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RESEARCH ARTICLE

MATERNAL AND PERINATAL OUTCOMES AMONG PREGNANT WOMEN WITH URINARY TRACT INFECTIONS

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ABSTRACT

Urinary Tract Infections (UTIs) are common during pregnancy because hormonal, physiologic and mechanical changes cause vesico-ureteral reflux and urinary stasis which facilitate bacterial growth. The association between UTI during pregnancy and high risk for adverse maternal and neonatal outcomes are widely reported globally although findings are inconsistent. This study therefore determined the association between UTI during pregnancy and risk for adverse maternal and neonatal outcomes in a tertiary hospital in Cape Coast, Ghana. A case-control prospective study lasting six months was carried out with 220 pregnant women with UTI (cases) and 200 without UTI (control) attending the Antenatal Clinic of Central Regional Hospital, Cape Coast. Participants were assessed at each ANC visit and during labour for several outcomes. Data were analyzed on SPSS 16. The study showed statistically significant associations between maternal UTI and adverse outcomes including foul-smelling liquor ($p=0.006$); premature rupture of membrane ($p<0.001$); intra-partum bleeding (APH and PPH; $p<0.001$). Neonatal outcomes included low birth weight ($p=0.014$), preterm delivery ($p<0.001$); Apgar score at 1 minute ($p<0.001$); stillbirth ($p=0.022$). Associations were not significant between maternal UTI and pregnancy-induced hypertension and baby's Apgar score at 5 minutes. We conclude that UTI in pregnancy adversely affects the mother and the neonate.

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INTRODUCTION

Pregnant women are particularly susceptible to Urinary Tract Infection (UTI). This is because normal gestation-induced hormonal, physiologic and mechanical changes result in increased risk of urinary stasis, vesico-ureteral reflux, altered glomerular filtration, increased urinary glucose concentration and alkalinity which ultimately facilitate bacterial growth (Mittal *et al*., 2005). These changes increase the risk of urinary infections which could be symptomatic or asymptomatic (Johnson *et al*., 2014). Studies on hospital-based prevalence of UTI in pregnancy in developing countries reveal the highest prevalence of 12.7% in Saudi Arabia (Almushait *et al*., 2013), 31.3% in Egypt (Dimetry, 2007), 47.5% in Nigeria (Okonko *et al*., 2009) and 56.5% in Ghana (Boye, 2012).

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Variations in the prevalence occur from one geographical location to another (even in the same country). These variations could be attributed to the perception of UTI, mode of screening and compounding risk factors (Obirikorang *et al*., 2012), poor perineal hygiene (Dimetry, 2007), and host behavioural factors in the populations studied. Risk factors for increased prevalence of UTI in pregnancy have been found to include low socio-economic status, low educational status, increasing maternal age (Parveen *et al*., 2011 and Perera *et al*., 2012), high parity[7], high sexual activity and past history of UTI (Perera, 2012 and Emiru *et al*., 2013). However Emiru *et al*. (Emiru *et al*., 2013) found no association with maternal age, educational level and parity. Amiri *et al.* (Amiri *et al*., 2009) also reported poor hygiene practices and high sexual activity as implicating factors. According to Boye *et al.* (Boye *et al*., 2012) the high prevalence in Ghana could be attributed to a combination of factors like low economic status and difficulty with personal hygiene among pregnant women.

Studies by Delzell and Lefevre (Delzell *et al*., 2000) have reported several adverse maternal and perinatal outcomes as a result of UTI in pregnancy including pre-eclampsia, amnionitis, intra-uterine growth retardation, low birth weight infants, pre-term deliveries and perinatal death. Emamghorashi *et al*. (Emamghorashi *et al*., 2012) also reported a significant association between maternal prenatal UTI, especially in the 3rd trimester, and neonatal UTI. The above mentioned outcomes can be devastating and emphasize the importance of diligent diagnosis and treatment of maternal UTI in pregnancy. In Ghana, as in many developing countries, UTI in pregnancy is challenging because it is sometimes asymptomatic. Therefore pregnant women who do not have symptoms of UTI may go through the whole pregnancy without diagnosis and treatment, and may end up with adverse outcomes. According to Macjeko and Schaeffer (Macejko, 2007), Smaill (Smaill, *et al*., 2007). Schnarr and Smaill (Schnarr *et al*., 2008) all women should be screened for bacteriuria in the first trimester, and those with recurrent urinary tract infections should have repeat bacteriuria screening throughout pregnancy. This should be the standard of obstetrical care. However in Ghana this is not the case. Most hospitals (even teaching hospitals) do not carry out routine urine microbial screening during pregnancy. In addition, many women book too late in pregnancy for effective treatment of UTI to be achieved. In a study of prevalence of UTI in pregnancy in Cape Coast metropolis, Boye, *et al* (Boye *et al*., 2012) found the highest incidence in the second trimester of pregnancy and stated that urinary tract infection culminating from poor diagnosis during pregnancy puts pregnant women at high risk of serious complications. While there are many studies focusing on the prevalence of UTI and asymptomatic bacteriuria in Ghana, (Boye *et al*., 2012; Obirikorang *et al*., 2012 and Turpin *et al*., 2007) there is paucity of data on the complications or adverse effects of UTI on mothers and their newborn, hence the need for this study. The purpose of this study was to determine the maternal and perinatal birth outcomes of UTI in pregnancy in a tertiary health care institution in Cape Coast, Ghana.

