Review

Colonisation with extended-spectrum β-lactamase-producing Enterobacteriaceae in pregnant/post-partum women: Systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 19 November 2018
Received in revised form 26 May 2019
Accepted 10 June 2019
Available online 15 June 2019

A B S T R A C T

Objectives: Maternal colonisation with extended-spectrum β-lactamase (ESBL)-producing microorganisms can lead to transmission of such pathogens to neonates, resulting in considerable morbidity. The aim of this study was to determine the global prevalence of maternal colonisation with ESBL-producing Enterobacteriaceae (ESBL-E).

Methods: A systematic review of PubMed, Embase, Scopus, Web of Science and ProQuest databases as well as the grey literature was performed. Studies reporting the prevalence of ESBL-E colonisation during pregnancy or postpartum period were included. Prevalence data were grouped by geographic region. The pooled prevalence and 95% confidence interval (CI) was estimated by meta-analysis using a random-effects model.

Results: Nineteen studies with reports from 16 countries (seven studies from Africa, one study from South America, two studies from Asia and nine studies from Europe) reporting data for 7352 pregnant/postpartum women were included. The pooled prevalence of ESBL-E colonisation was 8% (95% CI 5–10%). Prevalence estimates were 15% (95% CI 5–24%) in Africa, 6% (95% CI 4–10%) in South America, 5% (95% CI 4–6%) in Asia and 4% (95% CI 2–5%) in Europe. The pooled prevalence was higher in studies with low risk of bias (10%; 95% CI 7–13%) compared with those with high risk of bias (3%; 95% CI 2–3%).

Conclusion: There was heterogeneity regarding ESBL-E colonisation rates in different continents. The pooled prevalence rate was higher in Africa compared with other areas. Given that the highest rate was observed in Africa, implementing screening efforts for ESBL-E colonisation during pregnancy may be justified.

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https://doi.org/10.1016/j.jgar.2019.06.010
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1. Introduction

Extended-spectrum β-lactamases (ESBLs) are β-lactamase enzymes produced mainly by Enterobacteriaceae, a large family of Gram-negative bacteria. ESBLs have been detected in Escherichia coli, Klebsiella pneumoniae and Acinetobacter, among others [1]. ESBLs confer resistance to most β-lactam antibiotics, including third-generation cephalosporins and the monobactam aztreonam [2]. Production of ESBLs is considered the most common mechanism of resistance to cephalosporins among Enterobacteriaceae [3]. ESBL-producing Enterobacteriaceae (ESBL-E) can colonise various body parts, in particular the urinary and gastrointestinal tracts [4].

Undoubtedly, one of the major groups of patients affected by antimicrobial resistance and its consequences is pregnant women. ESBL-E colonisation in this particular group poses several threats to both maternal and fetal/neonatal health [1]. In addition to complicated maternal infections, especially urinary tract infections (UTIs) and pyelonephritis, the contribution of ESBL-E to obstetric complications (e.g. preterm labour), colonisation of very low birth weight (VLBW) infants [5] as well as perinatal transmission and subsequent neonatal infection [6] highlights the necessity to ascertain the global prevalence of maternal ESBL-E colonisation and its geographic distribution.

Whether there are true differences in terms of the prevalence of maternal ESBL-E colonisation in different geographic areas is unknown, and knowledge regarding this issue is clinically important. Some authors have stated the requirement for ESBL-E screening in mothers who give birth to preterm infants [7]. Whether such recommendations can be translated into applicable actions requires a true understanding of the epidemiology of ESBL-E.

