

Research



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Urinary tract infections and associated factors in HIV infected pregnant women at a tertiary hospital in Lusaka, Zambia

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Abstract

Introduction: Urinary Tract Infections (UTIs) remain among significant causes of morbidity and mortality in pregnant women in sub-Saharan Africa. Zambia shares this burden disproportionately compared to other countries and it is unknown to what extent HIV affects UTIs. This study investigated the prevalence of UTIs and associated factors among HIV infected pregnant women attending antenatal care at a tertiary hospital in Zambia. **Methods:** we conducted a retrospective review of medical records of Zambian HIV infected pregnant women who attended antenatal care at the women and newborn hospital between 1st January 2017 and 31st December 2017. We used a structured data extraction tool to extract data from the patient medical records using simple random sampling without replacement. Medical records of patients with known, diabetes and renal transplant were excluded. A logistic regression model was used to establish factors associated with UTIs. **Results:** we reviewed 380 medical records of pregnant women with a median age of 29 years (IQR: 22, 34). UTIs prevalence was 16.5%, (95% CI: 13.0, 20.7). Women with UTIs had lower gestational age than those without UTI (difference 3 weeks, $P < 0.0001$). Gestational age was independently associated with UTI (AOR: 0.96, 95% CI: 0.91-0.99). **Conclusion:** the burden of UTIs in this population was high compared to global estimates and gestational age predicts UTIs. Public health interventions should be directed at promoting an early screening of UTIs during pregnancy, preferably to educate HIV positive women to book for antenatal visit early so that screening could commence.

Introduction

Urinary Tract Infections (UTIs) are responsible for increased pregnancy-related morbidities in HIV infected women [1-3]. Complications of UTIs in pregnancy have been well studied in developed countries, and high rates of maternal and perinatal morbidities have been reported [4,5]. The maternal

and perinatal morbidities related to UTIs vary for different settings, though little has been done in sub-Saharan Africa [6].

A recent study in Tanzania [1] reported a rising trend of UTIs, from approximately 15% in 2009 to 21%, in 2017 with a preponderance of UTIs in the vulnerable HIV infected pregnant women. Other studies have reported that women with HIV infection have a threefold-greater risk of experiencing UTIs than HIV-negative women [7,8]. The reduced immune system associated with HIV infection may account for this increase in the observed UTIs.

Several studies have documented various predictors of UTIs [9-11]. Among the factors reported to be associated with UTIs are, single marital status, CD4 count below 200 cells/ μL and the presence of symptoms predicted UTIs [12,13]. The reported association between low CD4+ counts with UTI among HIV-infected pregnant women can be explained by the severity of immunosuppression and the increased likelihood for opportunistic conditions and/infections, including UTI, preeclampsia, oxidative stress [14-16]. Contrary, other studies have shown no association between UTI and marital status [17,18]. The lack of association with marital status can be attributable to the differences in cultural practice, hygiene and norms on sex issues in different areas [19].

UTIs are common among HIV-infected pregnant women and if left untreated, can lead to poor maternal and foetal outcomes [19-21]. Additionally, 20% to 30% of affected women may develop acute pyelonephritis [22,23] which may lead to septicaemia, anaemia, premature rupture of membranes, renal dysfunction, transient preterm labour, intrauterine growth restriction (IUGR), low birth weight and preeclampsia [24,25]. Additionally, asymptomatic bacteriuria (ASB) places the women at risk of preterm birth and delivery of low birth weight infants [26]. Despite the evidence of high prevalence rates of UTIs in HIV infected population, in other settings, there is a paucity of data on associated factors in the Zambian HIV

infected pregnant women population. This study investigated the prevalence of UTIs and associated factors in HIV infected pregnant women at a tertiary hospital in Lusaka, Zambia.

