

Burden of Asymptomatic Bacteriuria Amongst Nigerian Pregnant Women: A Protocol for Systematic Review and Meta-Analysis

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Protocol

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Abstract

Background

Asymptomatic bacteriuria can be a cause of adverse pregnancy and neonatal outcomes if undetected and untreated. Pregnant women are usually routinely screened with urine cultures at antenatal booking. However, the exact burden of asymptomatic bacteriuria in Nigeria is unknown. Our protocol is aimed at determining the pooled prevalence of asymptomatic bacteriuria amongst Nigerian pregnant women as well as the associated risk factors and pregnancy outcomes.

Methods

Nine databases: PubMed, African Journal Online, Google Scholar, Cochrane Library, CINAHL, Embase, ResearchGate, Scopus, and Web of Science will be searched using a search strategy that is developed by combinations of MeSH terms, keywords, text words, and entry terms. Only observational studies published or retrievable in the English Language will be included. Studies must be conducted in Nigeria. The primary measurable outcome of this study is the prevalence of asymptomatic bacteriuria in pregnant women. Identified studies will be screened, selected, and deduplicated in DistillerSR. Data items will be extracted into predefined forms in the DistillerSR. Reports including Prisma flow chart, quality scores, risk of bias, and study outcomes will be generated in DistillerSR. Extracted data items will be exported into the Comprehensive Meta-analysis Software version 3 for quantitative analysis. Methodological, clinical, and statistical heterogeneity will be assessed for all the studies. Publication bias will be assessed using Funnel plots. There will be a subgroup analysis of pooled prevalence using categorical variables. The primary outcome will be expressed in pooled prevalence, standard error, variance, and 95% CI of variance. Quantitative risk factors and pregnancy outcomes will be used for meta-regression. The reporting of the systematic review and meta-analysis will be according to PRISMA 2015 Statement.

Discussion

The pooled prevalence of asymptomatic bacteriuria in Nigeria will be examined in relation to associated risk factors and pregnancy outcomes. The study will be published in a peer-reviewed scientific journal.

Trial Registration Number

This protocol is registered with the Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42020213810

Background

Asymptomatic bacteriuria is significant bacterial colonization (10^5 colony-forming units (cfu)/mL) [1–5] of urine and urinary tract but without any of the symptoms of infections. Studies have shown variations in the incidence in pregnancy which is reported to range from 2.0 % to as high as 21.0 % [1,2,6,7]. If not treated, it may progress to acute pyelonephritis in about 30 % of cases [8]. The resulting urosepsis has

been associated with various adverse feto-maternal outcomes including anaemia in pregnancy, low birth weight, and preterm birth [2,3,9,10].

The rates of asymptomatic bacteriuria may be the same in pregnant and non-pregnant women [11]. However, the course in the latter may be benign while the former will likely lead to a more adverse outcome if not treated. This is so because of the physiological changes in pregnancy that favour stasis in the urinary pathway. These changes include progesterone-induced decreased tone of the ureter, renal pelvis, and the bladder, pressure on the ureter, and displacement of the bladder from the pelvis into the abdomen by the gravid uterus [12].

The prevalence of asymptomatic bacteriuria in pregnant women is affected by many risk factors [13–15]. Some of the factors include socioeconomic status, history of recurrent urinary tract infection, diabetes mellitus, and anatomical abnormalities of the urinary tract, sickle cell disease, and retroviral disease [14–15]. Sickle cell disease has been found to even double the risk in some studies [16]. To prevent the progression of asymptomatic bacteriuria, some developed countries adopt routine urine culture at the antenatal booking clinic as a standard form of care. This, however, is not done in Nigeria. Rather urine dipstick test is the norm; probably because the magnitude of the problem at the national level is unknown, likewise the attendant economic burden.

There have been some isolated studies, with no pool, to estimate the national burden [17–21]. To bridge this knowledge gap, we aim to carry out a systematic review and meta-analysis to qualitatively and quantitatively evaluate the prevalence, assess the associated risk factors and pregnancy outcomes of asymptomatic bacteriuria in pregnancy. The result of this study will likely be useful to health care policymakers seeking to standardize our medical care protocol to this vulnerable group and thereby reducing the associated adverse maternal and perinatal outcomes.

Method And Design

Objective

The main objective of this study is to determine the pooled prevalence of

asymptomatic bacteriuria in Nigerian pregnant women as well as the associated risk factors and pregnancy outcomes.