Two previous meta-analyses regarding the prevalence of ESBL-E in paediatric patients reported a pooled prevalence of 14% in paediatric UTI combining data from 16 primary studies [8] and a pooled prevalence of 9% in paediatric bloodstream infections using data from 23 primary studies [9]. Two separate meta-analyses regarding gastrointestinal colonisation with such organisms reported a similar pooled prevalence of 18% in solid-organ transplant patients [10] and residents of long-term care facilities [11]. A previous study in the UK focusing on women of reproductive age reported that 20% of subjects were ESBL-E carriers [12]. We identified only a single recent review confined to 10 studies from Africa [13], which estimated the maternal ESBL-E colonisation/infestation rate as 17%. Therefore, providing a more comprehensive estimate of the prevalence of maternal ESBL-E colonisation and its distribution in broader geographic regions appears necessary. In addition, several authors have asserted that the prevalence of ESBL carriage is increasing in the community. For example, it was demonstrated that in the period 2002–2011, the community carriage rate of ESBL-E in Europe increased significantly by 0.5% per year [14]. However, little is known about a possible similar trend in pregnant women. Difficulties in the development of novel antimicrobials to treat infected patients highlight the importance of recognising colonised patients in order to find preventive ways to avoid the spread of multidrug-resistant Gram-negative bacteria, although at present no reliable decolonisation methods exist for such organisms [12].

The objectives of this review were to estimate the prevalence of maternal colonisation with ESBL-producing bacteria globally and to determine the heterogeneity of prevalence measures in different geographical areas as well as the methodological quality of the primary studies. In our opinion, the findings of this review would represent contemporary estimates regarding the epidemiology of ESBL-E in pregnancy/postpartum period and will have implications for clinicians, researchers and infection control programmes. Furthermore, geographical areas with limited or no prevalence data will be identified.

2. Methods

This systematic review and meta-analysis was prepared according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 checklist [15].

2.1. Eligibility criteria

All cross-sectional studies (descriptive or descriptive-analytical) reporting the prevalence of laboratory-confirmed ESBL-E colonisation among women during pregnancy or postpartum period (within 6 weeks after delivery) as well as the culture technique used identify ESBL-E were eligible for inclusion in the meta-analysis. ESBL-E colonisation was defined as isolation of ESBL-E through culture from vaginal, rectal or perianal samples. No age limit was imposed.

Exclusion criteria were studies that reported UTIs, asymptomatic bacteriuria or specific populations of women, including women with genital infection, human immunodeficiency virus (HIV) infection, gestational diabetes mellitus, those admitted to the intensive care unit (ICU) and those with any obstetric/neonatal complications (i.e. preterm labour, VLBW infants, and mothers of neonates who required neonatal ICU admission). Case reports, case series, outbreak reports (to avoid overestimation) and review articles were excluded. Studies without clear reporting of the prevalence or extractable figures to calculate the prevalence of ESBL-E (i.e. number of colonised patients with ESBL-producing pathogens divided by total number of patients tested), despite contact with the authors, were also excluded.
No language restriction was imposed. Studies reported in languages other than English were translated to English using Google Translation service and consultation with an official translation centre, if required. Published reports in journals (original articles and letters) as well as abstracts presented at conferences/meetings and unpublished data were eligible. If studies were reported both at a conference and as full-text in a journal, only the full-text was included.

2.2. Information sources

Studies were identified by searching electronic databases as well as hand-searching of pertinent articles between 10 October 2008 and 10 October 2018. For the electronic bibliographic database search, the PubMed, Embase, Scopus, Web of Science and ProQuest databases were searched. In addition, LILACS (Latin American and Caribbean Health Sciences Literature Database), abstracts of European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) meetings [via the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) eLibrary] [16], International Congress on Infectious Diseases (ICID) abstracts (via International Journal of Infectious Diseases) [17], the US Centers for Disease Control and Prevention (CDC) website and Google Scholar were searched using key words.

2.3. Search

The electronic databases were searched (1 October 2018) both using controlled vocabulary [Medical Subject Headings (MeSH) for PubMed and Emtree for Embase] and free-text words without any language restriction. Appendix 1 presents the search strategy for

![Flow diagram](image-url)

Fig. 1. Flow diagram of selection of studies reporting the prevalence of colonisation by extended-spectrum \( \beta \)-lactamase-producing Enterobacteriaceae (ESBL-E) during pregnancy/postpartum period. WoS, Web of Science; ECCMID, European Congress of Clinical Microbiology and Infectious Diseases; ICID, International Congress on Infectious Diseases; UTI, urinary tract infection; NICU, neonatal intensive care unit.
Table 1
Characteristics of the included studies reporting the prevalence of colonisation with extended-spectrum $\beta$-lactamase-producing Enterobacteriaceae (ESBL-E) among pregnant/postpartum women in countries grouped by United Nations region.

