ASYMPTOMATIC BACTERIURIA: SCREENING AND PREVALENCE AMONG PREGNANT WOMEN ATTENDING CLINIC AT MUHIMBILI NATIONAL HOSPITAL:

A cross sectional study.

By

Dr G.L.K.Kamugisha (MD Dar)

A dissertation submitted in partial fulfilment of requirements for the degree of Master of Medicine (Obstetrics & Gynaecology) of the University of Dar es Salaam.

University of Dar es Salaam

September 2002.

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the University of Dar es Salaam a dissertation entitled: *Asymptomatic bacteriuria: Screening and Prevalence among pregnant women attending clinic at Muhimbili National Hospital,* **in partial fulfilment of the requirements for the degree of Master of Medicine (Obstetrics and Gynaecology)**

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Date: 14th October 2002

DECLARATION AND COPY RIGHT

I, Gelase Kalibashubao Kamugisha, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for similar or any other award.

Signature----------

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DEDICATION

This work is dedicated to my parents Lauren and Antonia Kalibashubao who opened my eye to education, and all patients who suffered in any way because of the little knowledge I had.

ABSTRACT

Background: Prevalence of Asymptomatic bacteriuria in pregnancy ranges from 2.0% to 23.9% and if not attended about 20% to 40% of these will develop symptomatic disease. None of various screening methods have been found to have satisfactory sensitivity and specificity.

Objective: To determine the reliability of nitrite reductase and leucocyte esterase methods in screening for ABU in pregnant women.

Settings: Muhimbili National Hospital - Antenatal clinic

Study design: Cross sectional

Population: Pregnant women attending antenatal clinic.

Methods: Systematic sampling was used and morning urine samples were screened using Dipstick methods. Bacterial culture and antimicrobial susceptibility was done. Analysis was done using EPI info version six and specificity and sensitivity were calculated.

Results: The prevalence of ABU was 23.0 %. Both nitrite reductase and leucocyte esterase tests had poor sensitivity ranging from 10.5% to 65.8%. *Klebsiella spp* and *E.coli* were the commonest microorganisms comprising 44.8% and 23.2% respectively.

Conclusion: ABU represents a considerable public health problem among pregnant women attending MNH-ANC and leucocyte esterase and nitrite reductase tests are not ideal for screening

Recommendation: There is a need to look for other screening tests.

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ABBREVIATION

MNH-Muhimbili National Hospital

ANC-Antenatal care

ABU-Asymptomatic bacteriuria

USA-United States of America

RR-Relative Risk

CLED-Cysteine Lactose Electrolyte deficiency Medium

MCH-Maternal &Child Health

RPC- Research and Publication Committee

MUCHS- Muhimbili University College of Health Science

SES-Socio Economic Status

INTRODUCTION AND REVIEW OF LITERATURE

Infections of the urinary tract are especially common in women. This has been attributed to the short urethra, which is approximately three to four centimetres and the proximity of the urethra to the vagina that is colonised with various organisms from the gastro-intestinal tract[1,2].

Ureteral dilatation tends to occur from the sixth week of gestation reaching a peak at 24 weeks in approximately 90% of pregnant women, and this remains so until delivery. Increased bladder volume and decreased bladder tone along with decreased ureteral tone contribute to increased urinary stasis and vesical ureteral reflux resulting in bacteria colonisation of the urinary bladder [3,4]

Other factors that may contribute to the development of bacteriuria during the third trimester include increase in the length of the kidney by 1cm and the slight change in position of the bladder becoming an abdominal rather than a pelvic organ. These changes tend to make the bladder hold almost double its volume without discomfort[3,4]. As a result of an enlarging uterus there is physical blocking of the ureters, which in turn contributes more to ureteral dilatation and urine stasis. Furthermore, the physiologic increase of plasma in pregnancy and a decrease in ability of the kidney to concentrate urine may cause a decrease in the natural antibactericidal activity of urine and hence in

presence of bacteriuria may increase susceptibility to infection[3,4]. Bacteria, which are normally present in the vagina and distal urethra through ascending infection, may lead to colonisation of urinary system. Direct massaging of the urethra during sexual act and instrumentation of urinary system may also facilitate ascent of bacteria and hence colonisation of the urinary system[2].

Epidemiologically, infection of the urinary tract is divided into community and nosocomial acquired infections[5]. Anatomically it is divided into lower and upper urinary tract infection while in clinical practice it is divided into asymptomatic and symptomatic bacteriuria[5]. Asymptomatic bacteriuria (ABU) is defined as persistent bacterial colonisation of the urinary tract without urinary tract symptomatology[3]. Bacteriuria is considered significant when 10^5 microorganisms or more are isolated per millilitre of a properly collected mid stream urine specimen[1,3,4].

