

The prevalence and management strategies of gestational urinary tract infections (UTI) in Kisumu County, Kenya

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ABSTRACT

Background: Urinary tract infections (UTI) contribute to substantive proportions of adverse pregnancy outcomes. Current national statistics in Kenya show high maternal mortality (488/100,000) and neonatal mortality (24/1,000) rates. Kenya continues to report increasing prevalence and incidence rates of UTI associated with maternal and neonatal deaths. Kisumu County in western Kenya has a high maternal mortality rate of 495/100,000 with uncaptured maternal morbidity relative to the national average. However, information on the epidemiology of gestational UTI in the County, is limited. Semi-urban Chulaimbo and Nyahera Sub-County hospitals were used as model facilities to establish the burden of UTI during pregnancy and the specific clinical diagnosis and therapeutic management strategies.

Methods: Socio-demographic, laboratory and clinical history data was extracted from 416 pregnant women's maternal child health data sets from health records between February 2019 to February 2020 using pre-designed data collection forms. Descriptive analysis was used to summarize the study population's demographic characteristics. Chi-square test was used to establish proportionality. Qualitative data were thematically summarized. For all analyses, $P \leq 0.05$ was considered statistically significant.

Results: The study population had a mean of two (2) (± 1.14) ante-natal (ANC) visits; a mean mothers age of 23.92 (± 6) years old; a mean parity of 2 (± 2) and a mean haemoglobin level of 10.73 (± 1.8). About 56% (233/416) of the mothers attended the first ANC visit at varied gestational age. Only 1.4% (6/416) had a clinical history capturing UTI infection out of the total prevalence of 57.9% (241/416) diagnosed UTI positive by routine ANC profile deep stick urinalysis test. These clinical history data sets 1.4% (6/416) revealed a broad-spectrum therapeutic management of gestational bacterial infections using first line antibiotics.

Conclusions: Most UTI positive cases go without specific clinical diagnosis and management, posing a high risk of antibiotic drug resistance and development of specific bacterial allied gestational complications.

Key words: Urinary tract infections, pregnancy, clinical diagnosis, therapeutic management, western Kenya.

BACKGROUND

Urinary tract infection (UTI) is the most common bacterial infection during pregnancy and can manifest as symptomatic or asymptomatic causing high morbidity and mortality rates in low-and-middle-income countries (LMIC) (2,3). Uncomplicated UTI present with frequency, urgency, dysuria, or supra pubic pain in women with a normal genitourinary tract (4). Complicated UTI is associated with functional or structural abnormalities of the genitourinary tract, with the involvement of either the bladder or the kidneys (4–8). Asymptomatic UTI is a persistent, actively multiplying bacterial infection within the urinary tract without any symptoms of infection. Its prevalence depends on parity, race and socio-economic status. Untreated asymptomatic bacteria may lead to development of acute symptoms of infections during pregnancy with serious consequences in form of fetal and maternal morbidity. For example, the infection has been associated with maternal anaemia, acute pyelonephritis, preterm labour, septicaemia and even possible death of the mother. Asymptomatic UTI can also cause intra-uterine growth restrictions, prematurity, and low birth weight of the fetus and sometimes even fetal mortality (9).

Recent WHO statistics show that 810 women die annually due to preventable causes related to pregnancy and childbirth (2). Majority (94%) of these maternal deaths occur in developing countries following poor access to healthcare services (10,11). Despite the standard diagnosis and management of UTI in-line with Ministry of Health (MOH) recommendations, current national statistics in Kenya show 488/100,000 maternal and 24/1000 neonatal mortality rates (12,13). This depicts a huge disparity in health service provision as compared to developed countries with minimal maternal mortality rate reported at 7/100,000 in 2017 (2,14). In Kenya, UTI was reported at a prevalence of 27% in the general population and it still remains of great public health importance (15,16). Gestational UTI contribute to substantive proportions of adverse pregnancy outcomes manifesting as different maternal and neonatal morbidity

