Infectious morbidity of speculum versus digital examinations in preterm prelabor rupture of membranes: a systematic review and meta-analysis

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ABSTRACT

Objective: To estimate the effect of speculum examination only versus digital cervical examination on maternal infectious morbidity in women with preterm prelabor rupture of membranes by performing a systematic review and meta-analysis.

Materials and methods: We explored MEDLINE, Scopus, Embase, CINAHL, ClinicalTrials.gov and Cochrane Central Register of Controlled Trials for studies comparing the rate of a composite maternal infectious morbidity (either chorioamnionitis, endometritis or both) in women with preterm prelabor rupture of membranes that underwent a speculum only versus digital cervical examination at the time of diagnosis. Two reviewers separately ascertained studies, obtained data, and gauged study quality. The rate of a composite maternal infectious morbidity (either chorioamnionitis, endometritis or both) were compared and odds ratios (ORs) with 95% confidence intervals (CIs) were estimated.

Results: Four cohort studies, reporting on 1213 women were identified. The median point prevalence of the composite maternal infectious morbidity was 26% (interquartile range 15–35%) in women who had a speculum examination only compared to 33% (interquartile range 22–42%) in women who underwent a digital examination. The overall maternal composite infectious morbidity rate in women that had a speculum examination only was less compared to women that had undergone a digital examination (pooled OR 0.75, 95% CI 0.58–0.98, I² 17%). The weighted mean length of latency in women with preterm prelabor rupture of membranes was longer in individuals evaluated by speculum only versus digital examination, 6.6 d versus 2.9 d (mean difference 4.5 d, 95% CI 1.4 to 7.8, I² 99%).

Conclusion: Speculum examination only in women with preterm prelabor rupture of membranes is associated with less maternal infectious morbidity and longer latency periods.

Introduction

Preterm prelabor rupture of membranes is defined as the rupture of amniotic membranes prior to labor that occurs before 37 weeks of gestation and occurs in approximately 2-3% of all pregnancies in the United States [1]. Current international guidelines vary on how to make the physical diagnosis of preterm prelabor rupture of membranes with some endorsing either speculum, digital examination or cervical ultrasound [2] and others encouraging speculum examination only [1,3]. This stems from a concern that cervical digital examinations increase the risk of infection ascending into the uterine cavity and reduce the length of the latency period. Yet, the evidence supporting the recommendations of speculum over digital cervical examination in reducing infectious morbidity and increasing length of the latency period is conflicting. One study has shown an increased risk of maternal infection with digital cervical examination [4], while three studies noted no statistical difference [5–7]. Three studies observed a longer latency period with speculum examination only versus digital cervical examination [5–7] with one study observing no statistical distinction [4].

Cervical dilation is an important variable for clinical management in the setting of preterm prelabor rupture of membranes. While correlation of the visual assessment of cervical dilation to digital cervical examination has noted a moderate to strong association overall (range 0.69 to 0.78), this is reduced to a weak strength of association if the gestational age is less than 34 weeks [8–10].

Given the contradicting evidence described above, obstetricians may have difficulty determining best
practice. Our objective is to estimate the effect of speculum examination only versus digital cervical examination on maternal infectious morbidity in women with preterm prelabor rupture of membranes by performing a systematic review and meta-analysis.

**Material and methods**

This review was organized in accordance with Meta-analysis of Observation Studies in Epidemiology (MOOSE) guidelines [11]. The protocol was recorded with the prospective register of systematic reviews (PROSPERO: registration number CRD42020203831) on 11 August 2020 before introductory searches were commenced. The study was judged exempt from Institutional Review Board endorsement since it was deemed non-human subject research.