ABU has been found in 2% to 10% of the obstetrical population world wide[1,2]. In the USA, one study reported a prevalence of 8.3%, while studies from Pakistan and Thailand reported prevalences of 4.8% and 11.2% respectively[6,7,8]. In Nigeria and Ethiopia the reported ABU prevalence were 23.9% and 7.0% respectively[9] [10] In 1981, the prevalence

of ABU in Dar es Salaam was found to be 6.4% [11].

In a study done in USA a strong association between ABU with parity, race and low socio-economic status has been reported[1]. On the other hand, ABU has been reported to be inversely associated with education beyond high school and age above 30 years among African Americans [12]. A study in Trinidad showed that asymptomatic bacteriuria occurred more commonly among Negroes of low socio economic status than among East Indians who were better-of economically[13]. The prevalence was also found to be high with increasing parity and gestational age[13]. It was noted however that 80% of study participants were reluctant to reveal their income, making analysis of socio economic status difficult[13]. In a study done in Dar es Salaam Tanzania, the prevalence of asymptomatic bacteriuria was found to be high in the medium socio economic class[11].

Escherichia coli has been found to accounts for 80% to 90% of the organisms causing ABU in most studies[2,3,4,14]. Other gram-negative organisms include *Proteus mirabilis* and *Klebsiella pneumoniae*[3,4,14]. Although many studies done in developed countries show that *E. coli* predominates in ABU, studies done in Thailand and Nigeria have revealed coagulase negative staphylococcus to be the commonest

organism isolated[7,10].

Only 1% to 2% of the women seen in early pregnancy and found not to have bacteriuria at that time do develop bacteriuria in late pregnancy [1,4] Though pregnancy does not increase the prevalence of ABU in women, it does enhance the rate of progression to symptomatic disease. Studies have demonstrated that 20% to 40% of pregnant women with ABU detected in early pregnancy and not treated will develop acute symptomatic infection later in pregnancy including cystitis and acute pyelonephritis[2]. Up to 30% of patients with untreated asymptomatic bacteriuria develop acute cystitis[3]. The symptoms of cystitis include dysuria, haematuria, urinary frequency, urgency and suprapubic discomfort in the absence of upper urinary tract symptomatology. However symptoms that are consistent with cystitis occur frequently in pregnant women without urinary tract infection[4].

Acute pyelonephritis is the most severe form complicating ABU and occur in 1%to 2% of all pregnancies[2,3]. Previous history of pyelonephritis, urinary tract malformation or renal calculi has been associated with increased risk of infection, and recurrence rate of up to 23% has been reported in patients with such a history[2,3].

Complications of acute pyelonephritis are primarily due to tissue damage mediated by bacterial endotoxins and cytokines elaborated by macrophages in response to these endotoxins[15]. These, trigger the symptomatology ranging from just costovertebral angle tenderness to evidence of damage in multiple organ systems[15]. A frequent and dramatic finding is thermo regulator instability characterized by high spiking fever and hypothermia, the temperature fluctuating between 34^{0}C and 42^{o}C, and decreased systemic vascular resistance[15]. Respiratory insufficiency has been reported to occur in 2% to 8% of women with pyelonephritis in pregnancy while alteration of alveolar capillary membrane permeability by endotoxins and cytokines released may result in pulmonary oedema. Clinically, patients present with dyspnea, tachypnea and hypoxaemia resembling adult respiratory distress syndrome. Anaemia defined as haematocrit of less than 30% has been reported to occur in 25% to 60% of antepartum patients with pyelonephritis[15]. Transient renal dysfunction depicted by decreased creatinine clearance has been reported to occur in 25% of women with antepartum pyelonephritis[4,15]. Although up to 15% of pregnant women with pyelonephritis have been found to have bacteraemia, only a small proportion have been found to develop full-blown clinical manifestation of septic shock [15].

Meta analysis done by Romero et al[15], showed that non-bacteriuric patients had 50% lower risk of preterm delivery RR 0.50 (95% CI 0.36 – 0.70) and 35% lower risk of having a low birth weight infants RR 0.65 (95% CI 0.57 – 0.74) when compared with patients with untreated ABU[2]. This finding suggests that ABU could only be one of the factors in the complex issue of prematurity[2,4].In the year 2000, 18.4% of mothers delivered at Muhimbili National Hospital had low birth weight infants[21] Schieve et al[15] reported that, the presence of significant bacteriuria was associated with premature labour, hypertensive disorders of pregnancy, and anaemia. Though this does not prove a cause and effect relationship, several trials have demonstrated that antibiotic treatment decreases the incidence of pre-term birth and low birth weight infants[4,16]. Inspite of these complications and the evidence that intervention in ABU reduces the risks, a study done in Greece showed that only 20% of the obstetricians screen their antenatal patients[17]. Several other randomised controlled trials addressing benefits of screening and treatment compared with no treatment of ABU in pregnancy have been carried out, the majority with the results which favour the former[2,4].A treatment trial of ABU in USA reduced the incidence of acute pyelonephritis from 4% to 0.8%, meaning that if patients with ABU were to be identified and treated, 80% of cases of pyelonephritis in pregnancy would be prevented[18]. A study by Elder et

al[15], showed that the treatment of ABU in pregnancy reduced the rate of persistent bacteriuria during pregnancy from 86% to 11% [2].