complications and deaths in Kenya (17,18). Regionally, North Eastern report the highest burden of maternal mortality rate (MMR) at 2,014/100,00 live births followed by Nyanza with 546/100,000, then, Eastern 400, Rift Valley 377, Coast 328, Western 319, Central 289, and Nairobi at 212/100,000 (2,19). These statistics vary in the different Counties within Kenya with Mandera having the highest reported MMR at 3,795, Wajir 1,687, Turkana 1,594, Marsabit 1,127, Isiolo 790, Siaya 691, Lamu 676, Migori 673, Garissa 646, Taita Taveta 603, Kisumu 597, Homa Bay 583 and Vihiga 531(12,20,21). A relative reduction in the burden of maternal mortality was realized following improved access to early screening and awareness, hence, in 2020, Kisumu County in western Kenya reported a maternal mortality rate of 495/100,000 still considerably high as compared to national statistics reported at 488/100,000 (22,23). The high burden of maternal mortality is directly attributed to haemorrhage (severe bleeding), obstetric labour, eclampsia, sepsis and ruptured uterus; and indirectly attributed to illness aggravated by pregnancy including HIV/AIDs, anaemia, cardiovascular cause and malaria (24,25). Previous findings have reported 21.5% prevalence of UTI in pregnant women in Nairobi (16), 11.9% in children aged 2 months in rural settings (26,27). Previous findings (28) show a general association of UTI and pregnancy-related complications among women in Ethiopia. Untreated UTI infections pose a high risk of pyelonephritis, premature delivery and fetal mortality among pregnant women, these conditions are also associated with impaired renal function and end stage renal disease among paediatric patients (29,30). Although previous findings report pregnancy-related mortality (21,23,31,32), the prevalence rates of UTI associated maternal complications experienced annually are yet to be investigated. Early screening, improved hygiene and effective antibiotic treatment of gestational UTI hold a great potential to reduce maternal and neonatal morbidities and mortalities in Kisumu County. The need to understand the epidemiology and biology of UTI associated complications among pregnant women in Kisumu County calls for a robust data set to define UTI public health burden during gestation

and the associated health complications. This study therefore, targeted Chulaimbo and Nyahera Sub-County hospitals as a model to establish UTI prevalence and specific clinical diagnosis and therapeutic management strategies among pregnant women seeking maternal child health (MCH) services from Chulaimbo and Nyahera Sub-County hospitals within Kisumu County.

METHODS

Study Area. This study was carried out in a hospital set-up within Kisumu County, Kenya. Kisumu County sits on a 2,085Km² land, with a total population of 1,081,485, as at previous census done in 2018 hence a population density of 495 people/Km². It is administratively divided into seven Sub-Counties including Kisumu Central (78,737 people), Kisumu East (69,988 people), Kisumu West (61,187 people), Nyando (65,751 people), Muhoroni (67,955 people), Seme (46,063 people) and Nyakach (62,024 people). Most residents in this county reside in the rural areas having 461,189 verses 429,354 people in the urban areas. Considering the environmental indicators, 52% of the total population access safe water while 47% have improved sanitation. Kisumu County reports a high fertility risk at 60% in women aged 20-29 and women younger than 20 years. Fertility risk inequalities are evident across all socio-demographic and socio-economic stratum. Health-seeking behaviour is affected by distance to the facility (33). In Kisumu County, 42% of women have distance issues to health service access, which are above the national rate at 20%. Kisumu County reports high (70%) ANC use as recommended by the WHO, however, only 27% receive all the components of ANC services including; blood pressure measurements, provision of a blood sample, provision of a urine sample, tetanus vaccination, Intermittent preventive treatment of malaria in pregnancy (IPTp), deworming treatment and iron-folic acid supplements (23). Maternal mortality rate (MMR) is 495/100,000 higher than the National MMR at 488/100,000, neonatal mortality rate (NMR) 39/1000 higher than the national NMR at 24/1000, child mortality rate (CMR) of 24/1000, infant mortality rate (IMR) of 54/1000 versus the National IMR at 31/100,000 and under-five mortality rate of 79/1000. Each Sub-County has a Sub-County level hospital with the capacity to offer ANC services, perform adequate microbiology diagnostic assays and run antibiotic susceptibility tests that reveal a high burden of multidrug resistance (MDR).

