# WHO recommendations for induction of labour

The WHO guidelines on induction of labour are valid and useful and can be implemented in all under-resourced settings. The recommendations are likely to be cost–effective and acceptable to pregnant women, their obstetricians and policy-makers in under-resourced settings.

**RHL guideline appraisal by Goonewardene M, Rameez MFM, Kaluarachchi A, Perera H**

## 1. INTRODUCTION

Induction of labour (IOL) needs to be considered when the risk–benefit analysis indicates that delivering the baby is a safer option for the baby, the mother, or both, rather than continuing the pregnancy, and when there are no clear indications for caesarean section and no contraindications for vaginal delivery.

Post-term gestation, prelabour rupture of membranes (at term and preterm) and fetal growth restriction are the leading indications for IOL (1). Other situations in which IOL may be indicated include medical disorders (such as hypertensive disorders of pregnancy), suspected fetal macrosomia, intrauterine fetal death, multiple gestations, chorioamnionitis and even maternal request (1–3). Globally, in medium-to-large health-care facilities, it is estimated that approximately 10% of all deliveries involve IOL, ranging from 1.4% in Niger to 35.5% in Sri Lanka (3).

The primary goal of the WHO recommendations for IOL is stated to be the improvement of the quality of care and outcomes for pregnant women undergoing the procedure in under-resourced settings (3). The objective of this appraisal was to determine the value of the WHO recommendations in improving quality of care and outcomes for pregnant women undergoing the procedure in under-resourced settings.

## 2. METHODS OF THE REVIEW

All four authors of the present appraisal had a preliminary discussion about the Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument and how it should be applied to the WHO guidelines. Next, each author independently applied the instrument and a total score and a standardized score (out of a maximum of 100) was obtained for each domain, as described in the AGREE document (4). The comments made by individual authors on each item and the overall assessment were discussed to arrive at a consensus. In appraising the guidelines the authors kept in mind the following questions:

- Do the recommendations in the guidelines enable health-care professionals and policy-makers to introduce interventions that help to reduce the impact of the problem the guidelines seek to remedy?
- Are there any clinical/health system/policy questions that the guidelines do not address?
- Do the guidelines include the steps that would be needed at the health system and clinic levels to put the recommendations into practice?

## 3. RESULTS OF THE REVIEW

The total scores awarded by the four authors to the WHO recommendations were as follows: scope and purpose: 42/48 = 88%; stakeholder involvement: 38/64 = 59%; rigour of development: 85/112 = 76%; clarity and presentation: 44/64 = 69 %; applicability: 38/48 = 79%; and editorial independence: 30/32 = 94%.

The objectives, the clinical questions covered and the women to whom the guidance applies are stated clearly in the guidelines. Although several stakeholders, including specialist obstetricians and lay women had been involved in formulating the recommendations, apparently only one consumer representative and one expert in IOL reviewed the recommendations after they were formulated.

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The strength of each recommendation in the guidelines is labelled as "weak" or "strong". Apparently, the strength was determined on the basis of, among other factors, the quality of the available evidence and whether the recommendation was likely to be modified as a result of further research. The authors of this appraisal felt that in some cases the strength attributed to certain recommendations could mislead the readers of the WHO guidelines. For example, recommendation No. 17 (outpatient IOL not recommended) is noted as being "weak". This may lead some clinicians and policy-makers infer that the recommendation is a suggestion rather than as a strong statement that IOL should not be practised as an outpatient procedure. The same also applies to intravenous oxytocin alone being recommended for IOL. In addition, the authors of this appraisal believed that in formulating recommendation Nos. 1 and 2 on IOL at 41 weeks' gestation insufficient evidence from Asia and Africa may have been used. Moreover, possible adverse perinatal outcomes may not been considered sufficiently in deciding on the strength of recommendation Nos. 1–4.

## 4. DISCUSSION

Overall, the WHO guidelines on IOL are valid and useful and can be implemented in all under-resourced settings.

### 4.1 Scope and coverage of the guideline

The scope and coverage of the guidelines are appropriate to the context of the topic. Of the 16 recommendations, the authors of this appraisal fully agreed with the eight strong recommendations (i.e. Nos. 5, 8–12, 14 and 15) made regarding IOL in women with prelabour rupture of membrane, the use of oral and vaginal misoprostol, vaginal prostaglandins and balloon catheter for labour induction, and sweeping of membrane to reduce the need for induction (3).

In women with gestational diabetes mellitus (GDM), there is a high risk of perinatal morbidity and mortality, with stillbirths accounting for the majority of cases involving perinatal death. Most cases of stillbirth are associated with poor control of glycaemia during pregnancy. Hypertension, placental insufficiency, growth restriction or macrosomia also contribute to increased perinatal morbidity and mortality in GDM (5). The recommendation on GDM has been based on a single trial of 200 women who had received insulin and had good control of glycaemia. As could have been expected, no perinatal deaths occurred in this trial. However, the risk of macrosomia was reduced by IOL at 38 weeks and there were three cases of mild shoulder dystocia in the expectant management group. Even in the expectant group, 50% of women underwent IOL for a variety of obstetrics reasons. Because of the rarity of adverse outcomes, even the authors of the Cochrane review concluded that firm conclusions could not be drawn from this study and that there may have been little advantage in delaying delivery beyond 38–39 weeks and that IOL may have been a reasonable option for these women (6). Expectant management after 40 weeks could have adverse perinatal outcomes in women with GDM, especially in under-resourced settings, and the safety of such expectant management needs to be established.

In the women who had IOL at 38 weeks for suspected fetal macrosomia, the significant reduction of clavicular and arm fractures due to shoulder dystocia (RR 0.2, 95%CI 0.05 – 0.79) is important and should be considered as a priority outcome in this particular situation (7). In under-resourced settings without ultrasound scanning facilities, the clinical expertise available and the women’s informed choice will need to be considered when managing women with suspected fetal macrosomia.