The specific objectives include:

1. To determine the pooled prevalence of asymptomatic bacteriuria amongst pregnant Nigerian women.
2. To evaluate the associated risk factors such as socioeconomic status, history of recurrent urinary tract infection (UTI), diabetes mellitus, and anatomical abnormalities of the urinary tract, sickle cell and retroviral diseases for asymptomatic bacteriuria in the pregnant Nigerian women.

3. To assess pregnancy outcomes such as preterm birth, anemia, and pyelonephritis in asymptomatic bacteriuria

Review Questions

1. What is the pooled prevalence of asymptomatic bacteriuria amongst pregnant Nigerian women?
2. What are the frequencies of the risk factors associated with asymptomatic bacteriuria in pregnancy?
3. What are the frequencies of adverse fetomaternal outcomes associated with asymptomatic bacteriuria?

Study Characteristics

a. Study Design:

This is a protocol for systematic review and meta-analysis of observational studies that reported the prevalence of asymptomatic bacteriuria amongst pregnant women in Nigeria. There is no time restriction. Other types of study designs are excluded including interventional studies, comments, and editorials.

b. Inclusion criteria

1. Observational studies e.g., cross-sectional, case-control, cohort, retrospective, and historical cohort studies;
2. the study must report the prevalence of asymptomatic bacteriuria in pregnancy as a primary outcome.
3. the study must be retrievable in the English language.
4. **the study must be available in electronic databases.**

c. Exclusion criteria

1. Letters to editors, reviews, commentaries, and editorials.
2. Duplicate of same studies.
3. Studies with secondary but no primary outcome.
4. Studies on the prevalence of asymptomatic bacteriuria but not in pregnancy.
5. Interventional studies including randomized clinical trials and quasi-clinical trials.
6. Non-Nigerian studies or studies on Nigerians in the diaspora.
7. Grey literature will not be included.

PICOs

Participants are all pregnant Nigerian women with asymptomatic bacteriuria.

Intervention: there is no intervention.

Comparator: there is no comparator.

Outcomes: the primary outcome is the proportion of asymptomatic bacteriuria in pregnant women in Nigeria. Secondary outcomes are: - a) frequencies of risk factors including recurrent UTI, SCD, HIV infection, parity, urinary tract abnormalities, urethral catheterization, and pyelonephritis; and b) pregnancy outcomes will include the proportion of preterm delivery, intrauterine growth restriction, neonatal sepsis; and puerperal sepsis.

Effect size for the primary outcome is the prevalence

Effect size for secondary outcomes is prevalence except for categorical variables that serve as moderators.

Information sources

The search will employ sensitive topic-based strategies designed for each

database. The following databases will be searched: CINAHL, Embase, PubMed, Web of Science, Google scholar, African journals online (AJOL), Scopus,

ResearchGate, and Cochrane Library. Only observational studies that are

conducted in Nigeria and retrievable in the English Language will be included.

Search strategy

The search strategy will include MeSH terms, text words, and entry terms. The

Search strategies used in databases are as shown in Table 1.

Data Extraction and Management

Three main tools will be used to manage data: DistillerSR, CMA software version 3 and Microsoft Excel.

a. Screening: Identified studies will be independently and blindly screened in pairs using the DistillerSR software at the following levels:

1. Level 1: study design: only observational studies will be included.
2. Level 2: screening of titles and abstracts of identified studies using search strategy.
3. Level 3: full texts will be screened using search strategy.
4. Level 4: Snowballing of articles to identify more relevant studies.
5. Level 5: Studies will be screened for primary and secondary outcomes.

6. Level 6: Studies will be screened for risk of bias using NIH Quality assessment for observational studies.

Conflicts during screening will be resolved by a third reviewer, who serves as a tiebreaker.

b. Selection process: Studies will be selected based on study design, inclusion/exclusion criteria, and screening outcomes. Full-text articles will be obtained for all included studies. Primary outcomes must be reported in all eligible studies. Authors of eligible articles with missing data will be contacted by email and telephone. Depublication of eligible studies will be performed using the DistillerRS.

c. Data collection process: Extractable data item will be collected into predefined forms created in the DistillerSR. Extractable data items from eligible studies will include:

1. Surname of first author and year of publication
2. Proportion of asymptomatic bacteriuria in pregnant Nigerian women (prevalence)
3. Mean patient's age
4. Risk factors: recurrent UTI, SCD , HIV infection, parity, urinary tract abnormalities, urethral catheterization, and pyelonephritis
5. Pregnancy outcomes: the proportion of preterm delivery, intrauterine growth restriction, neonatal sepsis; and puerperal sepsis.
6. Method of detecting bacteriuria: dipstick, culture, and PCR

The effect size for primary outcome is prevalence. Effect size for most of the secondary outcomes is prevalence.