Data collection was targeted at Chulaimbo and Nyahera Sub-County hospitals in Kisumu East Sub-County since they contain the second largest population in the County. Furthermore, these hospitals serve a semi-urban population and have enhanced health services attributed to the presence of AMPATH program. These combinations of semi-urban location and having variety of other services qualified Chulaimbo and Nyahera Sub-County hospitals as the most appropriate data collection points for the current study.

Study Design. This was a hospital-based study that adopted a prospective study design in which pregnant women's hospital data extraction was done from health records over one year from February 2019 to February 2020.

Study Population. The study population comprised of datasets from all women who attended MCH services from Chulaimbo and Nyahera Sub-County hospitals within Kisumu County from the month of February 2019 to February 2020 (See Supplementary Data I).

Sample Population. The sample population included datasets from all pregnant women who attended MCH services from Chulaimbo and Nyahera Sub-County hospitals within Kisumu County from the month of February 2019 to February 2020.

Inclusion criteria

Data from healthy pregnant women permanently residing in Kisumu County without any chronic infection, attending MCH services from Chulaimbo and Nyahera Sub-County hospitals and who presented with UTI infections at the hospital from February 2019 to February 2020.

Exclusion criteria

Incomplete data sets from pregnant women and data from non-pregnant women were not eligible for the study.

Sample size determination. Sample size was calculated using Fisher's formula (34) at 50% UTI prevalence rate resulting N=365. As a precautionary measure, we considered an attrition

rate of 10% (N=36.5) to give a final sample size of N=402. Therefore, in the current study, a total of 416 MCH datasets were collected over one year from February 2019 to February 2020.

Sampling technique

Data from health records was extracted from Chulaimbo and Nyahera Sub-County hospitals records through purposive sampling.

Quantitative data collection

Serialised electronic data capturing forms were used to collect socio-demographic and clinical data. Health records were interrogated to assess gestational UTI clinical diagnosis and therapeutic management.

Qualitative data collection

Key informant interviews (KII) were conducted with 15 health care workers involved in direct care of pregnant women at Chulaimbo and Nyahera Sub-County hospitals. The interview guide focused on levels of UTI concern among health care workers, healthcare worker attention to pregnancy complications and health care worker directed UTI prevention and treatment strategies.

Clinical Laboratory UTI diagnosis

As a way of confirming the specific bacteria associated with the UTI in the targeted population, a sub-set of 12 aseptically collected midstream urine samples were randomly selected from pregnant women attending ANC services from Chulaimbo and Nyahera Sub-County hospitals. These samples were microbiologically analysed and identified bacterial isolates subjected to antibiotic susceptibility tests (AST).

Pilot testing

Prior to data collection, electronic data capturing forms were pretested on 10 MCH ANC data sets from Chulaimbo Sub-County hospital, which were not included in the final analyses.

Following piloting, these electronic data capturing forms were adjusted for clarity and consistency.

Data Analysis

Data collected was recorded and safely saved in Excel spreadsheets. These were transferred to SPSS v21 database for analyses at the Department of Biomedical Sciences and Technology of Maseno University. Descriptive analysis was used to summarize the study population's demographic characteristics. Chi-square tests were used for proportionality tests. A $P \leq 0.05$ was considered statistically significant for all the analysis.

RESULTS

The study population had a mean of two (2) ANC visits (± 1.14 ; Min 1- Max 7); a mean mothers age of 23.92 years old (± 6 ; Min 10 – Max 43); a mean parity of 2 (± 2 ; Min 0-Max 8); mean gravidae of 3 (± 2 , Min 1- Max 10); mean gestational age of 24.5 weeks (± 7.7 Min 3- max 38) and a mean haemoglobin level of 10.73(± 1.8 , Min 5 – Max 15). 56 % (233/416) attended the first ANC visit at varied gestational age during their pregnancy especially between 24 and 28 weeks (**Table 1**). Only 1.4% (6/416) had a clinical history capturing UTI infection while a total prevalence of 57.9% (241/416) were UTI positive following their diagnosed routine ANC profile deep stick urinalysis test (**Table 2**).

The proportion of pregnant women with asymptomatic UTI infections were 57.9% (241/416), significantly high compared to those with negative UTI infection status 42.1% (175/416) (χ^2 , $p < 0.001$). Clinical UTI history important for informed therapeutic management was performed for only 2.5% (6/241) cases who tested positive following deep stick urinalysis test. The remaining 97.5% (235/241) had no clinical history captured and no appropriate treatment administered. The datasets with clinical history captured revealed that a total of 1.4% (6/416) antibiotic therapy was mainly done by administration of first line broad-spectrum antibiotics.