<table>
<thead>
<tr>
<th>First author</th>
<th>Study date</th>
<th>Country</th>
<th>Sample</th>
<th>Studied population</th>
<th>Total population</th>
<th>Colonised patients [n (%)]</th>
<th>Specific organism distribution (n)</th>
<th>ESBL-E confirmation test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa (n=7 studies)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herindrainy [25]</td>
<td>2016</td>
<td>Madagascar</td>
<td>Stools and endorectal swabs</td>
<td>All pregnant women living in study areas</td>
<td>275</td>
<td>54 (19.6)</td>
<td>NR</td>
<td>DDST, CA-SFM guidelines</td>
</tr>
<tr>
<td>Sáez-López [23]</td>
<td>2013</td>
<td>Morocco</td>
<td>Vagina</td>
<td>Asymptomatic pregnant women during antenatal control or at delivery in maternity hospital</td>
<td>320</td>
<td>0 –</td>
<td></td>
<td>DDST, CLSI guidelines</td>
</tr>
<tr>
<td>Sáez-López [23]</td>
<td>2014</td>
<td>Mozambique</td>
<td>Vagina</td>
<td>Asymptomatic pregnant women during antenatal control or at delivery in hospital</td>
<td>200</td>
<td>1 (0.5)</td>
<td><em>E. coli</em> (1)</td>
<td>DDST, CLSI guidelines</td>
</tr>
<tr>
<td>Fortini [26]</td>
<td>2011</td>
<td>Nigeria</td>
<td>Stools</td>
<td>Healthy pregnant women admitted to hospital</td>
<td>101</td>
<td>32 (31.7)</td>
<td><em>E. coli</em> (32)</td>
<td>Disk diffusion and genotyping, EUCAST guidelines</td>
</tr>
<tr>
<td>Kaba [27]</td>
<td>2016</td>
<td>South Africa</td>
<td>Stools</td>
<td>Asymptomatic pregnant women living in three subdistrict locations near Cape Town Postpartum women at a medical centre</td>
<td>90</td>
<td>4 (4.4)</td>
<td>NR</td>
<td>DDST, CLSI guidelines</td>
</tr>
<tr>
<td>South America (n=1 study)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Villar [29]</td>
<td>2012</td>
<td>Argentina</td>
<td>Rectal</td>
<td>Perianal swabs of asymptomatic pregnant women at a laboratory</td>
<td>259</td>
<td>16 (6.2)</td>
<td><em>E. coli</em> (14), <em>E. cloacae</em> (1), <em>Citrobacter koseri</em> (1)</td>
<td>CDT, CLSI guidelines</td>
</tr>
<tr>
<td>Asia (n=2 studies)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathak [30]</td>
<td>2008</td>
<td>India</td>
<td>Perianal</td>
<td>Asymptomatic pregnant women attending for routine antenatal care at teaching and non-teaching hospital outpatient clinics</td>
<td>710</td>
<td>109 (15.4)</td>
<td><em>E. coli</em> (109)</td>
<td>CDT, CLSI guidelines</td>
</tr>
<tr>
<td>Nanayakkara [31]</td>
<td>2015</td>
<td>Sri Lanka</td>
<td>Vagina</td>
<td>Asymptomatic mothers admitted for delivery at a teaching hospital</td>
<td>250</td>
<td>4 (1.6)</td>
<td><em>E. coli</em> (2), <em>Klebsiella spp.</em> (2)</td>
<td>DDST, CLSI guidelines</td>
</tr>
<tr>
<td>Europe (n=9 studies)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zamfir [32]</td>
<td>2014</td>
<td>Germany</td>
<td>Perianal</td>
<td>Asymptomatic pregnant women with a planned vaginal delivery upon admission at two clinics</td>
<td>763</td>
<td>20 (2.6)</td>
<td><em>E. coli</em> (20)</td>
<td>CDT, EUCAST guidelines</td>
</tr>
<tr>
<td>Patyi [33]</td>
<td>2014</td>
<td>Hungary</td>
<td>Stools/ anorectal</td>
<td>Pregnant women at delivery in hospital</td>
<td>751</td>
<td>19 (2.5)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Knowles [34]</td>
<td>2015</td>
<td>Ireland</td>
<td>Rectal</td>
<td>Rectal swabs received for GBS screening in a maternity hospital</td>
<td>123</td>
<td>2 (1.6)</td>
<td>3 isolates in 2 patients: <em>E. coli</em> (2), <em>Proteus mirabilis</em> (1)</td>
<td>CDT, EUCAST guidelines</td>
</tr>
<tr>
<td>Rettedal [35]</td>
<td>2012</td>
<td>Norway</td>
<td>Rectal</td>
<td>Asymptomatic pregnant women attending pre-delivery consultation at a teaching hospital</td>
<td>901</td>
<td>26 (2.9)</td>
<td>27 isolates in 26 patients: <em>E. coli</em> (26), <em>K. pneumoniae</em> (1)</td>
<td>CDT, EUCAST guidelines</td>
</tr>
<tr>
<td>Kaczmarek [36]</td>
<td>2008</td>
<td>Poland</td>
<td>Rectovaginal</td>
<td>Isolates of asymptomatic pregnant women at an academic microbiology department</td>
<td>100</td>
<td>0</td>
<td>–</td>
<td>DDST</td>
</tr>
<tr>
<td>López-Cerero [38]</td>
<td>2013</td>
<td>Spain</td>
<td>Rectovaginal</td>
<td>Asymptomatic pregnant women giving birth at an academic centre</td>
<td>406</td>
<td>39 (9.6)</td>
<td>–</td>
<td>DDST, CLSI guidelines</td>
</tr>
<tr>
<td>Sáez-López [39]</td>
<td>2012</td>
<td>Spain</td>
<td>Vagina</td>
<td>Asymptomatic pregnant women at antenatal visits at maternity department of a hospital (603 with normal gestation and 35 with preterm labour/premature membrane rupture)</td>
<td>638</td>
<td>0</td>
<td>–</td>
<td>DDST, CLSI guidelines</td>
</tr>
<tr>
<td>Gysin [40]</td>
<td>2015</td>
<td>Switzerland</td>
<td>Vagina/ perineum/ rectal</td>
<td>Asymptomatic pregnant women at routine follow-up visit at a university hospital</td>
<td>181</td>
<td>5 (2.8)</td>
<td><em>E. coli</em> (5)</td>
<td>NR</td>
</tr>
</tbody>
</table>