Methods

Study design and setting: we conducted a retrospective review of medical records of Zambian HIV infected pregnant women attending antenatal care between 1st January 2017 and 31st December 2017. This study was conducted at the Women and Newborn Teaching Hospital of the University Teaching Hospitals in Lusaka urban, Zambia. The hospital is the largest referral centre in Zambia for obstetrics conditions. On average, the hospital attends to 28,800 pregnant women each year and about 18,000 births are recorded at this hospital annually. It receives referrals from over 25 clinics from the surrounding areas of Lusaka and the rest of the country.

Sample size: the study was powered to detect a prevalence of 44% [27] at 80% power, a significance level of 5% and a 95% confidence level. Contingency to account for medical records with incomplete data was set at 10%, giving a minimum of 90% of the information in the participants' medical records, which allowed for multiple imputations of missing data at the analysis level. The minimum required number of records was calculated at 380.

Data collection: the case records were obtained from the registry department and information on demographic and clinical characteristics of HIV infected pregnant women was extracted. Case definition of UTI: a UTI case was defined as a positive urine culture. For this data, a midstream urine sample of women admitted with symptoms suggestive of UTI was collected for culture. A laboratory technician performed a routine urine culture and confirmed positive results. We excluded women with a urine culture-negative (no growth), missing of documented urine culture test, multiple pregnancies, underlying renal disease and files with incomplete data. We used a simple

random (computer-generated random numbers) sampling technique to select records without replacement. Once a medical record was selected, if the participant was ineligible, the record was not replaced.

Statistical methods: for descriptive statistics, the median (interquartile range [IQR]) for continuous values (i.e. age of the mother [years], gestational age and number of antenatal visits) was calculated after testing for the assumption of normality using Shapiro-Wilk W-test and QQ-plots graphically (result not shown). For the comparison of baseline characteristics, we used the ^aPearson chi-square test and ^bFisher's exact test for categorical variables.

Investigator's best model selection approach was used to ascertain a suitable multiple regression model to predict the presence of UTI from all variables known about the individual. We then used UTI case status as an outcome and selected variables as exposures to carry out bivariate analysis and subsequently included factors with p-value below 0.20 into an unconditional logistic regression model, employing the forward selection approach and level of significance of 0.05. The likelihood ratio test was used to drop out variables one by one from the model until we reached the priori set of variables (based on the investigator's experience in Zambian clinical setting). A predicted probability distribution was done to illustrate the chance of UTIs given the gestational age of the pregnancy. To avoid inflating the type-I error rate and loss of power, continuous predictor variables (e.g. gestational age) were not categorised in the regression model. All statistical tests were done at the significance level of alpha 0.05 and 95% confidence interval. Data were analysed using Stata/IC version 15 (Stata Corporation, Texas, TX, USA).

Study variables

Independent variables: clinical and socio-demographic characteristics, age, marital status, number of antenatal visits, education level,

gestational age and occupation. Dependent variable: UTI among pregnant women which was a binary qualitative variable and classified at two levels as presence versus absence.

Ethical statement: ethical clearance was granted by ERES converge ethics committee (approval number 2018-Feb-043) and additional permission was obtained from the management of the Women and Newborn Hospital. The confidentiality of all records was safeguarded to the extent ethically possible and all laboratory, reports, study data and data extraction forms are coded by numbers only. Databases are password protected.

Results

Clinical and demographic characteristics of participants: we reviewed 380 medical records of pregnant women. With the Shapiro-Wilk normality test and Q-Q plots confirming data were not normally distributed, we determined that the median maternal age was 29 years (IQR: 22, 34) and median gestational age 36 weeks (IQR: 30.5, 39). Additionally, the median haemoglobin levels and parity of the participants were 11g/dl (IQR; 9.1, 12) and two children (IQR; 1, 3), respectively. The majority of them attended antenatal clinic at least three times 262 (69%), 303 (79.7%) were married, 76 (20%) were single and 1 (0.3%) was a widow. Furthermore, 159 (41.8%) had attained tertiary level education, 147 (38.7) secondary and 74 (19.5%) managed a primary level of education. The majority of the women 170 (44.7%) were in informal employment, 111 (29.2%) were unemployed and 99 (26.1%) were in formal employment (Table 1).