Clinical laboratory diagnosis of specific aseptically collected midstream urine samples revealed the presence of Coagulase Negative *Staphylococcus*, Gram Positive Bacilli and *Streptococcus agalactae*. Antibiotic susceptibility tests showed likely resistance to commonly administered first line antibiotics including; ciprofloxacin, amoxiclavuic acid, ampicillin, tetracyclin, ceftriaxone, sulfamethoxazole trimethoprim, ampicillin and gentamycin, but sensitivity to various antibiotics that are not available easily to such hospital set-ups such as Imepenem, erythromycin, chloramphenicol and clindamycin (**Table 3**).

Further qualitative results revealed that urinary tract infection during pregnancy was moderately of a concern among pregnant women seeking antenatal services at both facilities, and most (79% of the health workers) focused attention, on recurrent urinary tract infection and premature delivery as complications observed. Prevention strategies highlighted by most (63%) of the health workers to minimize the occurrence of urinary tract infection during pregnancy were education and counselling. In addition, majority (76%) of the health workers indicated that it is often, greatly emphasized, to pregnant women who test positive for a urinary tract infection that advice on personal hygiene and increasing water intake as the main ways of reducing UTI infections. Furthermore, most (71%) health care workers insisted on follow-up on the progress of those who test positive for a UTI at subsequent antenatal care visits. Finally, the specific management and treatment method for urinary tract infection highlighted by most (70% of health workers) was giving cefixime and nitrofurantoin based on physical assessment and personal judgment and assessment of severity. These antibiotics were considered in the absence of a drug susceptibility tests at the clinics.

DISCUSSION

This study was set to determine the prevalence of gestational UTI, associated clinical diagnosis and the therapeutic management strategies. Socio-demographic, laboratory and clinical history data was extracted from 416 pregnant women's MCH data sets in Chulaimbo and Nyahera Sub-County hospital facilities' health records between February 2019 to February 2020 using pre-designed data collection forms.

Current research findings reveal asymptomatic gestational UTI prevalence of 57.9% (241/416) by routine empirical deep stick urinalysis test, which gives non-specific UTI associated aetiological bacterial agent findings. The current rate of gestational UTI prevalence in this region is much higher as compared to 27.6% reported in the general population among adults attending medical care in Kiambu level 5 hospital (15), and 21.5% among pregnant women attending ANC in Nairobi, Kenya (16). Other similar hospital-based studies in Sub-Saharan Africa have shown varying prevalence rates of gestational UTI infections; 3.7% Mbale, Uganda (35), 35% in Mbarara Uganda (36), 15.7 % in Ethiopia (28) and 20% and 35.5% in Tamale Central and Tamale Teaching hospitals in Ghana (37) and 18.8% in Sri Lanka, following urine culture and biochemical analysis during investigations. A systematic review of studies on the prevalence of gestational uro-pathogens and their antimicrobial resistance patterns in developing countries in Asia and Africa reported an overall rate of 13.5%. Gram-positive bacteria accounted for 15.9%, and Gram-negative bacteria accounted for the majority of infections (83.7%) with *Escherichia coli* being the most predominant uro-pathogen present in all the 26 studies included in the review. This review further reported resistance to antimicrobial drugs that are regularly used in developing countries with high resistance to ampicillin (67.2%). However, all the identified uro-pathogens showed relative sensitivity to ciprofloxacin (71.2%), nitrofurantoin (65%) and ceftriaxone (74.1%) (38). These previous observations are comparable to our findings, as their results shows that among pregnant

women, the prevalence was at 55% in Benin City (39), and 56% in Onitsha (40), with an overall subtle variation in the rate of UTI in the different populations attributable to a variety of factors including parity, maternal age, gestational age, level of education and cultural practices.