Although multiple screening tests for ABU have been developed over the past several years, most of them have low sensitivity and have a low positive predictive value. However they have also been shown to be very specific when compared with a gold standard, that is urine culture[3]. In one study, urinalysis was compared with urine culture and was found to have a sensitivity of 18 %, a specificity of 97% and the positive predictive value was 43%[8]. Due to low sensitivity screening for ABU using simple urinalysis is not recommended[7]. Other screening methods such as leukocyte esterase dipstick method, has been shown to have a sensitivity of 17%, while that of nitrite dipstick was 57%[3]. Urine for gram stain though expensive, has been reported to have a sensitivity of 90% and specificity of 83%[2,3]. The most recent promising results have been obtained by using Uri screen (Diatech diagnostic Ltd), which is a rapid enzyme urine-screening test. This test has been reported to have a sensitivity of 100% and a specificity of 81% when compared with urine culture[4]. With a 6% prevalence of ABU, screening and treatment of ABU to prevent pyelonephritis based either on the leukocyte esterase, nitrite dipstick or urine culture may be more cost beneficial when compared with no screening[19,20]. However, when compared with the dipstick

method, the urine culture method is not cost beneficial. Only at high ABU prevalence rates (at or above 9%) does urine culture become cost beneficial when compared with dipstick method[19]. Even at a low ABU prevalence (e.g. 2%), still screening and treatment based on the dip stick method remains cost beneficial[19].

As evidenced above, effective treatment reduces the risks associated with ABU[2,16]. When selecting drugs for use during pregnancy, well established agents with well-known properties are generally preferred to newer ones. Studies have reported a physiological increase in glomerular filtration rate of about 50% thus making elimination of hydrophilic drugs that are excreted by the kidney to be much faster. This problem may necessitate increasing the dose[21]. Commonly used drugs are the beta-lactamase resistant penicillins and cephalosporins, amino glycosides and nitrofurantoin. In the USA amoxycillin is commonly used while in Canada trimethoprim and nitrofurantoin are commonly used, and in the UK penicillins and cephalosporins are commonly used. In Tanzania there are no guidelines and this is complicated with the high resistance rates among beta lactamase group of penicillin of up to 42% in some isolates[16].

STATEMENT OF THE PROBLEM AND RATIONALE:

There is wide range of prevalence of ABU, from as low as 2.0% to as higher as 23.9% and recent studies showing a tendency towards an increase[1,2,8,9]. An association between ABU and both low socio economic status and low level of education has been observed in some studies[1, 12,13]. If undiagnosed and untreated 20 % to 40% of those with ABU will develop symptomatic disease with its consequences on pregnancy outcome of premature labour and low birth weight infants[2]. Moreover there is evidence of high rate of low birth weight infants among women delivering at MNH unit[22]. It is evident that treatment of ABU is accompanied with reduction in rates of premature labour and low birth weight infants[2,3,15]. Furthermore it has been shown that despite obstetricians knowing about the problem they seem to give very little attention[17]. There are no recent studies that have been carried out to establish the magnitude of ABU among pregnant women in Tanzania. Given a fall in per capita income from US$283.6 in 1981 to US $261.1 in 2001[23] and the high cost of urine culture which is the method commonly used in reaching the diagnosis, plus an arena of high rates of resistance among commonly used antimicrobial agents, which adds a burden to our limited resources [16,19], it has been found pertinent to evaluate the performance of leucocyte esterase and nitrite tests as

screening methods for ABU, with a view of determining if they could be adopted as a part of ANC routine tests.

RESEARCH QUESTION

Do the dipstick methods for detection of ABU by leucocyte esterase and nitrite test have acceptable sensitivity and specificity?

HYPOTHESIS:

The dipstick method for detection of ABU by leukocyte esterase and nitrite test has acceptable sensitivity and specificity.

BROAD OBJECTIVE:

To determine the prevalence and evaluate the sensitivity and specificity of nitrite and leucocyte esterase dipstick methods in the screening of ABU in pregnant women.

SPECIFIC OBJECTIVE:

1. To determine sensitivity and specificity of dip stick methods in diagnosis of asymptomatic bacteriuria.
2. To determine the prevalence of asymptomatic bacteriuria among pregnant women attending MNH-ANC
3. To describe socio-demographic characteristics associated with ABU in

pregnancy.

4.To determine the bacterial causes of ABU and their antimicrobial susceptibility pattern.

