Research paper

Bacterial Profile and asymptomatic bacteriuria among pregnant women in Africa: A systematic review and meta analysis

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ABSTRACT

Background: Different physiologic changes that occur during pregnancy, such as Hydroureter, dilatation of the renal pelvis, glycosuria and aminoaciduria, and low urine production predispose pregnant women for ascending urinary tract infection. Globally, 2% to 15% of the pregnant women have urinary tract infection without specific symptoms. Therefore, this study aimed to estimate the prevalence of asymptomatic bacteriuria (ABU) in pregnant women in Africa.

Methods: Systematic search of published studies done on PubMed, EMBASE, Web of Science, SCOPUS, PsychInfo, CINAHL, and google scholar for gray literature. All published observational studies until October 30, 2020 were included. This meta-analysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Quality of studies was assessed by modified Newcastle-Ottawa Scale (NOS). Meta-analysis was carried out using a random-effects method with the double arcsine transformation approach using the STATA™ Version 14 software. Trim and fill analysis was done to correct presence of significant publication bias. The study protocol is prospectively registered on PROSPERO, registration number CRD42020212601.

Findings: From 3393 obtained studies, 48 studies from 12 African countries involving 15, 664 pregnant women included in this Meta-analysis. The overall pooled prevalence of asymptomatic bacteriuria among pregnant women in Africa after correction for publication bias by trim and fill analysis was found to be 11.1% (95% CI: 7.8, 14.4). The most common bacterial isolates involved in the etiology of ABU was Escherichia coli with pooled prevalence 33.4% (95% CI: 27.3 - 39.4)

Interpretation: Asymptomatic bacteriuria is substantial among pregnant women in Africa. Therefore, all pregnant women should be tested for the presence of asymptomatic bacteriuria. A screening program must be based not only on the incidence but also on a cost-efficacy evaluation and a microbiological evaluation.

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1. Introduction

Due to the hormonal and physiological changes during pregnancy: women’s are more susceptible to infections. Different physiologic changes that occur during pregnancy, such as Hydroureter, dilatation of the renal pelvis, glycosuria and aminoaciduria, were responsible for the stasis of urine and create the best medium for the growth of different species of bacteria [1,2]. Also, low urine osmolality due to physiologic change facilitate bacterial colonization and increase ascending infection increased in addition to the dysfunctional vesicoureteral reflex and ureteric valves [2].

Asymptomatic bacteriuria (ABU) in pregnancy is defined as the presence of ≥ 100,000 colony-forming units (CFU) /ml of urine taken from a clean catch midstream urine specimen in the absence of specific symptoms of acute urinary tract infection [1,3]. Globally, it happens in 2% to 15% of all pregnancies [3]. Pregnancy boosts the progression from asymptomatic to symptomatic bacteriuria. Due to this, ABU is a main risk factor for the development of urinary tract infections (UTIs) [4,5].

The most common organism responsible for 75–90% of bacteriuria in pregnancy is Escherichia coli [5,6]. Other microbial agents include, Proteus mirabilis, group B Streptococcus, Pseudomonas
Research in context

Evidence before this study

We systematically searched PubMed, EMBASE, Web of Science, SCOPUS, PsychInfo, and CINAHL to identify published studies. Grey literature searching done by Google and Google Scholar. All published observational studies written in English language, published until October 30, 2020 and studies that reported the prevalence of asymptomatic bacteriuria among pregnant women in Africa were included. The overall pooled prevalence of asymptomatic bacteriuria among pregnant women in Africa after corrected for Duval and Tweedie’s trim and fill analysis and was found to be 11.1% (95% CI: 7.8, 14.4).

Added value of this study

Our study confirmed that the prevalence of asymptomatic bacteriuria among pregnant women was significant and Escherichia coli is the most common bacterial isolates involved in the etiology of ABU.

Implications of all the available evidence

The findings may have great clinical implication on importance of testing all pregnant women for the presence of asymptomatic bacteriuria and microbiological evaluation.

aeruginosa, Klebsiella pneumoniae, Streptococcus sапrophyticus, Staphylococcus aureus, and Enterococcus faecalis [7].

The maternal and fetal outcomes related to ABU are numerous. Untreated ABU result in abnormal maternal outcomes such as development of pyelonephritis in 20–50% of cases [1,4–6, 8,9], higher rate of preterm labor, chronic infection resistant to drugs, preeclampsia, anemia, chorioamnionitis, endometritis and UTI in the postpartum period [2,5,7,8]. Fetal complications associated with ABU include prematurity, Intrauterine growth restriction (IUGR), low birth weight, increase in perinatal mortality, stillbirth, mental retardation and development delay [2,4,5].