The current study also shows significant omission of UTI status from the mothers' clinical history following laboratory antenatal care (ANC) profiling. Only 2.5% (6/241) datasets had a clinical history capturing UTI infection out of the total prevalence of 57.9% (241/416) with positive UTI diagnosis by urine culture. A review of the diagnostic and therapeutic challenges in the management of gestational UTI revealed that specific detection and effective treatment remain a vital clinical problem in low-middle-income countries (LMICs) (30). In addition, previous works recommend repeated cultures every trimester for improved asymptomatic bacteriuria detection rate (41,42). Despite the Ministry of Health's standard microbiological diagnostic procedures providing for bacterial culture and sensitivity tests, the LMICs have continued to carry out presumptive deep stick urinalysis for ANC profiling. These laboratory findings remain uncertain especially in regards to accurate identification of asymptomatic potentially pathogenic gestational bacteriuria. Inadequate relevant UTI history to clinicians hinders appropriate medication, hence, affected cases presenting with un-identified asymptomatic and un-characterised symptomatic UTI go un-noticed posing a future risk of gestational UTI associated complications. This is quite a worrying trend as the laboratory data in our settings demonstrated varied susceptibilities to various isolated pathogens. There is a general prescription of broad-spectrum antibiotics for UTI in this population and this might compromise future interventions due to suspected built up of resistant strains to the easily available broad-spectrum antibiotics.

Assessment of gestational UTI associated risk factors is highly advisable following the unmet challenges in the implementation of the ideal bacterial diagnostics for effective surveillance and proper clinical and therapeutic management (43).

Proper attention is missed out which may lead to recurrent UTI reinfections and ultimate life-threatening gestational UTI-associated complications. Previous review findings (44,45) reported no significant UTI association with primary pregnancy outcomes including pyelonephritis, preterm birth and secondary pregnancy outcomes including low birth weight, and Apgar score. On the contrary, some study findings report increasing positive association of gestational UTI with maternal anaemia, acute pyelonephritis, preterm labour, septicaemia and even possible death of the mother, intra-uterine growth restrictions, prematurity, and low birth weight of the fetus and fetal mortality (9). Gestational asymptomatic bacteriuria (ASB) has been associated with premature and low birth weight, a relationship that is not supported by other studies (46–48). Indeed, most of the healthcare workers in our set-ups mentioned some management strategies, which might be effective in reducing the prevalence of UTI in women. However, there were no clear follow-up strategies to ensure compliance and re-testing of the women who tested UTI positive. These mixed ideologies lead to controversial findings that require proper up-to-date implementation of the standard UTI diagnostic and management policy implementation for effective antibiotic therapy and ultimate healthy populations.

As previously stated above, misdiagnosis and inappropriate characterization of both asymptomatic and symptomatic UTI may lead to symptomatic treatment using broad-spectrum antibiotics posing a great risk for the development of multidrug resistant (MDR) bacterial strains (49,50). Previous findings reveal a future potential for the development of multidrug resistance (51) attributed to specific UTI bacterial aetiological agents (52,53) following poor clinical and therapeutic management. This may explain the increasing incidences of UTI associated complications in African populations where conclusive confirmatory tests as per the recommended Ministry of Health guidelines are not implemented due to limited resources.

CONCLUSIONS

Current findings show a high prevalence of gestational UTI (57.9%). Only a handful of these cases get appropriate timely medication following clinical and therapeutic management. There is general lack of conclusive diagnostic test results in line with the Ministry of Health guidelines, which provide for bacterial culture and sensitivity tests. This leads to un-identification of UTI-specific aetiological bacterial agents prompting broad-spectrum antibiotic medications, a major risk for future antibiotic resistance, not conclusively addressed in the current study. There is paucity of information about common UTI associated aetiological bacterial agents in the target population. An investigation to identify specific UTI associated bacterial organisms will illuminate the possibility for development of alternative, more affordable point-of-care diagnostic platforms for enhanced UTI surveillance and specific antibiotic treatment (54,55). This will be vital in demystifying future forethought antibiotic resistance in populations at risk and ultimately a reduced burden of gestational UTIs and the associated poor pregnancy outcomes.