DDST, double-disk synergy test; CA-SFM, Antibiogram Committee of the French Society of Microbiology; NR, not reported; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; CDT, combined disk test; GBS, group B Streptococcus. **Note**: All studies reported community-acquired ESBL-E colonisation.

*Midyear of the study period.*
PubMed, and Appendix 2 shows the search strategy for Embase. The search results from all sources were entered into EndNote program.

2.4. Study selection

Two authors (MK and SA) independently screened the titles and abstracts of the search results for eligibility. The number of retained articles was compared and any disagreement was solved by discussion, reviewing the full-text of the articles and, if required, comments of a third author (AN). In the next stage, the full-texts of the articles were reviewed and, if eligibility criteria were met, the required data were extracted.

2.5. Data extraction

A data-gathering checklist was developed considering the required variables. The included full-text articles were reviewed independently by two authors (NJ and AN) and the required data were extracted. Any disagreement or unclear data were resolved by trying to contact the authors of the report. The authors were also contacted for further information if required. The gathered variables included: last name of first author; year of sampling; year of publication; country; continent; sample analysed in the laboratory (stool, rectal, vaginal); studied population; total number of subjects; number of subjects recognised as colonised with ESBL-E; responsible organism; frequency of organisms; and ESBL-E confirmatory diagnosis method used.

