WHO recommendation against routine antibiotic administration for women with prelabour rupture of membranes at (or near) term

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Recommendation

Routine antibiotic administration is not recommended for women with prelabour rupture of membranes at (or near) term.

(Low-quality evidence, strong recommendation)

Publication history

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Remarks

- “Routine” use implies administration of antibiotics in the absence of clinical signs of infection or any additional risk factors for infection.
- “Near term” in this context refers to 36 weeks gestation and above.
- Evidence for this recommendation was based on studies that included women with duration of ruptured membranes less than 12 hours. The GDG noted that while the available evidence clearly indicates that antibiotics do not confer any benefits under a clinical policy of immediate or early induction (within 12 hours of rupture), it is less clear for a policy of expectant or delayed induction longer than this timeframe. Nevertheless, the generally low rate of maternal infection in the control population in the included studies (< 5%) further supports the restriction of antibiotic use to women with PROM and clinical evidence of infections.
- The GDG noted that evidence is lacking on the potential benefits of antibiotic prophylaxis for women with prolonged rupture of membranes (> 18 hours) and active labour where the baseline risk of infection may be higher. As the risk of infection increases with the duration of labour, it is possible that women with prolonged labour and ruptured membranes may benefit from antibiotic prophylaxis, and this underlies the common clinical practice. The group acknowledges that in the light of current obstetric practice, it is unlikely that a randomized controlled trial will address the important question on the effect of antibiotic prophylaxis in prolonged prelabour rupture of membranes at term (> 12 hours) or prolonged labour with ruptured membranes.
- The GDG put its emphasis on potential side effects of antibiotics, particularly long-term effects among exposed children, as well as bacterial resistance and, therefore, made a strong recommendation.

Background
Bacterial infections during labour and the puerperium are among the leading causes of maternal mortality worldwide, accounting for about one tenth of the global burden of maternal deaths. While the number of deaths arising from these infections has decreased considerably in high-income settings, the situation has not improved in resource-limited settings. Most of the estimated 75,000 maternal deaths occurring worldwide yearly as a result of infections are recorded in low-income countries. Although the reported incidence in high-income countries is relatively low (between 0.1 and 0.6 per 1000 births), it is nonetheless an important direct cause of maternal mortality.

Apart from deaths and acute morbidities associated with infections during or following childbirth, long-term disabilities such as chronic pelvic pain, fallopian tube blockage and secondary infertility can also occur. Maternal infections around childbirth also have a considerable impact on newborn mortality, and an estimated 1 million newborn deaths are associated with such infections annually. In addition, infection-related morbidities and prolonged hospitalization can interfere with mother–infant bonding in the first days after birth.

**Methods**

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, guided by the GRADE approach. Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of maternal peripartum infections (2015).

A Cochrane systematic review was conducted on the use of prophylactic antibiotics for women with prelabour rupture of membranes (PROM) at 36 weeks gestation or beyond for preventing infectious morbidities. In the review, randomized controlled trials relevant to the key question were screened by review authors, and data on relevant outcomes and comparisons were extracted. Evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgments for each outcome, and the estimated risks.

WHO convened a Guideline Development Group (GDG) meeting on recommendations on prevention and treatment of maternal peripartum infections in September 2015, where this recommendation was developed. The GDG comprised of a group of independent experts, who used the evidence profiles to assess evidence on effects on the pre-specified outcomes. GDG members discussed the balance between desirable and undesirable effects, overall quality of supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity, to formulate the recommendation. Remarks were added to clarify the recommendation, and aid implementation.

**Recommendation question**

For this recommendation, we aimed to answer the following question:

- Among pregnant women with prelabour rupture of membranes at or near term (P), does routine antibiotic prophylaxis (I), compared with no routine antibiotic prophylaxis (C), prevent infectious morbidities and improve outcomes (O)?

**Evidence Summary**

Evidence on the use of prophylactic antibiotics for women with prelabour rupture of membranes (PROM) at 36 weeks gestation or beyond for preventing infectious morbidities was extracted from a Cochrane systematic review of four trials involving 2639 women.

The trials were conducted in Chile, Egypt, Portugal and Spain.

Gestational age inclusion criteria varied slightly between trials (36 weeks in two trials and 37 weeks in
Two trials). All studies excluded women with multiple pregnancy and major obstetric complications. All studies used consistent criteria for diagnosis of membrane rupture and had protocols that attempted to minimize vaginal examinations. Pregnancy management protocols varied slightly between settings, mainly for induction policies.

The trials did not report on antibiotic side-effects and antibiotic resistance.