Of the 25 trials with 6660 women included in the Cochrane review on the use of intravenous oxytocin alone for induction of labour, only five trials with 691 women (all conducted before 1993) had recruited women with intact membranes. In all other trials women had both intact and ruptured membranes, or the trials were unclear about the women's membrane status. As expected, there were no significant findings in the group with intact membranes and that group did not contribute much to the overall outcomes (8). Thus, the safety of intravenous oxytocin infusions with intact membranes has not been established. Therefore, the conclusion that that intravenous oxytocin alone without rupture of membranes is effective and could be recommended for IOL may not be accurate. Although amniotomy alone is not recommended for IOL in the guidelines, it could still have a place in IOL in the presence of a scarred uterus or in situations in which oxytocin infusions

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and prostaglandins are contraindicated because of the risk of uterine rupture or hyperstimulation. Amniotomy, however, will also carry the risk of ascending infection and therefore would be contraindicated in women with genital infections (such as HIV) or those with a dead fetus.

The authors of this appraisal fully agree with the general principle that "women receiving oxytocin, misoprostol or other prostaglandin should never be left unattended". Hence, the statement "outpatient IOL is not recommended for improving birth outcomes" should have been a strong recommendation. The authors feel that in deciding on the strength of the recommendations patient safety must be the prime consideration and not lack of evidence and possibility of the recommendation being modified in the future. Labelling this recommendation as weak, may have rendered it unclear, possibly encouraging some clinicians to ignore it.

## 4.2 Implementation of the recommendations

It has been shown that maternal complications of pregnancy could increase after 40 weeks' gestation in low-risk women, especially nullipara (11). In low-risk pregnancy at term, it has been suggested that active management of risk through the use of preventive labour induction prior to possible development of utero-placental insufficiency or cephalo-pelvic disproportion can improve birth outcomes and reduce caesarean section rates (12, 13).

Since women in Asia and Africa have been shown to have a shorter duration of pregnancy compared with European women (14, 15), the authors of this appraisal recommend that clinicians in those regions should regard recommendation No. 1 (IOL for women known with certainty to have reached 41 weeks of gestation) as strong. The authors believe that the evidence which forms the basis for this recommendation was inadequate in terms of representation of Asian and African women in the studies. Of the 8085 women included in the Cochrane review only two studies involving 295 women were from India, four studies involving 747 women were from China and Thailand, and one study involving 600 women was from Turkey. This amounts to only 1642 (20%) women. There were no studies from Africa. There may also be situations in which IOL may need to be considered earlier in Asian and African women if uteroplacental insufficiency or cephalopelvic disproportion is suspected especially in nullipara. In under-resourced settings where ultrasound scanning facilities are not available to date pregnancies accurately, there would be a need to educate and motivate pregnant women to attend prenatal clinics early to allow clinical dating of the pregnancy. On the other hand, there is no rationale for IOL in an uncomplicated pregnancy at less than 38 weeks and no benefit could be expected from routine IOL at less than 38 weeks. Further evidence is required regarding benefits and undesirable effects of IOL between 38 and 41 weeks (12, 13).

Prostaglandins should be avoided in cases of scarred uteri and should be used with caution, and the dose reduced, in grande multipara (2). They should not be used without adequate monitoring of both the mother and the fetus and the availability of facilities for emergency caesarean section and neonatal resuscitation. Oral misoprostol is available in 25-µg tablets in many under-resourced settings.

Finally, all the recommendations are feasible in under-resourced settings. Although a cost analysis has not been carried out, the recommendations are likely to be cost–effective and acceptable to the pregnant women, their obstetricians and even policy-makers in under-resourced settings.

## 4.3 Recommendations for further updates of the guidelines

In the next update of the guidelines, it would desirable to have the recommendations reviewed by a wider group of clinicians, women of reproductive age and intrapartum care-givers prior to publication. It would also help to refine the methodology for determining the strength of recommendations in order to avoid possible misunderstandings. Furthermore, WHO should consider including a practical algorithmic guide with a second-line approach in cases of failure of the first-line IOL approach. Also, guidance on the management of serious adverse effects such as hyperstimulation would be desirable in future updates.

The nitric oxide donor iso-sorbide mononitrate, when administered vaginally, has been shown to be effective in cervical ripening and making the cervix favourable for IOL at term. Since nitric oxide donor iso-sorbide mononitrate does not cause uterine contractions, it has been shown that it could be safely used as an

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outpatient procedure. This would enable its use even in grande maltipara or women with scarred uteri (9,10). The use of this and other new drugs as well as IOL in women with fetal growth restriction have to be considered for future updates.

In addition to the basic indicators of IOL, the inclusion of the following outcome indicators in the main body of the guidelines would be of value for monitoring and evaluating the implementation of the guidelines: vaginal delivery not achieved within 24 hours; uterine hyperstimulation with fetal heart rate changes; severe neonatal morbidity and perinatal deaths; severe maternal morbidity or death; common side-effects; and maternal satisfaction with IOL.

In addition to what has been identified in the guidelines, the inclusion of the following as high-priority topics for research should be considered:

- Is nitric oxide donor iso-sorbide mononitrate administered vaginally a safe, feasible, effective and acceptable method for outpatient pre-induction cervical ripening?
- Should IOL be offered to women with suspected fetal macrosomia?
- In low-risk pregnancies at term (38–41 weeks gestation) is active management of risk by preventive IOL safe and effective in improving maternal and perinatal outcomes?
- Should IOL be offered at earlier gestations to non-Caucasian women?

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