Prevalence of UTIs: of the 380 study participants, 63 had UTIs, translating to a prevalence of 16.5% (95% CI: 13.0, 20.7). From the total number of subjects in each category who were diagnosed with UTIs 25/159 (15.7%) attained tertiary level of education, 24/147 (16.3%) secondary level and 14/76 (18.4%) attained primary level education. Additionally, 11/99 (11.1%) were in formal employment, 31/170 (18.22%) were in the informal

sector and 21/111 (18.9%) were unemployed, gestational age was less than 36 weeks 48/211 (22.7%), had less than two children 42/240 (17.5%), had haemoglobin levels of less than 11 g/dl 36/194 (18.6%) and had visited antenatal clinic less than three times 46/262 (17.6%). There was a significant association between gestational age and UTIs ($P < 0.001$). On the contrary, there was no association between maternal age, parity, occupation, marital status and education (Table 2).

Factors associated with UTIs at Women and New Born Hospital: regression analysis to predict the presence of UTI from all variables known about the participant was undertaken. Table 3 shows the results of the bivariate and multivariable analysis to assess factors associated with UTIs.

Bivariate analysis: single women compared to married (OR 1.61, 95% CI; 0.86, 3.00), women in informal (OR 1.78, 95% CI; 0.85, 3.75) and unemployed (OR 1.87, 95% CI; 0.85, 4.10) compared to those in formal employment had higher odds of being diagnosed with UTI. An increase in the number of antenatal visits (OR 0.88, 95% CI; 0.69, 1.10) and age of a woman (OR 0.98, 95% CI; 0.94, 1.20) reduced the odds of having UTI though random chance finding could not be ruled out. On the other hand, a unit increase in gestation reduced the odds of having a UTI (OR 0.95, 95% CI; 0.91, 0.99).

Multivariable analysis: a unit increase in gestational age was independently associated with reduced odds of having a UTI (AOR 0.96, 95% CI; 0.91, 0.99). This reduction could be as high as 0.99 to as low as 0.91, with probability 0.95 from the population where this sample came from. Additionally, being single (AOR 1.46, 95% CI; 0.66, 3.22) and occupation (i.e. informal (AOR 1.76, 95% CI; 0.84, 3.75), unemployed (AOR 1.71, 95% CI; 0.77, 3.81) compared to formal) both increased the chance of UTIs though this was not significant. While education (i.e. secondary (AOR 0.79, 95% CI; 0.37, 1.64) or tertiary (AOR 0.75, 95% CI; 0.36, 1.59) compared to primary) and a unit increase in the number of antenatal visits (AOR 0.95, 95% CI; 0.73,

1.18) predicted less chance of urinary tract infections controlling for all variables in the model though random chance finding could not be ruled out.

Predicted chance of UTI given gestational age of a woman: the predicted chance of UTIs given the gestational age of a woman is shown in Figure 1. Inferring from the figure, an increase in the gestational age of a woman reduced the chance of having UTIs.

Discussion

This study assessed the prevalence and associated factors of UTIs among HIV infected pregnant women at Women and Newborn Hospital in Lusaka, Zambia. Our findings revealed a UTI prevalence of 16.5% in the period between 1st January 2017 and 31st December 2017 in this setting. An increase in gestational age predicted less chance of UTIs in this population. There was no significant association with maternal age, parity, occupation, marital status and education. This prevalence was relatively higher than the reported range of 1.9% to 10% in a recent systematic review and meta-analysis of the prevalence of asymptomatic bacteriuria [28]. However, analysis of regional estimates suggests higher trends that are comparable to our findings; 14.2% in Zimbabwe, 28% in Tanzania and 17.31% in Nigeria [2,29,30]. We only found a lower reported prevalence in South Africa of 5% [31]. This could suggest a higher disease burden in our settings or differences in the approach of these studies.