**Any antibiotic versus placebo or no antibiotic (all women) (EB Table 8a)**

- Two trials compared antibiotics with placebo, and two other trials compared antibiotics versus no treatment. All trials compared different antibiotics and routes of administration. Two trials tested IV ampicillin with IV or IM gentamycin, one trial tested parenteral ampicillin/subactam, and one trial intravenous cefuroxime and clindamycin for 48 hours then oral cefuroxime and clindamycin for a further 24 hours.
- There were no significant differences between groups for maternal infectious morbidities: suspected or proven chorioamnionitis (RR 0.65, 95% CI 0.34 to 1.26; 4 trials, 2639 women), endometritis (RR 0.34, 95% CI 0.05 to 2.31; 4 trials, 2639 women) or wound infection (RR 0.79, 95% CI 0.36 to 1.72; 3 trials, 1906 women). Data on postpartum pyrexia had high levels of heterogeneity ($I^2 = 93\%$) and were presented separately for two trials (RR 0.97, 95% CI 0.58 to 1.61; RR 0.11, 95% CI 0.01 to 0.88). There was no difference in reported maternal adverse effects (RR 2.93 95% CI 0.12 to 71.63; 4 trials, 2639 women). There were no cases of serious maternal outcome, postpartum septicaemia or maternal deaths reported in any of the trials.
- There was no significant difference between groups in perinatal mortality (RR 1.98, 95% CI 0.60 to 6.55; 4 trials, 2639 infants), though two studies had no cases. Furthermore, no difference in stillbirth was shown when comparing antibiotics with placebo or no antibiotics (RR 3.00, 95% CI 0.61 to 14.82; 3 trials, 1906 infants). There were no cases of neonatal mortality in the three trials reporting this outcome (1906 infants).
- There was no significant difference in probable early-onset neonatal sepsis (RR 0.69, 95% CI 0.21 to 2.33; 4 trials, 2639 babies) or definite early-onset neonatal sepsis (RR 0.57, 95% CI 0.08 to 4.2; 4 trials, 2639 babies). There were no significant differences for neonatal meningitis (RR 0.33, 95% CI 0.03 to 3.11; 4 trials, 2639 infants), neonatal pneumonia (RR 0.33, 95% CI 0.01 to 7.96; 4 trials, 2639 infants), admission to NICU (RR 1.23, 95% CI 0.82 to 1.85; 3 trials, 1906 infants) or length of hospitalization in NICU (MD 0.05 days, 95% CI -0.09 to 0.19; 1 trial, 1640 infants). There were no cases of respiratory distress syndrome in two studies.

**Antibiotics versus no antibiotics: by timing of induction of labour (EB Table 8b)**

- Three trials involving 2478 women were included in the subgroup analysis of timing of induction of labour.
- There was no significant difference between comparison groups for early (< 12 hr) or late (≥ 12 hr) induction subgroups with respect to chorioamnionitis and/or endometritis (early induction: RR 1.15, 95% CI 0.64 to 2.08; 1 trial, 1640 women; late induction: RR 0.34, 95% CI 0.08 to 1.47; 2 trials, 838 women).
- No significant differences were found between comparison groups in the subgroups for perinatal mortality (early induction: RR 3.00, 95% CI 0.61 to 14.82; 1 trial, 1640 infants; late induction: RR 0.98, 95% CI 0.14 to 6.89; 2 trials, 838 infants). Data on stillbirths were only available for the early induction subgroup, for which no statistically significant difference was found (RR 3.00, 95% CI 0.61 to 14.82; 1 trial, 1630 women).
- There were no significant differences between comparison groups in the two subgroups with respect to neonatal mortality.

**Implementation considerations**

- The successful introduction of this recommendation into national programmes and health-care services...
depends on well-planned and participatory consensus-driven processes of adaptation and implementation. The adaptation and implementation processes may include the development or revision of existing national guidelines or protocols based on this recommendation.

- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.
- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations, and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
- In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.

**Research implications**

The GDG identified that further research on the following high-priority questions is needed:

- What is the contribution of the duration of rupture of membranes and length of labour on maternal and neonatal infectious morbidity among women with PROM at term?
- What are the benefits of initiating prophylactic antibiotics after prolonged rupture of membranes at term?

**Related Links**


Supporting systematic review:

**Wojcieszek AM, Stock OM, Flenady V. Antibiotics for prelabour rupture of membranes at or near term. The Cochrane database of systematic reviews. 2014(10):Cd001807.**

**References**


Organization. 2011.


Citation

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