before it becomes a total disaster. Lancet Clinical Laboratories in Zimbabwe, one of the largest group of laboratories in Zimbabwe and Broadly in Africa a significant increase in detection multi-drug resistant pathogens, resistant to the first, second- and third-line antimicrobial agents was documented, which has left very narrow alternative for antimicrobial therapy for infectious disorders. Despite the huge number of antimicrobial agents available, UTI infections still is a major threaten to pregnant women in Zimbabwe. In a report assessing the prevalence of asymptomatic bacteriuria and drug sensitivities of the common causative organisms in antenatal women at Harare and Mbuya Nehanda hospital. indicated that the prevalence of asymptomatic bacteriuria is antenatal women was 23% and the main causative agents were E. coli, Streptococci, staphylococci and Klebsiella which are also the causative agents for UTI (Zakazaka, 2017). Informal evidence is showing AMR cases among UTI infected pregnant women in Zimbabwe particularly Harare submitting urinary samples to Lancet Laboratory but not so many studies have been carried out to characterise its patterns. Despite others

investigations on antimicrobial were conducted, the matter has received less attention other than few comments by stakeholder with no evidence empirically.

II. METHODS

Study Design

The study used a retrospective cross-sectional research design based on quantitative approach where secondary data information were gathered on the whole study population at a single point of time.

Study Setting

The investigation was carried out at the Lancet Clinical Laboratories Mutare. The laboratory was chosen because it serves as a reference centre therefore having a huge number of in and out patients and reflecting patients from big geographic areas in Manicaland province Zimbabwe. Secondary's data for patients were collected in year 2021.

Study Population

The study was centred on all pregnant women's urinary samples analysed at Lancet Clinical Laboratories in 2021. The results that were obtained in this study were applicable to this study population.

Study Participants

All pregnant women, who submitted urinary samples to Lancet Clinical Laboratories, during 2021 January to 2021 December were included. Female patients who are not pregnant and male patients submitting samples at Lancet Laboratory from January 2021 to December 2021 were excluded

Sample Size

The sample size was derived from the target population. The sampling was conducted using random sampling for participants.The size of the sample was calculated using the single size population formula below8, relaying on 95% confidence interval in addition from previous report 14% estimated prevalence rate of antimicrobial resistance was considered and our population being infinite. Formula: N= [Z2P (1-P)]/d2 Where: N=the needed sample size Z= the critical value associated with the level of confidence/significance (1.96 for 95%) P= the estimated prevalence (0.14) D =degree of precision chosen for the study (0.05) N=185

Measurement method

The data collection method used in study was the observational method. This method was applied during reviewing of the microbiology results in the original laboratory data base. We looked for all pregnant women urine culture results where UTI was suspected and compiled a record of pregnant women UTI negative results and pregnant women with UTI positive results, the isolated organisms from the UTI, their prevalence, susceptibility tests results and any antimicrobial resistance characteristics.

Data Analysis and organization of data

The data for this research is presented in form of line and bar graphs and tables through the application Graph pad 6 to illustrate the data statistics and the key findings were analysed and

interpreted descriptively. The results from sample cultures were used to characterize the type of microbial organisms' growth, determine the prevalence of UTI and to investigate antimicrobial susceptibility test. Proportions and mean values of study subjects were used to characterise the characteristics of the variables of the enrolled respondents.

Ethics Considerations

The ethical clearance for the study was taken from the Institutional Ethics committee which assisted in obtaining the clearance from for collecting secondary data

III. RESULT

1. Demographic, socio-economic, and clinical factors of study participants

In this present investigation a total of 185 women being pregnant with urinary tract infection were engaged. As indicated in Table 1, the majority of the study participants were in the age range less than 25 and 30-35 years (32% and 22%) respectively. using the residential address on the patients request forms, majority of these women originate from low-cost areas and they account for 51%. Higher proportion of the urinary tract infected women 54% were known to have a history of previous urinary tract infection and in their majority 49% were found to be in their second trimester based to the clinical history.