Another plausible explanation could be due to different admission criteria in different countries and hospitals and the fact that most cases during antenatal visits are managed on an outpatient basis. Besides, the populations studied differ. For example, the study by Kaduma [2] was a matched case-control study looking at the risk of UTIs in preeclampsia and non-preeclamptic controls, the controls alone had a prevalence of 16.8%. The other possible reason could be that the diagnosis criteria and infrastructure in the region is different from

country to country. For instance, in the findings of a study done in South Africa, they reported that the cost of the standard urinary culture was a limiting factor for the routine urine screening [31]. It is for this reason that other screening methods have been proposed, which include urine dipsticks, gram staining, bioluminescence assays, microscopic urinalysis and dipslide urine cultures.

Omoriegie and Eghafona (2016), in their study on UTIs among asymptomatic HIV patients in Benin-Nigeria, reported a significantly higher prevalence among HIV patients compared to non-HIV infected subjects (27.45% versus 17.31%, respectively, $P=0.038$) [30]. In the present study, we, however, did not review medical records for HIV-negative pregnant women and hence were not able to compare the differences. This is potentially for future work. The other aspect to the present findings is that the women were treated in similar fashion (tenofovir 300mg, lamivudine 300mg and efavirenz 400mg) which is currently the first line of treatment for HIV infection according to the Zambian national guidelines [32] and data was not available on the stage of the disease. This may have influenced the prevalence as persons with advanced stages of HIV infection are more prone to develop UTIs than those with well-controlled or undetectable viral load counts [30]. Other studies have found that HIV status does not play a role in the severity of the UTI [31,33]. Reasons could possibly be that the patients were on different antiretroviral drugs, which help to reconstitute the immune system and the severity of the HIV infection was not reported in their findings. Moreover, since the present study excluded incomplete medical records, it can be argued that the prevalence of UTI among HIV-infected pregnant women may be higher in this setting.

The findings further revealed that an increase in gestational age predicted less chance of UTIs controlling for other variables in the model. This is particularly important when planning public health interventional studies that need the targeted population at risk for UTIs. In a review based on critical assessment of literature by Schnnar J and

Small F, 2008, of the pregnant women screened between 12 and 16 weeks gestation, 80% were identified to have asymptomatic bacteriuria [34]. In the Zambian setting, a higher proportion of pregnant women book for antenatal care in the late second trimester [35], presenting a challenge for early diagnosis and management. Up to 30-40% of pregnant women with asymptomatic bacteriuria develop symptomatic UTI later in pregnancy if ASB is undetected and untreated compared to 1.8% non-bacteriuric controls [35,36]. This complication may lead to adverse pregnancy outcomes like preterm birth, the premature rupture of membranes and pyelonephritis [31]. Therefore, it is very important that screening is done at the booking visit [37].

Our findings bring out some important aspects with regard to gestational age. It is in the early weeks of pregnancy where the mothers are at increased risk for UTIs (Figure 1). Therefore increasing awareness to encourage early attendance for antenatal care services at the hospital can improve early diagnosis [34]. Most European and North American clinical practice guidelines recommend screening for ASB as a routine pregnancy test [38]. In the Zambian setting, just like in many other settings, screening related guidelines have not yet been implemented to optimise pregnancy outcomes through the use of evidence-based practice [29].

Limitations: the use of the retrospective design in research may affect the completeness and accuracy of data to be collected. Care was taken to only use records with at least 90% complete information. External validity-single site study and lacks generalisability to other populations.

Conclusion

The prevalence of UTIs among HIV-infected pregnant women at the Women and Newborn Hospital in Zambia is 16.5%. An increase in gestational age predicted less chance of UTIs in this population. Efforts to improve clinical outcomes of HIV-infected pregnant women should be directed at early screening for UTIs in this setting.