Maternal and fetal complications that may arise due to infection can be prevented by timely detection and treatment [1,4,8]. Urine culture is the gold standard diagnostic technique for ABU which occurs during pregnancy [5]. It’s recommended that three up to seven days antibiotics therapy reduces the risk of symptomatic UTI by 80 to 90% [4]. Also, antimicrobial treatment of ABU will reduce the risk of risk of having a low birth weight baby from 15% to 5% and pyelonephritis from 20 to 35% to 1–4% [2].

Since the risk of asymptomatic bacteriuria was increased by prior history urinary tract infection, pre-existing diabetes mellitus, increased parity, and low socioeconomic status [10]; understanding the magnitude and bacterial isolates of asymptomatic bacteriuria in Africa is important in reducing the complications related to it. Even though, there were several studies conducted on the prevalence of asymptomatic bacteriuria, there are disagreements on the result of the studies. Therefore, this meta-analysis was aimed to estimate the overall prevalence of asymptomatic bacteriuria among pregnant women in Africa.

2. Methods

2.1. Study protocol

The study protocol was registered and published in the PROSPERO international prospective register of systematic reviews with registration number (CRD42020212601). This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for literature search strategy, selection of studies, data extraction, and result reporting [11]. To download, organize, review, and cite related articles Endnote (version X8) reference management software for Windows was used.

2.2. Study design and search strategy

We systematically searched PubMed, EMBASE, Web of Science, SCOPUS, PsychInfo, and CINAHL to identify published studies. The following search key terms were used to include studies from above mentioned database: “pregnant women”, “pregnant mother”, “pregnancy”, “Urinary tract infection”, “bacteriuria”, “UTI”, “asymptomatic bacteriuria”, “bacterial profile”, “Asymptomatic Urinary Tract Infection”, and “Uropathogens”. The Boolean operators (AND and OR) combination were used to search databases. The PubMed search terms with their Boolean operators of this review was attached as an additional file (Additional file 1). In addition, manual hand searching done by Google and Google Scholar to include studies that reported the prevalence of asymptomatic bacteriuria among pregnant women in Africa.

2.3. Study selection

The relevant studies were obtained after titles and abstracts screening of retrieved record. The screening was done by two independent authors (N.A, and T.T) and when the discrepancies occur it was resolved by the third authors (M.T)

2.4. Eligibility criteria

All published observational studies written in English language, published until October 30, 2020 and studies that reported the prevalence of asymptomatic bacteriuria among pregnant women in Africa were included.

Studies were excluded if:

1. Studies that reported the prevalence of ABU without laboratory test
2. Methodologically poor studies with 0–5 points on Newcastle-Ottawa Scale (NOS) were excluded

2.5. Quality assessment of included studies

The quality of each study was assessed using the modified Newcastle-Ottawa Scale (NOS) for cross-sectional studies [12]. The scale contains eight sections, and evaluated the included articles based on the selection, comparability, exposure assessment, and outcome. The point score and interpretation were: Points of 0–5 considered as low quality, 6–7 as moderate quality and 8–10 as high quality. We included articles with a minimum score of 6 on NOS

2.6. Data extraction

We prepared a form in Microsoft Excel 2013 spreadsheet for data extraction. The format was prepared to extract the following important variables from the articles: The first author’s name, publication year, region, design, type of sample collected, sample size, sampling method, the prevalence of asymptomatic bacteriuria and microorganisms involved in bacteriuria. The extraction was done by two independent authors (N.A, and T.T) and any discrepancy that occur during the extraction process was resolved by a third author (M.T).

2.7. Statistical analysis

An inverse-variance weighted random effects meta-analysis model using the double arcsine transformation approach [13] was
used to pool the prevalence of asymptomatic bacteriuria among pregnant women in Africa. Statistical analyses were done by using Stata version 14.0. The heterogeneity test of the studies was assessed using Higgins I-squared (I^2) and p-value. The value of I^2 was taken as 0–24% may not be important, 25–49% indicates moderate heterogeneity, 50–75% indicates substantial heterogeneity and over 75% indicates considerable heterogeneity [14]. The Source of heterogeneity was analyzed by subgroup analysis and Meta-regression. Publication bias was tested statistically by Egger's tests and viewed graphically by the funnel plots. Due to presence of publication bias the result was corrected by Duval and Tweedie's trim and fill analysis.