**Search strategy and eligibility criteria**

An electronic investigation with no language boundaries using the databases of MEDLINE via the PubMed interface, Scopus, Embase [Excerpta Medica Database], CINAHL [Cumulative Index to Nursing and Allied Health Literature], ClinicalTrials.gov and Cochrane Central Register of Controlled Trials [CENTRAL] was completed to identify articles that reported on infectious morbidity in individuals with preterm prelabor rupture of membranes that compared those who received a speculum examination only versus digital cervical examination at the time of initial assessment. The primary exploration was performed by one author (M.T.) with support from a qualified medical librarian in systematic reviews from inception through July 2021. Unpublished collected works (i.e. “grey literature”) were evaluated by searching Google Scholar and the ProQuest Dissertations & Thesis database. For Google Scholar searches, the first 100 results were screened based on the assumption that the most applicable results would emerge first. Articles were detected using a combination of the following Medical Subject Headings: “premature rupture of membranes” and “digital examination.” References from recovered articles were hand explored for supplementary articles. The final form of the Medical Subject Headings was applied by a second author (A.A.) separately and no additional articles were ascertained. The full search strategy is presented in Appendix 1, available in the Supplemental Materials. The authors of two identified studies were contacted for further information. Authors indicated that material in a follow up article contained subjects from their preceding publication and this follow up article was excluded from this analysis to avoid the potential double counting of subjects [12]. Authors of one other trial did not respond to request [13].

**Study identification**

Two independent reviewers (M.T., A.A.) evaluated the electronic searches for eligible studies by title and abstract. All determined articles were recovered in full and evaluated for inclusion. Studies were qualified for inclusion if they assessed women with preterm prelabor rupture of membranes that had a speculum examination only at presentation and were compared to women who had a digital cervical examination. Data were accepted from cohort, case–control, and cross-sectional studies. No randomized controlled trials were available.

**Risk of bias, outcome measures and synthesis of results**

Two reviewers (A.A. and S.M.) independently rated the quality of incorporated articles using a modified Newcastle Ottawa Scale (NOS) for cohort studies [14]. Discrepancies were resolved through interchange with a third author (M.T.). A weighted Fleiss’ kappa coefficient was calculated to estimate inter-rater conformity [15]. The overall qualities of articles were rated as follows: low risk of bias (NOS score 7–9), high risk of bias (NOS score 4–6), and a very high risk of bias (NOS score 0–3) [16]. The primary outcome was the rate of a composite maternal infectious morbidity (either chorioamnionitis or endometritis). Chorioamnionitis was diagnosed with two or more of the following symptoms: temperature of 38°C or greater, uterine tenderness, maternal tachycardia, fetal tachycardia, or leukocytosis. Endometritis was diagnosed by maternal temperature of 38°C or greater and uterine tenderness with no other source of infection. A planned analysis of the individual components of the composite maternal infectious morbidity for the rate of chorioamnionitis only, the rate of endometritis only, and the length of the latency period, defined in the identified studies as the duration from membrane rupture until the onset of labor, was performed. One study [7] reported the length of latency as the median and range, and the mean and standard deviation were calculated from this information [17]. From the data from each article, two-by-two tables were generated and odds ratios (ORs) with their 95% confidence intervals (CIs) were computed. Summary statistics of continuous
Retrieved from searches of MEDLINE, Scopus, Embase, CINAHL, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials (n=47)

Articles retrieved in full (n=6)

Excluded after reading titles and abstracts (n=41)

Articles included in systematic review (n=4)

Excluded after reading articles in full (n=2)
• one study had duplicated patients
• one study did not report number of subjects in each group

Figure 1. Flow diagram of studies identified in the systematic review.

Results

Study selection

A flow diagram of the study assemblage method is exhibited in Figure 1. A total of 47 related studies were initially identified. After elimination of studies not pertinent to the subject of interest, six studies remained and were retrieved for complete analysis [4–7,12,13]. Two studies were eliminated, the first due to potential duplication of patients from a previous report and the second study because the number of subjects in the comparison groups were not reported [12,13]. In total, four studies with 1213 women that had preterm prelabor rupture of membranes were included in the review: 843 that had a speculum examination only and 390 with a digital examination [4–7].