MATERIALS AND METHODS:

Study setting – Muhimbili National Hospital (MNH)

MNH is the largest referral hospital in the country used as a University teaching hospital. MNH also attends the majority of high-risk antenatal patients in Dar es Salaam as well as normal pregnant women. The maternity unit is divided into four working units each headed by a consultant, two specialists and residents. It has four wards with a capacity of 160 beds. The delivery ward at MNH attends on average 40 deliveries a day, the majority being those attending the hospital ANC. There are four antenatal clinic sessions in a week, i.e. one for each firm. Each clinic session caters for about 80 pregnant women, the majority of whom are high-risk antenatal women. A bout 20 women attend MNH-ANC for the first time each session. The majority of first ANC attendees are referred from peripheral clinics on the basis of a specially designed risk screening ANC card (MCH4 in appendix V).

Study design

Cross sectional study was done at MNH ANC between August and

October 2001.

Study population

Pregnant women who attended antenatal clinic at MNH for the first time between August and October 2002.

Sample size

By the formula N= (z/D) 2 p (1-p)

Where N= sample size.

Power of the study at 80%

Z =1.96 for confidence interval of 95%

D = margin of error + 5%

P = prevalence quoted highest 10%

N= (1.96/0.05) 2 (0.1) (0.9) = 138.2976 ≈ 139

Expecting a response rate of 75%

Adjusting for expected drop out $\frac{139 \times 100}{75}$ =184.33

Sample size was= 185

Sampling technique:

Systematic sampling technique was used among those attending the clinic for first time

i.e. New patients per clinic = 20

Total number of clinics in a week was four

Total number of new attendees is 20 x 4 = 80

Duration of the study was three months

Total number of new attendees was: 80 x4 x 3 = 960.

Estimated sample size required was 185

Total number of attendees divided by sample size gave 5 as the width of the interval. i.e. 960 / 185 =5

Every fifth new attendee on a registration form was included in a study making an enrolment of four pregnant women per clinic.

1st client was the first to appear on the day of commencing the study.

Data collection:

Two research assistants (Nurse Midwives) were trained on recruitment procedures, filling questionnaires and proper instructions on collection of urine samples. Two training sessions of four hours duration each were conducted, one before and another after the pilot study. The one conducted before the pilot study emphasised on how to properly fill the questionnaire and collect urine samples that include:

(i) To have a full bladder for at least three to four hours before collecting a urine sample

(ii) Why morning specimen will be used in trying to achieve this goal.

(iii) The importance of keeping the container closed until the time of

collecting urine sample so as to maintain sterility.

(iv) Midway without interrupting the stream, a sterile container is plugged into the stream of urine and a sample collected.

(v) Importance of sending the sample to the laboratory in time.

(vi) Emphasising the specimen to be brought within three hours of collection.

(vii) How to elicit tenderness on the lumbar region."

Informed consent and ethical consideration

After the woman was selected, the objectives of the study were explained including the main procedures, methodology, issues of confidentiality and how she will benefit from the study (Appendix 1). After agreeing to participate in the study a written informed consent was obtained from her by signing a pre-designed consent form (Appendix II). A separate sheet was used to record pregnant women's particulars and identification numbers for easy follow up of those needing treatment after the results. Every pregnant woman was instructed to request for her results during the next visit. This facilitated easy access of those needing treatment. The research assistants interviewed the pregnant women using a structured questionnaire (Appendix III). The researcher crosschecked all questionnaires on the day of enrolment and any missing information was filled when the woman brought the sample the

next day.

Urine samples collection

Explanation was given to each woman on the necessity of having a well-collected urine sample as detailed above in the training session. The two research assistants were responsible with educating the women on how to properly collect a urine sample. The researcher attended some of the sessions. A sterile bottle with a screw cap was given to a pregnant woman after accepting to participate and signing a consent form for the study. A bus fare was provided so that the woman could bring the specimen the next day. Once specimens were received they were sent to the laboratory within one hour for processing.

Laboratory procedures.

One technician was responsible for processing all the urine samples without being aware of the objectives of the study. The specimens were sent to the laboratory by the researcher / research assistant within one hour of arrival and were kept in the refrigerator before processing if necessary.

Urinalysis

1.The specimens were evaluated for presence of nitrite and leucocyte

esterase activity using DiaScreen dipstick (CHRONIMED Minneapolis) using manufacturers instructions.

2.The nitrite test was scored positive when the reagent square turned into pink colour, and the leukocyte esterase test was scored positive when the reagent square matched the colour-coded "+"or"++". A test that was scored zero or trace was considered negative[19].

Urine culture

Using a standard loop, 1µl of well-mixed urine was inoculated into Cysteine Lactose Electrolyte Deficiency medium (CLED). The inoculated plate was incubated aerobically at 37°C for 18 –24 hours. Presence of 10^5 colony-forming units per millilitre of urine was interpreted as indicating significant bacteriuria[25]. The isolated bacterial colonies were identified using standard bacteriological techniques[26,28]. Antimicrobial susceptibility patterns were tested using Stokes method and reported as sensitive or resistant[27].