2. Microorganisms positivity rate

Urinary Prevalence of UTI in pregnant women who submitted samples at Lancet clinical laboratories in this present report was 60% (111 /185), the listed below bacterial uropathogens were isolated and identified: E. coli 52 (28.10%), S. aureus 17 (9.18%), Klebsiella pneumonia, 19(10.27%), enterobacter spp 11 (5, 94%), Proteus spp 5 (2.70%), pseudomonas spp (1.65%) and the Streptococcus species, 4(2.16%) isolates. Out of 111 cases with a significant bacterial growth, 60 (54%) was resistant to one or more drugs used in the laboratory and 51 (46%) had susceptibility to all the drugs. (Figure1)
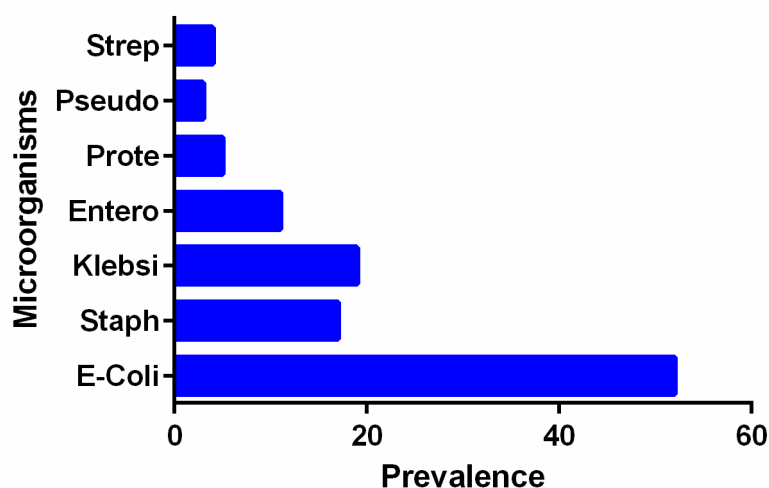

Figure 1: Prevalence of AMR by microorganism

3. Urinary tract isolated microorganisms' antibiotic resistance distribution

In descending manner the prevalence of AMR was as listed as follow, ampicillin 60%, vancomycin 45%, penicillin 40%, co-trimoxazole 36%, erythromycin 35%, gentamicin10 30%, nitrofurantoin 25%, ciprofloxacin 23%, cefotaxime 23% and chloramphenicol 15% (figure 2).
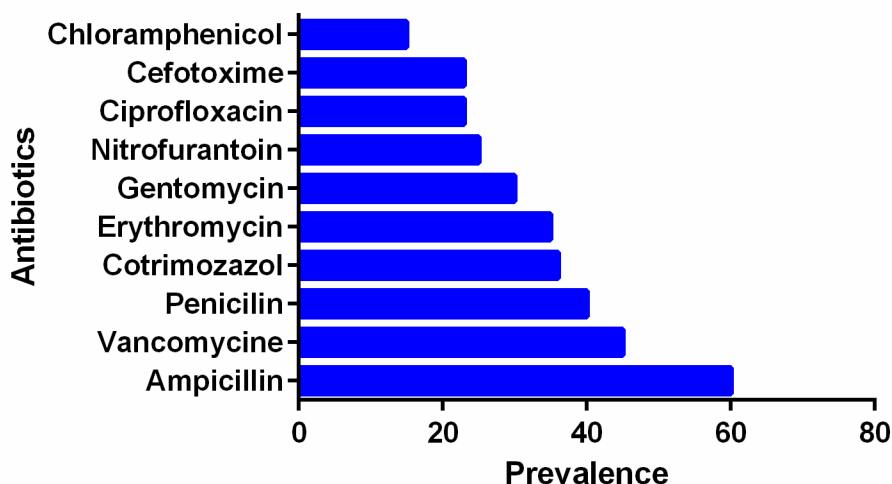
Figure 2: Prevalence of AMR stratified by antibiotic

4. Characteristic of antimicrobial resistance patterns of isolated urinary tract organisms

The characterisation of the patterns by differentiating between gram-positive and gram-negative antimicrobial resistance characteristics of UTI in pregnant women was evaluated. In the gram-positive bacteria cases, a total case of 17 (9.18%) Staphylococcus aureus were isolated, highest resistance was obtained by Ciprofloxacin, then followed by Chloramphenicol and the least resistance to Nitrofurantoin. The total number of Streptococci isolated was 4(2.16%). There was no application of Cefotaxime, Gentamicin, Penicillin and Ampicillin for strep Spp. Gram-negative bacteria isolates were more prevalent than gram-positive bacteria isolates. In the group of gram-negative isolates, the drugs most resistant to E. coli were; ampicillin, and the least resistant was nitrofurantoin. The drugs most resistant to Klebsiella were; ciprofloxacin and the least resistant chloramphenicol 0(0%). Most resistant to Enterobacter spp were; least resistant was ciprofloxacin 0(0%). Drugs in Gram positives category namely penicillin, cefotaxime, and chloramphenicol revealed 80-99% sensitivity. While for the gram-negative isolates drugs namely chloramphenicol demonstrated highest sensitivity (Figure2)

Table1: Demographic and clinical characteristics of pregnant women with UTI (n=185)