Patients and Methods

Design: Descriptive case-control prospective study was conducted during the period of September 2012 and March 2013.

Sampling: Four hundred and twenty (420) pregnant women in their third trimester seen in antenatal clinic of the Central Regional Hospital (CRH), Cape Coast, Ghana during the study period were purposively selected and enrolled in the study after informed consent had been obtained. These comprised two hundred and twenty (220) pregnant women with positive urine culture (cases) and200 healthy pregnant women without UTI (controls) matched for gestational age. Women with known underlining renal pathology or chronic renal disease and those on antibiotic therapy in the previous 2 weeks were excluded.

Personal data: Pre-tested questionnaires with a Cronbach's alpha coefficient of 0.75 were used to obtain information on relevant medical, obstetrical and socio-demographic characteristics; history of symptoms suggestive of UTI as well as history of antibiotic usage in the index pregnancy. Maternal haemoglobin, weight, height and body mass index (BMI) were also assessed and recorded.

Urine analysis: Clean catch, freshly voided mid stream urine samples (10-15 ml) were collected and analyzed within one hour. Standard calibrated quantitative loop (Cheesebrough *et al*., 2000) was used to inoculate urine sample on Cysteine Lactose Electrolyte Deficient (CLED) agar plates, MacConkey Agar (MCA) and Blood Agar (OXOID-England) and incubated for 24hrs at 37°C. Isolates were identified based on their colony morphology and growth characteristics. Individual colonies were suspended in normal saline to 0.5 McFarland and disc diffusion method was used to determine susceptibility of the isolates. Diagnosis of UTI was made when there was a positive urine culture with at least 10^5 colony forming units (CFU)/ml.

Outcome of pregnancy: Participants were monitored throughout their pregnancy at each antenatal visit until delivery and evaluated for presence of premature rupture of membranes and premature labour; pregnancy-induced hypertension, foul smelling liquor, bleeding (ante-partum and post partum) and mode of delivery. Neonates born to participants in both case and control groups were assessed for gestational age, live/stillbirth, birth weight, Apgar score at one minute and five minutes. Conditions indicative of the general health status of the neonates were also noted.

Ethical consideration: Institutional Review Board of the University of Cape Coast approved the study and ethical clearance was obtained from the Central Regional Hospital. Participants also gave their informed consent and participation was voluntary.

Data analysis: Data were analyzed on SPSS version 16.Odds ratio and 95% confidence interval were calculated among the categorical parameters by applying the Fishers' exact test.

RESULTS

Causative organisms

The major micro-organisms isolated from women with UTI were E*scherichia Coli* (54.1%), *Staphylococcus aureus (*34.1%) *Klebsiella pneumoniae* (4.1%) and minor bacteria groups constituting 7.3%. (Figure1). Isolates were sensitive to diverse antibiotics. Only one case of *Pseudomonas aureginosa* was isolated and was resistant to all antibiotics used for the susceptibility test. Although microorganisms were isolated from the urine of the 220 cases used in the study 168 (76.4%) reported symptoms suggestive of UTI while 52 (23.6%) were asymptomatic. Table 1. shows the socio-demographic characteristics of the subjects in the study. The number of women with no formal education was significantly higher in the group with UTI than in the control group. The 220 pregnant women with UTI (cases) were aged 27 ± 8.5 years and the control group of 200 non-UTI pregnant women were aged 28± 7.8. Other personal factors include the BMI of 22±4.8kg/m^2 (for cases) and 23±5.9kg/m^2 (for controls). Haemoglobin levels were 12.1±2.3g/dl and 11.9±3.1g/dl for

the cases and the controls respectively. UTI was significantly associated with the educational level of subjects (=18.278, p<0.001; OR=2.888; 95% CI: 1.744-4.864 (the odds of non-literate mothers having UTI was almost three times the odds of other groups). Level of income was also significantly associated with UTI in pregnancy (=63.464, p<0.001); but UTI was not significantly associated with parity (number of times given birth).