Pilot study

A pilot study was carried out to test the questionnaire, specimen collection and processing procedure. The questionnaire was pre-tested three times before obtaining a final version used in collecting the data. After getting a final version of the questionnaire, a total of twenty

pregnant women were interviewed and requested to bring the urine samples the next morning. Sixteen women brought the samples at the specified time. Four women did not bring the urine samples. Culture revealed significant bacteriuria in three samples during the pilot study.

Exclusion criteria:

1. Pregnant women who were on any form of antibiotic treatment in the preceding two weeks before the study were excluded.
2. Pregnant women who had dsyuria and lumbar pain that suggested symptomatic bacteriuria

NB. For lumbar pain objective examination to elicit tenderness was performed.

Definition of terms:

1 Asymptomatic bacteriuria was diagnosed when there was no symptoms reported by a pregnant woman but urine culture was positive.

2. A urine culture was defined as positive when 10^5 colony-forming units of a single uropathogen per milliliter of urine were isolated.
3. A urine culture was defined as contaminated when there was a mixed growth of any density or a pure culture of less than 10^5 colony-forming units per milliliter of urine.

4. A urine culture was defined as negative when there was no bacteria growth.
5. For the purpose of this study all contaminated samples were classified as negative.
6. A nulliparous woman is one who has not delivered an offspring weighing 500g or more or a 24 weeks gestation or more[29].
7. A primipara woman is one who has given birth to one new born weighing 500g or more or 24 weeks gestation or more[29].
8. A multiparous woman is one who has given birth more than once of an offspring weighing 500g or more or 24 weeks gestation or more.[29]
9. Married in this study refers to staying with the partner under the same roof.

DATA ANALYSIS:

Mini-analysis

Socio-economic status

A researcher designed the score chart for the analysing SES as there was no set up standard for this country due to inconsistency of income. (Appendix IV)

1.Each item in a questionnaire was given a score.

2.The total highest score was 24,and the total lowest score was 2.

3.The score less or equal to 14 was taken as low socio-economic status.

4.The score from 15 to 20 was taken as medium socio-economic status.

5.The score equal or greater than 21was taken as high socio-economic status.

Social class was graded as low, medium or high.

Overall analysis

This was done using EPI-INFO-VERSION -6 statistical programme

Sensitivity, specificity, positive predictive value and negative predictive value were used in evaluating the performance of dipstick methods in diagnosing ABU taking urine culture as the gold standard.

$$\text{Sensitivity} = \frac{\text{True positive x100\%}}{\text{True positive + False Negative}}$$

$$\text{Positive predictive value} = \frac{\text{True Positive x100}}{\text{True positive + False positive}}$$

$$\text{Specificity} = \frac{\text{True Negative x 100\%}}{\text{True Negative + False positive}}$$

$$\text{Negative Predictive Value} = \frac{\text{True Negative x 100}}{\text{True Negative + False Negative}}$$

Variables analysed

Dependent variables: Urinalysis and urine culture results

Independent variables: Age, parity, socio-economic status, level of

education and marital status.

Statistical analysis-Chi square test was used to compare proportion and p-value of < 0.05 was considered significant

Limitations of the study:

1. Lumbar pain could be difficult to differentiate with backache, which is a common symptom among pregnant woman.
2. Socio-economic status though strongly associated in most studies with asymptomatic bacteriuria its evaluation might be very unreliable due to inconsistency of source of income in the society studied. Furthermore there is no set up standard for evaluating socio economic status in the country.
3. Some problems may be encountered during collection of urine sample despite the intense training on how to properly collect it.

Ethical considerations

1. Pregnant women who were found with significant bacteriuria were offered prescriptions according to sensitivity pattern of the uropathogen isolated.
2. Pregnant women with symptoms for bacteriuria were included in the study to enable them obtain the appropriate treatment after culture and sensitivity results. However they were excluded during

analysis.

3. Identity number was offered to each participant for ensuring confidentiality.

Approval by College Research and Publication Committee of MUCHS was sought, and permission was granted.

RESULTS

During the study period a total of 184 pregnant women were recruited. Ten women had positive symptoms and signs suggestive of urinary tract infection and were excluded from the study. Nine women did not bring urine samples. So a total of 19 women were excluded leaving 165 women who were included in the analysis. A total of 38 women had significant bacteriuria giving ABU prevalence of 23.0%.

Prevalences of ABU in relation to socio demographic characteristic.

Table I shows the prevalence of ABU in different socio-demographic groups of pregnant women. The prevalence of ABU was 30.4%, 21.6%, and 22.2% for the age groups <20, 20-30, >30 years respectively (p-value =0.659). The prevalence of ABU was 25.0% and 23.1 % among pregnant women in medium and low socio economic status respectively and none in the high socio economic class. Among 70 nulliparous, 17 (24.3 %) had ABU, while among 84 women of parity one to four 19 (22.6%) had ABU. Among the 11 women who had five or more previous deliveries 2 (18.2%) had ABU. There was no significant association between parity and the prevalence of ABU. (p-value =0.895)

Table I. Prevalence of ABU in relation socio-demographic characteristics of pregnant women.