Study characteristics and quality assessment

Attributes of the included studies are shown in Table 1. Of the four studies included, all were cohort studies (three from single institutions and one a secondary analysis of a multicenter randomized controlled trial). Two studies were performed in the United States, one from Israel and one from Thailand. Two studies administered no antibiotics [4,5], one administered antibiotics for “positive cultures” only (either for group B streptococcus, chlamydia, or gonorrhea) [6] and one trial indicated that 38% of subjects overall received latency antibiotics (in the speculum or digital exam group) with multivariable analysis performed to control for original antibiotic administration [7]. Three studies administered no antenatal corticosteroids [4,6,7] and one gave 12 mg of dexamethasone for “two doses” then weekly until delivery [5]. All four studies were rated as low-risk of bias (mean NOS score: Adoni 8, Lewis 9, Sukcharoen 9, Alexander 8). The weighted Fleiss’ kappa coefficient comparing total NOS scores between the two reviewers for the quality of included studies noted substantial agreement (κ = 0.68). The weighted mean estimated gestational age when preterm prelabor rupture of membrane was diagnosed was available for three studies with no difference between individuals evaluated by speculum...
examination only versus digital examination, 29.5 versus 30.2 weeks of gestation (mean difference \(-0.47 \text{ weeks}, 95\% \text{ CI } -1.14 \text{ to } 0.21, I^2 87\%) [4,5,7]. Among the four studies evaluated, no differences were noted in mode of delivery in women that had a speculum examination only versus digital examination for the diagnosis of preterm prelabor rupture of membranes [4–7]. The median point prevalence of cesarean delivery was 33\% (interquartile range 26–37\%) in women who had a speculum examination only compared to 34\% (interquartile range 26–37\%) in women who underwent a digital examination. The overall cesarean delivery rate in women that had a speculum examination only was not different compared to women that had undergone a digital examination (pooled OR 0.98, 95\% CI 0.75–1.28, \(I^2 0\%\)).

Maternal infectious outcomes

The four included studies reported some type of maternal infectious morbidity (either chorioamnionitis or endometritis). Chorioamnionitis only was reported in one study [5], a composite of chorioamnionitis or endometritis was noted in one study [6], and both chorioamnionitis and endometritis were reported separately in two studies [4,7]. The median point prevalence of the composite maternal infectious morbidity was 26\% (interquartile range 15–35\%) in women who had a speculum examination only compared to 33\% (interquartile range 22–42\%) in women who underwent a digital examination. The overall maternal composite infectious morbidity rate in women that had a speculum examination only was less compared to women that had undergone a digital examination (pooled OR 0.75, 95\% CI 0.58–0.98, \(I^2 17\%\)) (Figure 2). Visual inspection of the funnel plot suggested no evidence of publication bias for studies on the overall rate of maternal composite infectious morbidity in women with preterm prelabor rupture of membranes and the Peters’ test had \(p = .40\). The funnel plot is presented in Appendix 2 in the Supplemental Material.

A planned analysis of women with chorioamnionitis only, endometritis only and length of latency was performed. Three studies reported on the outcome of chorioamnionitis [4,5,7]. The median point prevalence of chorioamnionitis was 18\% (interquartile range 10–23\%) in women who had a speculum examination only compared to 24\% (interquartile range 18–26\%) in women who underwent a digital examination. The overall chorioamnionitis rate in women that had a speculum examination only was similar to women that had undergone a digital examination (pooled OR 0.85, 95\% CI 0.60–1.19, \(I^2 26\%\)). Two studies reported on the outcome of endometritis [4,7]. The median point prevalence of endometritis was 6\% (interquartile range 4–9\%) in women who had a speculum examination only compared to 8\% (interquartile range 6–11\%) in women who underwent a digital examination. The overall endometritis rate in women that had a speculum examination only was similar to women that had undergone a digital examination (pooled OR 0.82, 95\% CI 0.50–1.33, \(I^2 0\%\)). All four studies reported the length of latency [4–7]. The weighted mean length of latency in women with preterm prelabor rupture of membranes was longer in individuals evaluated by speculum examination only versus digital examination, 6.6 d versus 2.9 d (mean difference 4.5 d, 95\% CI 1.4 to 7.8, \(I^2 99\%\)).

Discussion

This meta-analysis demonstrates that in the setting of preterm prelabor rupture of membranes, women who undergo a sterile speculum examination alone have decreased composite rate of maternal infectious morbidity and a longer duration of latency period when
compared with women that have a digital cervical examination.