Perinatal and Maternal Outcomes in Pregnancy

Table 2 shows the perinatal outcomes of pregnancy in the case and control groups. Maternal UTI was significantly associated with birth outcome (live birth/still birth (χ^2=5.221, p=0.022); baby's Apgar score at 1 minute (χ^2 = 27.499; p<0.001); gestational age (χ^2 = 14.594, p<0.001) and baby's birth weight (χ^2 = 6.071, p=0.014).

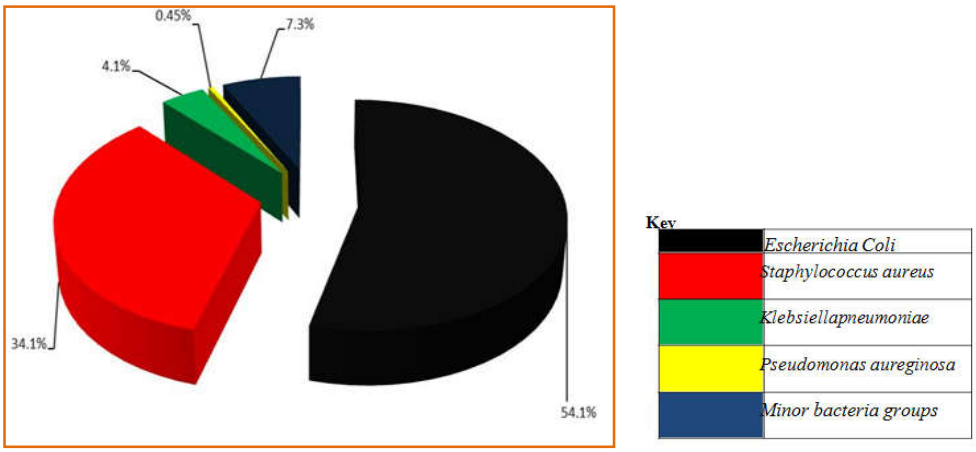

Figure 1. Pie chart showing common causative organisms of UTI in sample

Table 2. Perinatal Outcomes of Urinary Tract Infections in pregnancy for case and control groups

Parameters (Perinatal) Perinatal factors	Variables	Case (n=220)	Control (n=200)	Chi Square	Df	P-Values	Odd Ratio	CI*	
								Lower	Upper
Gestational Age	Preterm	42	13	14.594	1	0.000	3.359	1.785	6.734
	Term	178	187						
Birth Weight	< 2500g	62	36	6.071	1	0.014	1.782	1.123	2.862
	≥ 2500g	158	164						
Apgar Score at 1 min	< 7	71	22	27.499	1	0.000	3.827	2.293	6.611
	≥ 7	149	178						
Apgar Score at 5 min	< 7	54	42	0.747	1	0.387	1.222	0.773	1.943
	≥ 7	166	158						
Birth Outcome	Live	202	194	5.221	1	0.022	0.354	0.124	0.871
	Still Birth	18	6						
Sex of baby	Male	106	102	0.333	1	0.564	0.894	0.608	1.312
	Female	114	98						

Table 3. Maternal Outcomes of Urinary Tract Infections in pregnancy for case and control groups

Parameters (Maternal)	Variables	Case (n=220)	Control (n=200)	Chi Square	Df	P-Values	Odd Ratio	CI	
								Lower	Upper
Maternal factors	Maternal								
Foul Smelling liquor	Present	21	6	7.461	1	0.006	3.342	1.389	9.403
	Absent	199	194						
Premature Membranes	Present	36	10	13.871	1	0.000	3.667	1.826	8.053
	Absent	184	190						
Bleeding (APH/ PPH)	Present	41	13	13.871	1	0.000	3.261	1.730	6.548
	Absent	179	187						
Pregnancy - Induced Hypertension	Present	65	62	0.105	1	0.746	0.933	0.615	1.419
	Absent	155	138						
History of Previous Abortion	Present	17	15	0.105	1	0.746	1.497	0.497	2.160
	Absent	203	185						
Mode of Delivery	SVD	166	142	2.021	2	0.364			
	C/S	45	44				1.143	0.711	1.836
	ID	9	14				1.804	0.761	4.499