Character	Urine culture				Total	p-value
	Positive		Negative			
	n =38	(%)	n=127	(%)		
Age (years)						
<20	7	30.4	16	69.6	23	
20-	19	21.6	69	78.4	88	p= 0.658
30<	12	22.2	42	77.6	54	
Socio economic status						
Low	27	23.1	90	77.9	117	P=0.799
Medium	11	25.0	33	75.0	44	
High[a]	0	0	4	100	4	
Parity						
Nulliparous	17	24.3	53	75.7	70	
Para 1-4	19	22.6	65	77.4	84	p=0.85
Para≥5	2	18.2	9	81.8	11	
Education						
No education	4	28.6	10	71.4	14	
Primary	24	20.7	92	79.3	116	p=0.54
Secondary	10	28.6	25	71.4	35	
Martial status						
Married	34	23.4	111	76.6	145	
Unmarried	4	20.0	16	80.0	20	Fisher's exact p=0.553

[a] Not included in analysis due to small number (n=4)

The prevalence of ABU was 28.6%, 20.7%, and 28.6% for those with no formal education, primary education and secondary education and above respectively. There was no statistically significant difference in prevalence between the educational groups (p-value= 0.54).

The prevalence of ABU among pregnant women who were living with a partner was 23.4% compared to 20.0% among pregnant women who were not living with a partner. There was no statistically significant difference between the two marital status groups. (p-value =0.523)).

Performance of dipstick in diagnosing ABU.

Tables II and III show the sensitivity, specificity, positive and negative predictive values of nitrite reductase test and presence of leucocyte esterase when compared with urine culture. The sensitivity, specificity, positive and negative predictive values of nitrite reductase was 31.5%, 89.8%, 48.0%, and 81.4% respectively while that of leucocyte esterase was 44.7%, 78.7%, 38.6%and 82.6% respectively.

Table II.Sensitivity / specificity of nitrite reductase test compared to urine culture

	Urine culture				Total
	(+)	%	(-)	%	
Nitrite reductase					
+)	12	31.6	13	10.2	25
(-)	26	68.4	114	89.8	140
Total	38	100	127	100	165

Table III.Sensitivity/specificity of leucocyte esterase detection compared to urine culture.

	Urine culture				Total
	(+)	%	(-)	%	
Leucocyte esterase					
(+)	17	44.7	27	21.3	44
(-)	21	55.3	100	78.7	121
Total	38	100	127	100	165

Table IV shows the sensitivity, specificity, positive and negative predictive values when leucocyte esterase and nitrite reductase tests results are concordant compared with urine culture. The sensitivity, specificity, positive and negative predictive values was 10.5%, 97.6%, 57.1%, and 78.5%respectively. The sensitivity, specificity, positive and negative predictive value of the testing strategy when the reactivity of either leucocyte esterase enzyme or nitrite reductase is considered were 65.8%, 70.8%, 40.3%and 77.7% respectively (Table V).

Table IV. The sensitivity/specificity when nitrite and leucocyte esterase tests are concordant compared to urine culture.

		Urine culture				Total
		(+)	%	(-)	%	n
Concordant nitrite &leucocyte esterase						
	(+)	4	10.5	3	2.4	7
	(-)	34	89.5	124	97.6	158
Total		38	100	127	100	165

Table V. The sensitivity/specificity based on the reactivity of either nitrite or leucocyte esterase assays compared to urine culture

	Urine culture				Total
	(+)	%	(-)	%	n
Nitrite or leucocyte					
(+)	25	65.8	37	29.1	62
(-)	13	34.2	90	70.9	103
Total	38	100	127	100	165

Klebsiella spp was the commonest isolated bacteria contributing to 44.7% of all isolates followed by *Escherichia coli, Staphylococcus spp Enterobacter spp, Proteus spp* isolated in 23.2 %, 18.4%, 7.9% and 5.35. % respectively. (Table VI)

Table VI. Frequency distribution of microorganism causing ABU.

Organism	Number of isolates	Frequency
Klebsiella spp	17	44.7%
E. coli	9	23.7%
S. aureus	7	18.4%
Enterobacter spp	3	7.9%
Proteus spp	2	5.3%

The antimicrobial sensitivity of *Klebsiella spp* was 76.5%, 70.5%, 75.5%, 41.2% and 23.5 % to gentamicin, cefaclor nalidixic acid, nitrofurantoin and augumentin respectively. For the *E.coli* isolates, 88.8%, 66.6%, 77.7%, 33.3% and 33.3% were sensitive to gentamicin, nalidixic acid, nitrofurantoin, augumentin and cefaclor respectively. For the *Proteus spp* isolates only 50% were sensitive to cefaclor while the *Enterobacter spp* isolates were 100%, 100%, 66.6%, 66.6% and 33.3% sensitive to gentamicin, nitrofurantoin, cefaclor, nalidixic acid and augumentin respectively (Table VII)