2.6. Assessing the risk of bias in primary studies

To determine the risk of bias in each study separately, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies was used [18]. This checklist consists of nine items addressing issues related to prevalence studies such as sampling frame, adequate sample size, appropriate statistical analyses and valid methods to describe the condition. For each item, four possible answers are available: ‘yes’, ‘no’, ‘unclear’ and ‘not available’. The studies were first reviewed separately by two authors (MK and NJ) and then, through discussion and comments by a third author (AN) if required, the final critical appraisal was completed. To categorise the studies, a total score was calculated for each study as follows: ‘yes’ to any of the 9 items scored 1; and ‘no’, ‘unclear’ or ‘not available’ responses scored 0. Studies with total scores of 8 or 9 were considered as having a low risk of bias and lower scores (≤7) were regarded as having a high risk of bias.

2.7. Synthesis of results

Prevalence data were grouped by geographical region based on the classification proposed by the United Nations Statistics Division, which includes Africa, Americas, Asia, Europe and Oceania [19]. The heterogeneity of prevalence measures was determined by the $I^2$ statistic and a value >75% indicated a high level of heterogeneity. To estimate the pooled prevalence and 95% confidence interval (CI), meta-analysis was performed using a random-effects model and ‘metaprop’ command [20]. Since some studies reported a prevalence rate of <5%, 'binomial exact method' [via cimethod(exact) option] was applied in the meta-analysis. Analysis was carried out using Stata Statistical Software: Release 12 (StataCorp LP, College Station, TX, USA).

2.8. Assessing publication or reporting bias

Publication bias was checked by inspecting the funnel plot of the prevalence rates and performing Begg’s test and Egger’s test.

Table 2: Quality assessment of the included studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for studies reporting prevalence data.

<table>
<thead>
<tr>
<th>First author</th>
<th>Africa (n = 7 studies)</th>
<th>US (n = 1 study)</th>
<th>Europe (n = 9 studies)</th>
<th>Asia (n = 2 studies)</th>
<th>Mexico (n = 1 study)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was the sample frame</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>appropriate to address the</td>
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<td>population?</td>
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<tr>
<td>Were the participants</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>sampled in an appropriate</td>
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<td>way?</td>
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</tr>
<tr>
<td>Was the sample</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>size adequate?</td>
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<tr>
<td>Were the study subjects</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>and the setting described in</td>
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<td>detail?</td>
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<td>Was the data analysis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>conducted with sufficient</td>
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<td>coverage of the identified</td>
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<td>sample?</td>
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<tr>
<td>Were valid methods used</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>for identification of the</td>
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<td>condition?</td>
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<tr>
<td>Was the condition measured</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>in a standard, reliable way</td>
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<td>for all participants?</td>
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<tr>
<td>Was there appropriate</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>statistical analysis?</td>
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<tr>
<td>Was the response rate</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>adequate and, if not, was the</td>
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<td>low response rate managed</td>
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<tr>
<td>appropriately?</td>
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</tbody>
</table>
Based on the Egger’s or Begg’s test, when the publication bias was non-ignorable (Begg’s or Egger’s tests P-value < 0.05), the trim-and-fill method was used to adjust for publication bias [22].

3. Results

3.1. Study selection

A total of 7489 records were identified, of which 1692 were duplicates. A further 5420 citations were excluded during screening of the titles and abstracts. Of the remaining 377 records, 359 were excluded for various reasons, such as not reporting ESBL-E colonisation, ESBL-E colonisation reported but no pregnant women investigated, and pregnant women with symptoms of genitourinary infection. Finally, 18 records met the inclusion criteria and were included the review [23-40]. One article [23] included data from two distinct geographic areas in Africa and the data were entered as two distinct studies. This translated to a total of 19 studies from 16 countries (Fig. 1). The included studies comprised seven studies from Africa [23–28], one from South America [29], two studies from Asia [30,31] and nine studies from Europe [32–40]. We tried to contact the authors of seven studies. The authors of three studies did not reply [41–43]. In one study the author confirmed that no pregnant women were included [44]. One study was performed purely on laboratory specimens (urine and sputum) without further clinical variables [45], and in another study the required data to calculate the prevalence was not available [46]. The author of the last study provided the necessary information (i.e. total number of pregnant women), resulting in inclusion of the study in the meta-analysis [23].

3.2. Study characteristics

Table 1 summarises the characteristics of the included studies by continent. For studies that lasted for longer than 12 months, the midyear of the study period that actual sampling and laboratory evaluation was done was determined as the study date.