In the United States, with 2 to 3% of all pregnancies being complicated by preterm prelabor rupture of membranes, nearly 100,000 women annually will encounter this condition [1,23]. Guidelines from the American College of Obstetricians and Gynecologists suggest that digital cervical examination should generally be avoided when diagnosing preterm prelabor rupture of membranes with evaluations performed in such a manner that minimalizes the risk of introducing infection, such as with sterile speculum examination [1]. Digital examination of the cervix in term patients with ruptured membranes has shown to increase both the quantity of growth and numbers of isolated vaginal organisms in the endocervical canal [24]. In contrast, sterile speculum examinations alone did not introduce vaginal organisms into the cervix. Yet, evidence has been lacking that digital cervical examination increases the risk of maternal infectious morbidity in the setting of preterm prelabor rupture of membranes. Three studies noted increasing trends in either chorioamnionitis, endometritis, or both; however, none of these trends were statistically significant [5–7]. Only one study observed a statistically greater rate of chorioamnionitis, but not endometritis [4]. Our analysis of chorioamnionitis or endometritis separately noted no association of these specific maternal infectious morbidity with a digital cervical examination. It was only through the combining results of the composite maternal infectious morbidity with meta-analysis that a weighted effect was shown to occur with a digital cervical examination. This observation is supported by a high level of consistency among the studies. With the majority of women in these four studies having not received latency antibiotics it is difficult to draw conclusions what effect the administration of latency antibiotics will have on a composite maternal infectious morbidity in current practice and further study is needed.

Digital cervical examination in the setting of preterm prelabor rupture of membranes has been reported to be associated with a shortened latency period in some trials [5–7] but not others [4]. It has been speculated that digital cervical examination is associated with a shorter latency period due to the introduction of vaginal flora into the intraamniotic cavity or that a subclinical infection results in the release of prostaglandins and stimulates uterine contractions [5,6]. However, one must be cautious about the underlying reasons for such associations due to a risk of selection bias. Patients in whom delivery is imminent may be more likely to receive digital cervical examinations. From the studies identified for the current analysis, one is unable to determine what institutional protocols were in place if delivery was perceived to be forthcoming (i.e. a preference for a speculum or digital cervical evaluation). Further the duration of the latency period is inversely correlated with the gestational age at amniotic membrane rupture [25]. The one study in the present meta-analysis that noted no association of digital cervical examination with the length of latency had a greater proportion of women with late preterm prelabor rupture of membranes (i.e. between 34 and 37 weeks of gestation) [4]. While a longer mean duration of latency was noted in the current analysis with a speculum examination only (4.5 d), heterogeneity between studies was high.

This study has several strengths, including a prospectively disclosed protocol, a comprehensive search scheme, and that populaces were from varied parts of the world. Limitations of our study should be remarked. The studies available for this analysis did not stratify the risk of infectious morbidity by gestational age at the time of preterm prelabour rupture of membranes. In pregnancies that experience preterm prelabor rupture of membranes, the incidence of chorioamnionitis increases significantly with decreasing gestational age [26]. Current antenatal guidelines recommend the administration of antibiotics to prolong latency and a course of corticosteroids in women with preterm prelabour rupture of membranes prior to 34 weeks of gestation [1–3]. The effect of these treatment
modalities on maternal infectious morbidity and duration of latency in the context of preforming a specimen versus digital examination are not known. Due to the small numbers of individuals with chorioamnionitis and endometritis seen in the various studies one cannot rule out a type II error. A post-hoc power assessment of the differences measured for these secondary outcomes in the current meta-analysis indicates our sample size had a 51% and 15% power to detect a difference between the two groups for chorioamnionitis and endometritis, respectively. As with all meta-analysis, the usefulness of the conclusions is contingent on the quality of the primary studies included. Unrevealed or unmeasured effects not steadily reported could have altered the identified associations.

Conclusion
This study confirms the association of digital cervical examination with increased infectious morbidity and a shortened latency period in the setting of preterm prelabor rupture of membranes. This suggest that there is no evidence to change the current clinical approach of avoiding digital cervical examination in this clinical situation. Clinical approaches, such as sterile speculum examination in the setting of preterm prelabor rupture of membranes, that can prolong the latency period and potentially allow for the optimal administration of corticosteroid therapy will improve neonatal outcomes as well as reduce maternal infectious morbidity.

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