Table VII.The frequency distribution of bacterial pathogens isolated and antimicrobial sensitivity

Organism	Antimicrobiai agent						
	Cefaclor	Augumentin	Gentamicin	Nitrofurantoin	Nalidixic acid	Cloxacillin	Erythromycin
Klebsiella spp	12(70.5%)	4(23.5%)	13(76.5%)	7(41.2%)	13(76.5%)	ND	ND
E.coli	3(33.3%)	3(33.3%)	8(88.8%0	7(77.7%)	6(66.6%)	ND	ND
Proteus spp	1(50%)	0	0	0	0	ND	ND
Staphylococcus spp	ND	ND	ND	ND	ND	7(100%)	6(85.5%)
Enterobacter spp	2(66.6%)	1(33.3%)	3(100%)	3(100%)	2(66.6%)	ND	ND

Percentage in brackets represents a proportion of isolates susceptible to antimicrobial agent; ND= Not done
Cefaclor = Second generation cephalosporin; Augumentin =Ampicillin +clavulunic acid

DISCUSSION

The prevalence of ABU in pregnant women has been reported to vary from 2% to 23.9 % in different studies[1,2,7.8,9,10]. It is also well established that when not clinically managed 20–40 % of pregnant women with ABU may develop symptomatic disease with the following complications, cystitis, pyelonephritis and an increased risk of preterm delivaries[2,3,4,15] esterase.

In this study the prevalence of ABU was 23%. This was higher than most of other findings with prevalence ranging between 2% to10 %,[1,2,6,8,11] except for a study done in Nigeria that reported a prevalence of 23.9%[9]. One of the possible explanations could be the fact that most of the mothers attending the MNH clinic had a complicated pregnancy, and were in the low SES. (As evidenced by the distribution of sample according to socio economic status where more than 70% belonged to low socio economic status group and the remaining 26% to middle socio economic group with less than 3% belonging to the high socio economic group.)

In this study there was no significant association between ABU and socio demographic characteristics including age in agreement with a study by Olusanya et al[9]. Few studies have reported an inverse

association of the prevalence of ABU with age above 30 years[12]. This difference in findings could be explained by the difference in the socio economic status of the societies where the study was conducted and this society where this study was conducted.

Although many studies have shown a strong association between ABU and SES[1,12,13], there was no significant association between SES and ABU in this study. This could be explained by the difficulty in evaluating the SES in our society due to inconsistency in the source of income. Similar problems were encountered in other studies[13]. In the only study done in Dares salaam the prevalence of ABU among pregnant women was high in the middle socio economic class group[11].

In this study there was no significant association between parity and ABU. Though some studies have shown associations, the associations are not consistent; Olusanya et al[9] in Nigeria found significant difference between nulliparous and primipara pregnant women with nulliparous women affected more frequently than primipara, whereas a study done in Trinidad, the increasing parity was associated with increased prevalence of ABU[13].

There was no significant association between level of education and the prevalence of ABU in the current study. In a study among black

American population the prevalence of ABU was found to be inversely associated with education beyond high school[12]. The level of education of the study population in the current study where only 20% had attained secondary education could explain the observed difference with no such association in this study. When stratified further, it was found that less than 3% managed to study beyond secondary school in the current study making comparison even more difficult.

As evaluated in this study, the performance of Dipstick method using leucocyte esterase and nitrite test in diagnosing ABU was poor. Nitrite reduction test when considered alone had a sensitivity of 31.5% and specificity of 89.8%. On the other hand leucocyte esterase test when considered alone had a sensitivity of 44.7% and specificity of 78.7%. When the results of two assays are concordant the sensitivity fell to 10.5% while the specificity rose even further to 97.6%. When either of the assays reactivity is considered the sensitivity was 65.8% and specificity of 70.8%. A good screening test needs an excellent sensitivity, specificity, cost effectiveness and should be easy and quick to perform. In this study these assays had very poor sensitivity ranging between 10.5% when assays are concordant and 65.8% when either leucocyte esterase or nitrite reductase is used. With the sensitivity of 10.5% about 90% of women with ABU will be missed, but less than 3% will be