The odd ratio (OR=3.359; 95% CI: 1.785-6.734) showed that pregnant women with UTI were 3.4 times more likely to have preterm babies than those without UTI. Baby's Apgar score of less than 7 at one minute occurred 3.8 times more among mothers with UTI than among the control group (OR=3.827; 95% CI:2.293-6.611). Mothers with a positive urine culture (UTI) had more babies weighing less than 2500g at birth than those without UTI (OR=1.782; 95% CI: 1.123-2.862). Maternal UTI was not significantly associated with Baby's Apgar score at 5 minutes and sex of the baby. Table 3. Shows the maternal outcomes of pregnancy in both the cases and controls. Results show that maternal UTI was significantly associated with the presence of foul smelling liquor (χ^2 = 7.461, p=0.006, OR=3.342; 95% CI: 1.389-9.403); premature rupture of membranes (χ^2 =13.871, p<0.001, OR=3.667; 95% CI: 1.826-8.053) and intra-partum bleeding (both APH and PPH; χ^2 = 13.871, p<0.001, OR=3.621; 95% CI: 1.730-6.548). UTI in pregnancy was not significantly associated with occurrence of Pregnancy-induced hypertension (PIH) in the current pregnancy, history of previous abortion and mode of delivery (spontaneous vaginal delivery/instrumental delivery/Caesarian section).

DISCUSSION

This study uniquely identified adverse effects of UTI during pregnancy on birth outcomes in the mother and neonate. Premature rupture of membranes, foul-smelling liquor, haemorrhage (APH/PPH), preterm deliveries, low birth weight, Apgar score of less than 7 at one minute and still birth are important findings that will be discussed. Several studies [4,13,20,] have also found association of UTI during pregnancy with the risk of adverse perinatal and maternal outcomes such as low-birth-weight infants, premature delivery, and occasionally, hypertension/pre-eclampsia, stillbirth, Caesarean delivery and intra-uterine growth restriction. However other studies (Chen *et al*., 2010 and MacLean *et al*., 2001), did not find such associations. These inconsistent results could be due to selection bias, differences in settings, inadequate control of confounding factors and whether it was hospital-based or population-based study.

The significant prevalence of premature rupture of membranes found in this study is consistent with previous studies (Sayres *et al*., 2010 and Wax, 2010), but different from that of Vasconcelos-Pereira *et al* (Vasconcelos-Pereira *et al*., 2013). A possible mechanism has been proposed to explain how UTI in pregnancy causes the risk of premature rupture of membranes. UTI induces macrophages to release metalloproteinase which degrades amniotic membranes, predisposing them to rupture (Simmons *et al*., 2010 and Bhutta *et al*., 2010). The significant incidence of preterm deliveries, low-birth-weight neonates, and still births found in this study are similar to studies by Bhutta et al. (Bhutta *et al*., 2010) and Simmons *et al* (Simmons *et al*., 2010), who posit that globally, UTI is one of the most important and potentially preventable causes of early preterm birth and is responsible for up to 50% of extreme preterm births of less than 28 weeks of gestation. Other studies have explained that the increased incidence of preterm labour and delivery associated with UTI can result from inflammatory responses induced by cytokines and prostaglandins mediators triggered by the colonization of amniotic fluid by uropathogens. These bacteria produce collagenase and phospholipases A and C, which act as precursors of pro-contractile prostaglandins E2 and F2a, consequently triggering preterm labour (Wax, 2010 and Simmons *et al*., 2010). It has been reported that intrauterine infections are responsible for up to 50% of extreme preterm births of less than 28 weeks of gestation, where both neonatal morbidity and mortality are high[26]. These intrauterine infections may have resulted from inflammation of amniotic membranes and transplacental transfer of cytokines originating from maternal UTI (Bhutta *et al*., 2010 and Oda *et al*., 2008). The significant finding of foul smelling liquor in this study could be regarded as evidence of such intrauterine infection. This infection, according to Leticia *et al* (2013), causeschorio-amnionitis, affects oxidation and nutrition at the placental site and results in intrauterine growth restriction (IUGR) which is responsible for small-for-dates babies. This situation may justify the significantly high rates of low-birth weight, premature rupture of membranes and stillbirth in the current study. The strong association between maternal UTI and bleeding (before and after delivery) in the study may also be as a result of the intrauterine infection. However Mann *et al* (2009) conclude that maternal genito-urinary infection is generally not associated with small for gestational age (SGA).