What is known about this topic

- *UTIs are a significant problem in pregnancy and if left untreated can lead to adverse pregnancy outcomes;*
- *It affects HIV infected pregnant women more commonly than the HIV negative;*
- *Sub-Saharan Africa shares this burden disproportionately when compared to other developed countries.*

What this study adds

- *The prevalence of UTIs at a tertiary public health institution in Zambia;*
- *Increase in gestational age predicts less chance of UTIs in this setting.*

Competing interests

The authors declare no conflict of interests.

Authors' contributions

Moses Mukosha: conceptualization, data curation, investigation, writing original draft preparation, writing review and editing; Lukundo Nambela: data collection, investigation, writing review and editing; Bellington Vwalika: supervision, review and editing; Chiluba Mwila: review and editing; Micheal Chigunta: review and editing; Aubrey Chichonyi Kalungia: review and editing, data curation; Mwansa Ketty Lubeya: review and editing. All the authors have read and agreed to the final manuscript.

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Tables and figure

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Table 2: prevalence of UTI and characteristics of study participants with UTI

Table 3: factors associated with UTI at women and new born hospital

Figure 1: the predicted probability of urinary tract infections given the gestational age of the pregnant woman

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Table 1: clinical and social demographic characteristics of selected participants at women and new-born hospital, 2017 (n=380)

Variable	Categories	Frequency (%)
Age (years)	Less than 29	184 (48.4)
	30 and above	196 (51.6)
Gestation age (weeks)	Less than 36	211 (55.5)
	37 and above	169 (44.5)
Parity	0-2	240 (63.2)
	Above 2	140 (36.8)
Haemoglobin levels g/dl	Below 11	194 (51.5)
	12 and above	183 (48.5)
Number of antenatal visits	Below 3	262 (69)
	4 and above	118 (31)
Marital status	Married	303 (79.7)
	Single	76 (20)
	Widow	1 (0.3)
Education	Primary	74 (19.5)
	Secondary	147 (38.7)
	Tertiary	159 (41.8)
Occupation	Formal	99 (26.1)
	Informal	170 (44.7)
	Unemployed	111 (29.2)

Table 2: prevalence of UTI and characteristics of study participants with UTI

Characteristic	Variable	No subject	No (%) UTI	95% CL1	P-value ²
Age (years)	Less than 29	184	33 (17.9)	12.7, 24.3	
	30 and above	196	30 (15.3)	10.6, 21.1	0.491a
Gestation age (weeks)	Less than 36	211	48 (22.7)	17.3, 29	
	37 and above	169	15 (8.9)	5.1, 14.2	<0.0001a
Parity	0-2	240	42 (17.5)	12.9, 22.9	
	Above 2	140	21 (15)	9.5, 22	0.525a
Haemoglobin levels g/dl	Below 11	194	36 (18.6)	13.3, 24.8	
	12 and above	183	27 (14.8)	10.0, 20.7	0.323a
Number of antenatal visits	Below 3	262	46 (17.6)	13.2, 22.7	
	4 and above	118	17 (14.4)	8.6, 22.1	0.445a
Marital status	Married	303	46 (15.2)	13.3, 19.7	
	Single	76	17 (22.4)	13.6, 33	0.305b
	Widow	1	0		
Education	Primary	76	14 (18.4)	10.5, 29	
	Secondary	147	24 (16.3)	10.7, 23.3	0.825a
	Tertiary	159	25 (15.7)	10.4, 22.3	
Occupation	Formal	99	11 (11.1)	5.7, 19	
	Informal	170	31 (18.2)	12.7, 24.9	0.223b
	Unemployed	111	21 (18.9)	12.1, 27.5	
Total		380	63 (16.5)	13.0, 20.7	

1 Confidence interval for proportion in percentages; 2 Univariate analysis; a Pearson chi-square test; b Fischer's exact test; UTI-urinary tract infection; 95% CL=95% confidence interval