Risk of bias

The risk of bias in eligible studies will be assessed for the individual studies using the National Institute of Health (NIH) Quality assessment tool for observational studies. This will be cross-checked with the Cochrane tool of risk of bias assessment for the strength of the body of evidence.

The following areas shall be assessed and any study with extreme bias will be excluded following a consensus decision.

1. Method of testing and reporting at the outcome level
2. Reporting of study: whether proportion/ prevalence with confidence interval or number of cases / sample size are reported at the outcome level. Primary indexes from studies with similar design and report outcome will be converted to prevalence which is the primary effect size.
3. Heterogeneity will be assessed at the study level.
4. Publication bias will be assessed at the study level.
5. Sensitivity analysis will be done at the study level.

Assessment of Meta-bias

To test for heterogeneity: Cochran's Q value and its p-value, I^2 , τ^2 will be used. The effect size is the prevalence at a 95% Confidence Interval (CI, 95%). As a rule of thumb, I^2 values of less than 40% will be considered low heterogeneity while values > 40 but < 75 % will be considered moderate and values > 75% are high.

Data synthesis:

Both narrative synthesis and quantitative analysis will be performed.

All studies that report primary outcomes with or without secondary outcomes will be included for systematic review, with all measurable outcomes and sample size reported in a tabular format. Studies with primary indices that can be converted to prevalence will be converted in the CMA Software version 3.

Quantitative Analysis

Quantitative data will include pooled prevalence, standard error, and 95% CI. Both random and fixed effect models will be assessed, and the appropriate model will be taken based on the forest plots. Quantitative analysis will be done using the Comprehensive Meta-analysis CMA software version 3.

Further Analysis

Subgroups analysis will be done using categorical risk factors and pregnancy outcomes as moderators. Meta-regression will be done with mean maternal age and parity. A cumulative meta-analysis will be performed to check for the trend in the prevalence of asymptomatic bacteriuria over the years.

Presentation and Reporting of Results

The study selection process will be summarized in a Prisma flow chart according to the PRISMA 2015 Statement and PRISMA-P Checklist [24,25]. A table of the search strategy in various databases will be presented. A list of included studies will be summarized in a table. Quantitative data: prevalence, standard error, 95 % CI, P values, relative weights assigned to studies, and heterogeneity tests will be reported in the forest plots. A table of quality scores and risk of bias of each eligible study will be presented. Forest and regression plots to show subgroup analysis and meta-regression respectively will be presented as well.

Discussion

The study will discuss the burden of asymptomatic bacteriuria in pregnant Nigerian women based on the pooled prevalence. It will examine the risk factors associated with asymptomatic bacteriuria in pregnancy in Nigeria as well as the pregnancy outcomes. The outcome of this study will impact on the method of detecting asymptomatic bacteriuria, whether dipstick testing is adequate enough or not compared to urine cultures. The findings of this study will inform choice of preventive measures to be recommended by

policymakers. The strength of evidence for this study will be scored using the NIH Quality Assessment for Systematic Reviews and Meta-analysis. The final outcome will be published in a peer-reviewed scientific journal.

Abbreviations

AGCPN: Association for Good Clinical Practice in Nigeria

CINAHL: Cumulative index to Nursing and Allied Health literature

AJOL: African Journals online

UTI: Urinary tract infection

SCD: Sickle cell Disease

NIH: National Institute of Health

PCR: Polymerase chain reaction

PRISMA: Preferred Reporting Items for Systematic Review and Meta-analysis

PROSPERO: International Prospective Register of Systematic Reviews

Declarations

Ethics and Dissemination

Ethical approval will not be required, since this study will rely solely on the secondary source of data

Contributions: DO, EN, and HO conceived the project, DO, EN, HO, and AN designed the study, BA and IR did PubMed searches, screening and review; HO and DO did AJOL search, UA, MC, and NO did Embase and Scopus searches and review; SO, GO and AN did Google scholar and WebOS searches and DE and YG did searches and review for CINAHL database, CE and OA did searches on Cochrane Database while AD did review of Researchgate.

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Guarantor of the Review: Dr Emmanuel Nna

Ethics approval and consent to participate: None

Consent for publication: It is not applicable

Availability of data: All data from this study will be made public.

Competing interests: The authors declare no competing interest

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Tables

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1SearchStrategyASB.pdf](#)
- [PRISMAPchecklistBMCASBFinal.docx](#)