LIST OF ABBREVIATIONS

AMPATH - Academic Model Providing Access to Healthcare

ANC – Antenatal Care

ASB – Asymptomatic Bacteriuria

AST – Antibiotic Susceptibility Test

CMR – Child Mortality Rate

GCRF - Global Challenge Research Fund

IMR – Infant Mortality Rate

IPTp – Intermittent Preventive Treatment of Malaria in Pregnancy

KII – Key Informant Interviews

LMIC – Low-and Middle-Income Countries

MCH – Maternal Child Health

MDR – Multidrug Resistance

MMR – Maternal Mortality Rate

MOH – Ministry of Health

NMR – Neonatal Mortality Rate

MUERC - Maseno University Ethical Review Committee

UTI – Urinary Tract Infections

WHO – World Health Organization

DECLARATIONS

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by Maseno University Ethical Review Committee (MUERC) (Approval number MUERC/00959/21). An approval letter was also obtained from the Ministry of Health (MOH) local authorities for permission to access the hospital facility health records.

CONSENT FOR PUBLICATION: Not applicable

AVAILABILITY OF DATA AND MATERIALS: The datasets used during this study are available from the corresponding author on reasonable request.

COMPETING INTERESTS: Not applicable

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AUTHORS' CONTRIBUTIONS

ENT and SS conceptualised and designed the study. NTE, SS and EF, carried out data collection. NTE, SS, EF, TK, BO and CO analysed and interpreted data. All authors critically reviewed and approved the final manuscript for publication.

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HEALTH DATA PROTECTION

Health data was handled professionally and protected in line with the data protection Act No. 24 of 2019-Kenya Law. Data collected was securely stored in the Maseno University repository for future reference.

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Table 1: Baseline demographic characteristics (N = 416)

S/No	Variable	Mean	±SD	Minimum	Maximum	Frequency	Prevalence (%)
1	No. of ANC visits	2	1	1	7		
2	Mothers' Age (years)	23.92	6	10	43		
3	Parity	2	2	0	8		
4	Gravidity	3	2	1	10		
5	Gestational age (weeks)	24.52	7.7	3	38		
6	Haemoglobin level (g/dl)	10.73	1.8	5	15		
7	First ANC visit					233	56

Table legend: % Prevalence generated by proportionality tests using Ch-square. SD=Standard deviation; ANC=Ante-natal clinic.

Table 2: Clinical History and UTI status

S/No	Variable	Mean	±SD	Minimum	Maximum	Frequency	Prevalence (%)
1	Clinical History (N = 416)						
	Clinical UTI diagnosed cases					6	1.4
	Clinical UTI undiagnosed cases					410	98.6
2	UTI infection status (deep stick urinalysis) (N= 416)						
	Positive					241	57.9
	Negative					175	42.1

Table legend: % Prevalence generated by proportionality tests using Ch-square. SD=Standard deviation.

Table 3: Laboratory Analysis of the UTI Specimens

Gram Stain	Catalase Test	Hemolysis on Blood Agar	Coagulase Test	Novobiocin Disk	CAMP Test	Presumptive Identification	Antibiotic Tested
GNB						<i>Escherichia coli</i>	Sensitive to Imepenem. Resistant to Ciprofloxacin, Amoxicluvaic acid, Ampicilin Tetracyclin, Cetriaxone and Sulfamethoxazole Trimethoprim
GPB						Gram Positive Bacilli	
GPC	Positive	Gamma	Negative	Sensitive		Coagulase Negative Staphylococcus	
NGO						No Growth Obtained	
NGO						No Growth Obtained	
GPC	Negative	Gamma			Yet to Confirm	<i>Streptococcus agalactae</i>	Sensitive to Erythromycin, Chloramphenicol, Cetriaxone and Clindamycin. Resistant to Ampicilin and Gentamicin
NGO						No Growth Obtained	
GPB						Gram Positive Bacilli	
GPC	Negative	Gamma			Yet to confirm	<i>Streptococcus agalactae</i>	Sensitive to Erythromycin, Chloramphenicol, Gentamicin and Clindamycin. Resistant to Ampicilin and Cetriaxone
NGO						No Growth Obtained	
NGO						No Growth Obtained	
GPC	Positive	Gamma	Negative	Sensitive		Coagulase Negative Staphylococcus	

Table legends: Data were generated from laboratory analyses. GNB=Gram-negative Bacteria; GPB=Gram-Positive Bacteria; GPC=Gram-positive cocci; NGO=Neisseria gonorrhoea.