Table 3: factors associated with UTI at women and new born hospital

Characteristic	UTI present (n=63) 16.5%	UTI absent (n=317) 83.5%	Crude OR (95% CL)	Adjusted OR (95% CL)
Age (years)	29 (IQR, 22-34)	30 (IQR, 25-35)	0.98 (0.94, 1.02)	0.99 (0.93, 1.05)
Gestational age (weeks)	33(IQR, 29-36)	36(IQR, 31-39)	0.95 (0.91, 0.99)	0.96 (0.91, 0.99)
Number of antenatal visits	3 (IQR, 2-4)	3(IQR, 2-4)	0.88 (0.69, 1.10)	0.95 (0.73, 1.18)
Marital status				
Married	46(73)	257 (81.1)	ref	
Single	17 (27)	59 (18.9)	1.61 (0.86, 3.00)	1.46 (0.66, 3.22)
Widow	0	1 (0.32)		
Education				
Primary	14 (22.2)	60 (18.9)	ref	ref
Secondary	24 (38.1)	123 (38.8)	0.84 (0.40, 1.73)	0.79 (0.37, 1.64)
Tertiary	25 (39.7)	134 (42.3)	0.80 (0.39, 1.65)	0.75 (0.36, 1.59)
Occupation				
Formal	11 (17.5)	88 (27.8)	re	ref
Informal	31 (49.2)	139 (43.9)	1.78 (0.85, 3.73)	1.76 (0.84, 3.75)
Unemployed	21 (33.3)	90 (28.4)	1.87 (0.85, 4.10)	1.71 (0.77, 3.81)

95% CL=95% confidence interval; OR=odds ratio; values are medians and frequencies (percentages); IQR=interquartile range

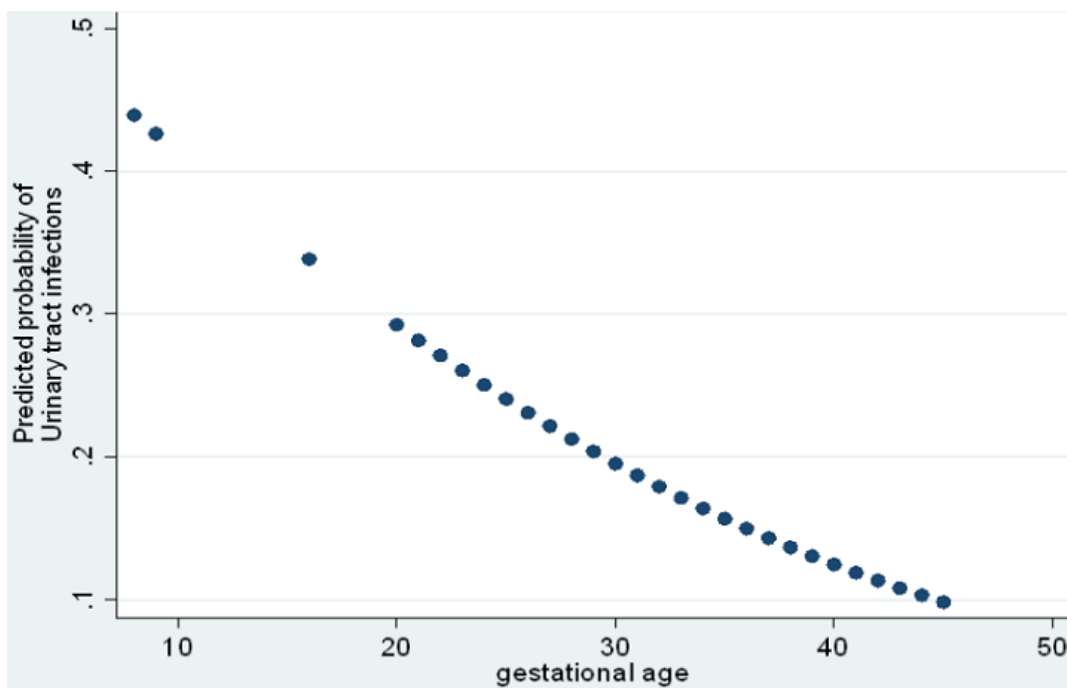


Figure 1: the predicted probability of urinary tract infections given the gestational age of the pregnant woman