The lack of association between maternal UTI and the presence of pre-eclampsia in this study is consistent with findings by MacLean (MacLean, 2001), Minassian *et al* (Alfred, 2013) but contrary to Conde-Agudelo *et al*. (Conde-Agudelo, 2008) who posits that UTI is strongly associated with preeclampsia in women with underlying renal infections. Women with known underlining renal pathology or chronic renal disease were excluded from this study which may explain this lack of association. The high association between maternal UTIand baby's Apgar score at one minute shows that maternalUTI could affect the ability of the baby to tolerate the birthing process within the first one minute of birth. This is especially likely to occur if there is associated reduced nutrition at the placental site and premature rupture of membranes. The insignificant association with baby's Apgar score at 5 minutes after birth is congruent with other studies (Mayor-Dray, 2009 and Vasconcelos-Pereira *et al*., 2013) and may mean that the adverse effect of UTI is less profound on the baby's tolerance level at 5 minutes after birth. The challenge of *Escherichia coli (E Coli*) with its multidrug resistant strains found to be the most predominant causative organism in UTI among pregnant women in this study needs to be addressed in order to reduce the risk of adverse maternal and neonatal outcomes. The value of 54.1% of *E Coli* isolates in the current study is close to the finding of 48.7% by Boye, *et al*[6] in the same location (Cape Coast, Ghana), but higher than 37.5% found in Egypt by Dimetry *et al* (2007), 42.1% in Nigeria by Okonko *et al* (2009) and 41.9% by Rizvi *et al* (2011). It is however lower than 67% in Sri Lanka (2012) and 88.15% in Bangladesh (2011). The most common predicting socio-demographic factors with UTIs in this study were income level and educational level but not parity. The association of income with prevalence of UTI is consistent with studies by Emiru *et al* (2013), Dimetry, *et al* (2007) but contrary to findings by Alfred *et al* (2013) who studied patients

in a private hospital in Benin, Nigeria. The lack of association in that study may be probably because private hospitals are predominantly attended by patients of the middle class and upper class. The association between UTI and level of education revealed in this study is also reported by Dimetry *et al* (2007), Parveen *et al* (2011), Perera *et al* (2012). The lack of association of UTI with parity is consistent with studies by Olsen *et al* (2000) in rural Tanzania and Emiru *et al* (2013)[0] in Ethiopia. This may be because of similarities in the childbearing patterns in these three African countries where women start childbearing early and tend to have many children. These homogenous groups of women are usually seen in the antenatal clinics.

Implications for Patient Care

The importance of pre-natal urine screening for bacteria to identify patients at risk is important. However some women with UTI who present themselves in hospital at the late stage of pregnancy may not benefit from effective treatment of the infection. Some pregnant women may have asymptomatic bacteriuria and most hospitals in developing countries like Ghana only routinely test pregnant women's urine for proteins and sugar and do urine culture only for patients with symptoms of UTI. This has great implications for quality and effectiveness of obstetric care, not only in the setting used for the study but also in other settings which do not carry out routine microbial screening of urine in pregnancy.

Conclusion and Recommendations

Based on the results obtained, we conclude that UTI during pregnancy increases the risk of maternal and perinatal outcomes like premature rupture of membranes, preterm delivery, intra-partum bleeding, low birth weight and low Apgar score at one minute. These findings underscore the importance of urine screening for bacteria in pregnancy to identify patients at risk so that they can be monitored throughout the pregnancy and adequately treated to reduce adverse outcomes, especially to the neonate. In many developing economies, facilities for neonatal intensive care for preterm and low birth weight babies are scarce. In order to forestall these risks and reduce perinatal morbidity and mortality, the current practice of only doing urine bacterial screening for pregnant women with symptoms needs to be reviewed. There is also need for specific policies and protocols in such settings in order to enhance obstetric care. We therefore recommend urine culture for every pregnant woman at first antenatal visit, repeated urine cultures during pregnancy for those with UTI and effective treatment of urinary infections to forestall adverse effects on mother and baby.

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