2.8. Ethics approval and consent to participate

Not applicable.

3. Role of the funding source

There was no funding source for this study.

4. Search results

Initially, a total of 3393 studies were retrieved from the databases and manual searching. From this, 30 duplicate were found and removed. The remaining 3363 articles were screened by their title and abstract and 3276 irrelevant studies were removed. Eight-seven full-text articles were assessed for eligibility, and 39 of them were excluded due to not reporting the outcome of interest, poor methodological quality and not based on laboratory. Finally, a total of 48 studies fulfilled the inclusion criteria and enrolled in the study (Fig. 1).

5. Study characteristics

A total of 48 articles with 15,664 pregnant women from 12 African countries was included in this systematic review and meta-analysis. Among included studies 46 were cross-sectional and 2 studies were case control study design. The sample size across the studies ranges from 100 [15] to 1830 [16] pregnant women. The highest number (27) of studies was included from West Africa and only one study was obtained from the Southern region of Africa. The lowest prevalence 3.8% of ABU was reported in Uganda [17] and the highest 63.3% was reported from Nigeria [18] (Table 1).

5.1. Prevalence of asymptomatic bacteriuria among pregnant women

The overall pooled prevalence of asymptomatic bacteriuria among pregnant women in Africa was 18% (95% CI: 15, 21) with heterogeneity index (I^2) of 97.47% (p < 0.001) (Fig. 2). Since the Eggers test was found significant, the final pooled prevalence was corrected for Duval and Tweedie's trim and fill analysis and was found to be 11.1% (95% CI: 7.8, 14.4).

5.2. Subgroup analysis

Subgroup analyses revealed a marked variation in the region of Africa with highest prevalence 22% (95% CI: 17, 28) in West Africa.
The presence of publication bias was evaluated graphically by funnel plots and statistically tested for the presence of small study effect by Egger test. The funnel plot indicated the presence of publication bias (Fig. 4) and after adjusting for publication bias by trim and fill analysis the funnel plot appeared symmetrical (Fig. 5). The presence of small study effect was evident by Egger test with p < 0.001.

### 6. Publication bias

The presence of publication bias was evaluated graphically by funnel plots and statistically tested for the presence of small study effect by Egger test. The funnel plot indicated the presence of publication bias as the graph appear asymmetrical (Fig. 4) and after adjusting for publication bias by trim and fill analysis the funnel plot appeared symmetrical (Fig. 5). The presence of small study effect was evident by Egger test with p < 0.001.

### 6.1. Type of bacterial isolates

Sixteen different types of bacterial isolates were extracted from studies included in this systematic review and meta-analysis. The most common bacterial isolates involved in the etiology of ABU in this systematic review and meta-analysis was *E. coli* with pooled prevalence 33.4% (95% CI: 27.3 - 39.4) (Table 3).
anatomic abnormalities, age, previous history of UTI, multiple pregnancies, diabetes, lack of personal hygiene and socioeconomic status [64].

*E. coli* was the most common bacterial isolate which cause ABU in this systematic review and meta-analysis. This is similar with the report from Infectious Diseases Society of America Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults [63] and WHO [65], and Meta analyses of randomized clinical trials [66]. For health women *E. coli* had lower levels of virulence factors such as specific lipopolysaccharide, adhesions, toxins, mobility factors, and other proteins. But due to physiologic change in pregnancy the strain might have a higher level of virulence [64].

Although this systematic review and meta-analysis presented up-to-date evidence on prevalence of ABU in Africa, it might have faced the following limitations. First, lack of studies from central African countries and only one study included from South region of Africa, this may affect the generalizability of the finding to Africa and warrants further investigation in central and south regions of Africa on prevalence of ABU among pregnant women. Secondly, significant heterogeneity was observed cross-study despite the analysis was
conducted on random effect Meta-analysis model to manage it. Thirdly, there is significant publication bias in this meta-analysis which is evaluated graphically by funnel plots and statistically tested for the presence of small study effect by Egger test due to this the result should be interpreted cautiously. Hence, the pooled prevalence was corrected by Duval and Tweedie’s trim and fill analysis. Finally, lack of similar meta-analysis at other continents to compare with our finding which might have influenced the discussion of our result.