Characteristics	Patient (n)	Percentage (%)
Age in years		
<25	59	32
25-30	30	16
35-40	20	11
>40	35	19
Residence		
High cost	39	21
Median cost	51	28
Low cost	95	51
History of UTI		
Yes	100	54
No	85	46
Pregnancy trimester		
First	40	22
Second	91	49
Third	54	29

IV. DISCUSSION

The present investigation revealed a UTI prevalence of 60%, additionally the major etiologic agents being E. coli, Klebsiella and Staphylococcus aureus with their corresponding proportions of 52, 19 and 17 isolates respectively. These findings aligned with studies carried out in Ethiopia, however E. coli and Klebsiella are the major isolated bacteria (Kibret and Abera, 2014). The prevalence of AMR was discovery to be 54% with ampicillin having the biggest resistance as well as, vancomycin and penicillin. The weakest resistant was demonstrated by ciprofloxacin, cefotaxime and chloramphenicol. (UTIs) are the dominantly widely spreading infections observed in health care settings and the second widely infections found in the population generally (Valiquette, 2001). In this total population of the present investigation of 185 pregnant women, of which 111 we found them having positivity for UTI therefore stipulating that UTI had a prevalence of sixty percent (60%). These present findings had similarity with investigations carried out in Ebonyi state, Nigeria where the prevalence of 55% was documented, and a study conducted in India, which had a prevalence of 61%. These phenomena could be attributed to the similarity in methods of investigations. The low socio-economic status plays a role in vulnerability to this burden and accessibility to health care facilities could contribute for the high prevalence rate observed in report. The prevalence of bacterial UTI was age dependent and highest among the age interval (under 25) and (30-35) which represented a percentage of 32% and 22% respectively, this agreed with a study done in India (Al-Naqshbandi et al, 2019).

Furthermore, those finding are supported by the fact that women in these age groups are active sexually while symptomatic UTI displayed a huge prevalence due to the stated fact, in addition reproduction is related to UTI. Prevalence of UTI with regards to gestational trimester was known to be higher in the 1st (22%) and 2nd (49%) trimesters as compared to the third trimester (29%) this corroborate with investigation conducted in Uganda and India which indicated higher prevalence related to the 2nd and 3rd trimesters with the 1st trimester having the least association and disagree with investigation conducted in India where they discover UTI to be more prevalent in the 1st and 2nd trimesters (Sekikubo, 2017 ; Al-Naqshbandi et al, 2019 ; Lodise et al, 2022). This discrepancy may be accountable to either the vesico-ureteral reflux or alteration in urine stasis or a fall in urinary oestrogens and progesterone across the 3 trimesters of pregnancy. The prevalence of antimicrobial resistance in this report was 54%, Additionally the prevalence of the resistance of the different drugs was assessed, which are in decreasing order as listed below; ampicillin (60%), vancomycin (45%), penicillin (40%), co-trimoxazole (36%), erythromycin (35%), gentamicin (30%), nitrofurantoin (25%), ciprofloxacin (23%), cefotaxime (23%) and chloramphenicol (15%). These results coincide with other studies, such as in Uganda (Sekikubo, 2017) where the resistance levels of ampicillin, ciprofloxacin and nitrofurantoin have similarity in findings. However, differences were documented with other reports namely in study conducted in Ethiopia (Gizachew Z et al, 2019), which revealed a significant rising in resistance rates of ciprofloxacin and chloramphenicol. Resistance could be credited to easy accessibility to antibiotics over the counter in developing countries including Zimbabwe. Furthermore, the initial applications of antibiotics prior to the laboratories results of antimicrobial susceptibility can account to the rising resistance.

The present report implicated nitrofurantoin of having more susceptible to uropathogens than most prescribed drugs, this is of key value due to debates in phasing it out. There is need to resurface old drugs as they would be more effective, some of these drugs being nitrofurantoin and Fosfomycin this is specifically for resistant uropathogens[16]. There was a UTI prevalence of 60% which is still higher than most studies undertaken, this is implying the degree of menace urinary tract infections are in Zimbabwe. This raised concern due to adverse effects of untreated UTI on mother and foetus. The highest causative agent of urinary tract infections documented was E. coli. The prevalence of antimicrobial resistance was 54% with ampicillin, vancomycin

and penicillin being the most resistant and chloramphenicol, ciprofloxacin and nitrofurantoin being the least resistant

V. CONCLUSION

The prevalence of AMR was high with regards to AMR prevalence rates in a study conducted in Zimbabwe Bulawayo. This is mainly due to the misuse of drugs therefore re-enforcement of prescription-only policies is crucial.

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