labelled as having ABU due to high specificity of 97.6%. When either leucocyte esterase strip or nitrite reduction reactivity was used to indicate the presence of ABU the sensitivity reached 65.8% missing about 35% of women with ABU. This on the other hand compromised the specificity to 70.8%, making approximately 30% of the women without ABU being labelled as having ABU while they don't have it. The results of this study are similar to those by Tincello et al who obtained a sensitivity ranging between 8.2% when concordant leucocyte esterase and nitrite reduction tests were used and a sensitivity of 67.5% when either leucocyte esterase or nitrite reductase were used[20]. But they are slightly higher than those of Shelton et al, who found a sensitivity of 45% when either of the assays was considered positive[24]. Batchman et al in USA found that urine dipstick with nitrite reductase and leucocyte esterase had a sensitivity of 50.9%and specificity of 96.9%[14]. Robertson et al found that nitrite reduction assay had a sensitivity of 43.4% slightly higher than in this study where the sensitivity was 31.5%[6]. The leucocyte esterase assay in that particular study had a sensitivity of 77.45%, which is higher than in the current study of 44.7%[6]. From the above discussion there are no good screening assays for ABU. However the high prevalence of ABU in this study may justify the use of urine culture as a diagnostic tool especially in high-risk ANC. Further studies on cheap and rapid tests will have to be developed and evaluated

including the molecular biological techniques like urinary interleukin-8 which are current in progress[28].

The commonest microorganism isolated in this study was *Klebsiella spp.*, which contributed 44.7% of all isolates, followed by *E. coli* contributing 23.2% and *Staphylococcus aureus* 18.4%. Many studies have reported *E.coli* as a major causative organism in ABU[2, 3,4,14]. There are studies however that have reported organism other than *E.coli* as a major causative organism. Chongosomi et al in Thailand found coagulase negative staphylococci as a major causative agent comprising 46% followed by *E.coli* 24%. Olusanya et al in Nigeria found that *Staphylococcus spp* were responsible for 47% of all cases of ABU followed with *E.coli*, which contributed 21.3%[9]. Orrinet et al in Trinidad found *Staphylococcus spp* as a major causative microorganism contributing 40% of all isolates followed by *E.coli* 32%[13]. These differences could be explained probably by the nature of women studied majority of who were of high-risk pregnancies. In the study done in Dares salaam twenty years ago *Klebsiella spp* was second most common organism causing ABU after *E.coli* each accounting for 31.3% and 46.9% respectively[11].

In this study *Klebsiella spp*, which was the commonest microorganism

isolated, was not fully sensitive to any antimicrobial agent tested including, cefaclor 70.5%, gentamicin 76.5% and nalidixic acid 76.5 %. Regarding *E coli* isolates, 88.8% were sensitive to gentamicin, 77.7% were sensitive to nitrofurantoin and 66.6% were sensitive to nalidixic acid. All isolates of *Enterobacter spp* were sensitive to gentamicin and nitrofurantoin. Of the *Proteus spp isolated* only 50% were sensitive to cefaclor otherwise they were resistant to the rest of the drugs tested. All *Staphylococcus spp* were sensitive to cloxacillin while 85% of the isolates were sensitive to erythromycin. When the results of this study are compared to another study done twenty years ago in Dar es Salaam on ABU, the drugs still in use that were tested were Nitrofurantoin and Nalidixic acid[11]. The sensitivity of the isolates by then was 100% to Nalidixic acid. *E.coli* and *Klebsiella spp* isolated by then had sensitivity of 100% and 90% to Nitrofurantoin respectively[11]. In a study by Olusanya' et al in Nigeria[9], the antimicrobial agents tested still in use were Nalidixic acid and nitrofurantoin, *Klebsiella spp* and *E.coli* had sensitivities of 94.9% and 98.5% where as in this study their sensitivities were 76.5%and 41.2% respectively. While nalidixic acid could still have some use, the use of nitrofurantoin in pregnancy needs to be considered cautiously.

Twenty to forty percent of untreated ABU diagnosed patients will

progress to symptomatic disease,[1,2] and only 1% to 2% of bacteriuric pregnant women acquire the infection during pregnany[1]. From the findings in this study gentamicin is the drug that could be used as the first line while waiting for culture and sensitivity results. This could be combined with erythromycin or cloxacillin for taking care of *Staphylococcus spp.* Gentamicin attains high renal tissue concentration, cross the placenta and theoretically it could be ototoxic and nephrotoxic to the foetus. So there is a necessity of performing renal function tests for determining the serum concentration of the drug to adjust for toxicity.

CONCLUSION

ABU represents a considerable health problem among pregnant woman attending ANC at MNH as evidenced by the high prevalence of the condition. There were no any socio-demographic characteristics in this study that showed a significant association with ABU. The commonest microorganism isolated in this study was *Klebsiella spp.* Among the antibiotics tested there was no single agent that was 100% effective on all isolates. However gentamicin could be effective in about 70% of gram-negative bacteria while cloxacillin could be selected for ABU caused by *Staphylococcus aureus*. The leucocyte esterase and nitrite tests did not have satisfactory sensitivity to warrant its use as a screening assay.

RECOMMENDATION

1. There is a need for screening pregnant women attending MNH - ANC for ABU given the high prevalence of 23%.
2. The leucocyte esterase and nitrite dipstick strips are not sensitive enough for screening ABU in these pregnant women. While looking for an ideal screening test urine culture can be used because of the high prevalence of ABU in these high-risk pregnant women.

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