3.3. Risk of bias within studies

Table 2 presents the quality assessment for risk of bias in each study. Of the 19 included studies, 14 studies [23–26,28–32,35,37–39] were of ‘high quality’ and a low risk of bias and 5 studies [27,33,34,36,40] were categorised as high risk of bias.

3.4. Synthesis of the results

Overall, the 19 included studies [23–40] reported data for 7352 women. The pooled prevalence of ESBL-E colonisation was 8% (95% CI 5–10%). The pooled prevalence rates of ESBL-E colonisation were 15% (95% CI 5–24%) in Africa, 6% (95% CI 4–10%) in South America, 5% (95% CI 4–6%) in Asia and 4% (95% CI 2–5%) in Europe (Fig. 2). Three studies

![Fig. 2. Forest plot showing the prevalence of colonisation by extended-spectrum β-lactamase–producing Enterobacteriaceae in pregnant/postpartum women by geographical area. Three studies [23,36,39] that did not find any resistant organisms were not included.](image-url)
did not report any ESBL-E colonisation among the investigated subjects [23,36,39]. There was high heterogeneity ($I^2 = 95.16\%$).

The pooled prevalence of ESBL-E colonisation was 10% (95% CI 7–13%) in the studies with low risk of bias and 3% (95% CI 2–3%) in those studies with high risk of bias (Fig. 3).

Three studies did not report specific isolates recognised as ESBL-producers [25,27,33]. The remaining 13 studies reported various organisms cultured and identified as ESBL-producers. The most commonly reported organism was *E. coli*, with a pooled prevalence of 78% (95% CI 65–90%).

3.5. Publication bias

Results of the Begg’s test showed a z-value of 1.04 ($P = 0.3$) and Egger’s test showed publication bias of −4.96 ($P = 0.03$). The trim-and-fill method did not estimate any missing studies and did not adjust the random-effect estimate (Fig. 4). Considering these findings, it can be assumed that publication bias was ignorable.

4. Discussion

4.1. Summary of the evidence

The pooled prevalence of maternal ESBL-E colonisation was 8%, with the highest rate found in African studies (15%). Not all sampled women were positive for ESBL-producing bacteria, as in three studies (Morocco [23], Poland [36] and Spain [39]) no colonised mothers were reported. Although several guidelines such as those from the Clinical and Laboratory Standards Institute (CLSI), the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the Antibigram Committee of the French Society of Microbiology (CA-SFM) as well as methods (double-disk synergy test, combined disk test) were described by the authors to identify ESBL-producing organisms, the inclusion criteria were not limited to any specific guideline or laboratory method. This was primarily decided in order to obtain as much data as possible for a more accurate and comprehensive estimation of colonisation.

The highest rate of maternal colonisation with ESBL-producing bacteria was seen in Africa. This rate was higher than the rate reported from Asian studies, although only two reports from Asia were available.
with high heterogeneity. This finding is similar to a previous meta-analysis that demonstrated the highest global prevalence of maternal colonisation with group B Streptococcus in Africa [47]. The high rate of maternal colonisation in Africa may be explained by several factors, such as extensive antimicrobial use and challenges in implementing antimicrobial resistance surveillance action plans [48], that have been linked to a high prevalence of antimicrobial resistance. With respect to the quality of the primary studies, African studies had a low risk of bias. Therefore, the heterogeneity seen regarding the difference in pooled prevalence rates between studies with low risk and high risk of bias may be factitious due to geographical variation in maternal colonisation. Substantial variations existed within some regions. For instance, in Africa one study reported no mother with ESBL-E colonisation in Morocco [23], but two other studies reported high prevalence rates from Nigeria (31%) [26] and Madagascar (18%) [24]. In Europe, for example, although one study in Spain did not find laboratory evidence of ESBL-E colonisation from vaginal samples of 638 women in a hospital in Barcelona [39], another study reported a prevalence of 9.6% from rectovaginal samples of mothers in a university hospital located in Seville [38].

Most studies recruited laboratory samples at hospitals or mothers who presented for routine antenatal care or delivery at larger hospitals. This can potentially bias the estimated prevalence towards urban settings and underestimate the true prevalence in rural areas or smaller local health centres with probably poorer socioeconomic status. Only two studies [24,25] were true population-based studies.