The results of this meta-analysis indicated the prevalence of asymptomatic bacteriuria is substantial among pregnant women in Africa. Therefore, pregnant women should be screened for bacteriuria by urine culture at least once in early pregnancy. Positive pregnant women should receive standard antibiotics regimen and thereafter

Table 2
Meta-regression analysis of factors affecting between-study heterogeneity.

| Heterogeneity source | Coef | Std. Err. | P-value |
|----------------------|------|-----------|---------|
| Publication year     | -0.0722 | 0.0573 | 0.214 |
| Sample size          | -0.0003 | 0.0006 | 0.618 |

Table 3
Type of bacterial isolates extracted from studies included in the systematic review and meta-analysis of asymptomatic bacteriuria among pregnant women in Africa.

| S/N | Type of microorganisms [Ref] | Number of included study | Total sample size | Pooled prevalence (95% CI) | Study heterogeneity |
|-----|-----------------------------|--------------------------|------------------|---------------------------|-------------------|
| 1   | *E. coli* [14 – 21,23 – 25,28 – 34,38,39,42,44 – 53,55,56,58 – 61] | 37 | 2723 | 33.4 (27.3 – 39.4) | 92.8 < 0.001 |
| 2   | *S. aureus* [14 – 18,20 – 25,28 – 30,32 – 34,38,44,47,53,55,56,58 – 61] | 32 | 2634 | 23.9 (18.9 – 29.0) | 91.6 < 0.001 |
| 3   | CoNS [18,25,28 – 30,34,51] | 7 | 453 | 20.9 (8.0 – 33.8) | 91.1 < 0.001 |
| 4   | Klebsiella Spp [14,17,20 – 24,29,30,34,38,44,51,52,56,58 – 60] | 19 | 1673 | 12.2 (8.0 – 16.5) | 90.1 < 0.001 |
| 5   | *S. saprophyticus* [40,52,56,59 – 61] | 6 | 260 | 11.1 (7.3 – 14.9) | 0 0.524 |
| 6   | *C. albicans* [14,15,20,36,49,52,56,58,61] | 7 | 1311 | 10.0 (6.6 – 13.5) | 69 0.004 |
| 7   | *S. faecalis* [20,33,44,48] | 4 | 212 | 9.3 (5.0 – 18.1) | 85 < 0.001 |
| 8   | *Proteus mirabilis* [18,23,24,28,32,34,42,44,46,48,50,52,53,56,61] | 15 | 873 | 9.3 (5.6 – 12.9) | 80.7 < 0.001 |
| 9   | Streptococci species [15,25,28,35,40,49] | 6 | 492 | 9.0 (6.5 – 11.5) | 0 0.504 |
| 10  | Other coliforms [18,47,53,59] | 4 | 182 | 8.7 (1.1 – 16.3) | 66.1 0.031 |
| 11  | *K. pneumoniae* [15,16,18,25,28,31,32,34,35,39,44 – 46,55,60,61] | 16 | 1050 | 6.9 (3.9 – 9.9) | 72 < 0.001 |
| 12  | *Staphylococcus epidermidis* [20,42,55] | 3 | 82 | 6.7 (1.3 – 12.1) | 0 0.730 |
| 13  | *Proteus spp* [14,15,17,20,21,29,30,33,38,43,49,51,55,58] | 15 | 1801 | 6.2 (3.8 – 8.6) | 75.3 < 0.001 |
| 14  | *Pseudomonas spp.* [14,46 – 18,20,28 – 30,33,38,44,45,46,55,60,56,65] | 16 | 1375 | 4.7 (3.6 – 5.8) | 31.8 0.108 |
| 15  | *C. freundii* [18,28,35,56] | 4 | 173 | 3.3 (0.6 – 5.9) | 0 0.455 |
| 16  | *Enterococcus* [16,20,32,35,42,49,59,60,61] | 9 | 345 | 3.1 (1.2 – 5.1) | 6.7 0.379 |

CoNS* = Coagulase negative *Staphylococci.*
periodic screening for recurrent bacteriuria should be undertaken after therapy.

8. List of abbreviations

ABU: Asymptomatic bacteriuria, CoNS: Coagulase negative Staphylococci, NOS: Newcastle Ottawa Scale, PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses, UTI: Urinary Tract Infection,

9. Data sharing statement

The data analyzed during the current systematic review and meta-analysis is available from the corresponding author on reasonable request.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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There was no funding source for this study.

Contributors

NA developed the protocol and involved in the design, selection of study, data extraction, quality assessment, statistical analysis, results interpretation and developing the final and initial drafts of the manuscript, TT, MT, TL, GD, and MS involved in data extraction, quality assessment, statistical analysis and revising subsequent drafts. All authors read and approved the final draft of the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2021.100952.

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