There is evidence of intestinal carriers of ESBL-producing pathogens both in inpatient and outpatients [49]. As there is evidence that maternal colonisation is a major factor for transmission of such organisms to neonates who developed sepsis with ESBL-E [50], it seems essential to have an accurate understanding of the epidemiology of this condition. Thus, we decided to determine the prevalence of ESBL-producing bacteria among pregnant women, not among Enterobacteriaceae. It is likely that reporting the estimated prevalence rates among subjects will yield more practical findings for epidemiological purposes addressing pregnant women. Currently, there is no guideline or international consensus regarding routine screening of pregnant women for ESBL-producing bacterial colonisation. The current findings may have implications for programmers to consider screening methods, at least in areas with higher ESBL-E colonisation rates. A recent review from Africa including 10 studies reported an estimated prevalence of ESBL-E colonisation of 17% during pregnancy/postpartum period [13]. The prevalence estimate of 15% in Africa calculated in the current analysis is close to the abovementioned study, although differences in the inclusion criteria should be noted. Here we carried out the review by including those records that only reported colonisation rates among asymptomatic pregnant women. Those citations that reported pregnant patients for whom clinical infection (UTI, obstetric infection, sepsis, etc.) had been diagnosed were not included. However, the previous African review presented prevalence rates combining both colonised and infected patients. The approach to colonised versus infected patients may be different in clinical practice. Moreover, the messages conveyed to physicians or programmers regarding each of these states are different. Hence, we decided to report only the estimated colonisation rate.

4.2. Limitations

Some gaps were noticed regarding published results from broader geographic areas. No reports were found from North America or Oceania (Australia and New Zealand). Moreover, due to insufficient data in most studies, ascertaining potential risk factors for maternal ESBL-E colonisation was not feasible. Most studies recruited mothers from maternity hospitals or antenatal care facilities. This translates to the fact that further high-quality and preferably population-based studies are required, in particular from countries with no/limited data on maternal ESBL-E carriage.

5. Conclusions

There was heterogeneity regarding ESBL-E colonisation rates in different continents. The pooled prevalence rate was higher in Africa compared with South America, Asia and Europe. More population-based and high-quality studies, in particular from regions with limited reported data, are required for more accurate estimations. High rates in Africa may justify considering implementing screening efforts for ESBL-E colonisation during pregnancy.

Funding

None.

Competing interests

None declared.

Ethical approval

Not required.

Acknowledgments

The authors acknowledge the Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran for their support in conducting this study. The study was approved by Research Deputy of the university (No. 980525).

Appendix 1. PubMed search strategy

#1 beta-lactamases
#2 “beta lactamase”[tiab] OR #3 beta-lactamase*[tiab] OR #4 “beta lactamase”[tiab]
#5 “extended-spectrum beta-lactamase”[tiab] OR #6 “extended-spectrum β-lactamase”[tiab]
#7 “extended spectrum beta-lactamase”[tiab] OR #8 “extended spectrum β-lactamase”[tiab]
#9 “extended spectrum b-lactamase*[tiab] OR #10 “extended-spectrum beta-lactamase-producing*[tiab] OR #11 ESBL*[tiab]
#12 “drug resistance, microbial*[Mesh] OR #13 (drug resistance AND microbial)
#14 “antimicrobial drug resistance*[tiab] OR #15 “antimicrobial drug resistances*[tiab]
#16 (“antibiotic resistance” AND microbial[tiab]) OR #17 “antibiotic resistance*[tiab]
#18 (resistance AND antibiotic[tiab]) OR #19 “antimicrobial resistance*[tiab]
#20 “drug resistance, bacterial*[Mesh] OR #21 (”drug resistance” AND bacterial)
#22 “antibacterial drug resistance*[tiab] OR #23 (“antibiotic resistance” AND bacterial[tiab])
#24 “bacterial drug resistance*[tiab] OR #25 Enterobacteriaceae*[tiab]
#26 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25
#27 (pregnancy OR pregnancies[tiab]
References


