Isolated Oligohydramnios at Term as an Indication for Labor Induction: A Systematic Review and Meta-Analysis

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Introduction

Oligohydramnios is most commonly defined as an amniotic fluid index (AFI) ≤5 cm or the largest vertical pocket measuring ≤2 cm [1, 2]. It is considered a risk factor for adverse fetal outcome, as well as an indicator of the possible presence of maternal and/or fetal comorbidities. Hence, the identification of oligohydramnios usually mandates close fetal surveillance.

Isolated oligohydramnios (IO) refers to the presence of oligohydramnios without fetal structural and chromosomal abnormalities, without fetal growth restriction, without intrauterine infection, and in the absence of known maternal disease. The incidence of IO ranges from 1.17–1.84). There were no significant differences in cord pH <7.1 and meconium-stained amniotic fluid. In the single randomized trial comparing induction of labor with expectant management, no differences were found in any significant maternal or neonatal outcomes. Conclusion: Isolated oligohydramnios at term is associated with significantly higher rates of labor induction, Cesarean sections, and short-term neonatal morbidity.

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Key Words
Isolated oligohydramnios · Term pregnancy · Induction of labor · Expectant management

Abstract
Objective: To investigate whether isolated oligohydramnios at term is associated with increased rates of perinatal morbidity and mortality and whether induction of labor in term pregnancies with isolated oligohydramnios is superior to conservative management in reducing perinatal morbidity and mortality. Study Design: We searched databases from inception to May 2015. We included studies that evaluated isolated oligohydramnios at term and perinatal outcome. Each outcome was analyzed separately, performing a comparative analysis between the study and control groups. Results: Twelve studies were included with 35,999 women: 2,414 (6.7%) with isolated oligohydramnios and 33,585 (93.29%) with normal amniotic fluid index. Patients with isolated oligohydramnios had significantly higher rates of labor induction [odds ratio (OR) 7.56, confidence interval (CI) 4.58–12.48] and Cesarean sections (OR 2.07, CI 1.77–2.41). There were higher rates of an Apgar score <7 at 1 and 5 min (OR 1.53, CI 1.03–2.26, and OR 2.01, CI 1.3–3.09, respectively) and admission to the neonatal intensive care unit (OR 1.47, CI 1.17–1.84). There were no significant differences in cord pH <7.1 and meconium-stained amniotic fluid. In the single randomized trial comparing induction of labor with expectant management, no differences were found in any significant maternal or neonatal outcomes. Conclusion: Isolated oligohydramnios at term is associated with significantly higher rates of labor induction, Cesarean sections, and short-term neonatal morbidity.

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0.5 to 5% depending on the definition used and the population studied [3, 4]. When IO is diagnosed at term (>37 complete weeks of gestation), it is commonly considered a solid indication for labor induction [5]. It is well established that oligohydramnios is associated with an increased incidence of adverse perinatal outcome, possibly as a result of umbilical cord compression, an associated utero-placental insufficiency, and/or meconium-stained AF (MSAF). Therefore, recommendations for labor induction at term have evolved in an attempt to reduce the incidence of these adverse outcomes. However, original reports elucidating the association between oligohydramnios and adverse perinatal outcome included fetuses with structural anomalies, growth restriction and postmaturity syndrome, as well as mothers with various underlying medical conditions, and, thus, may not apply in cases of IO [6–14]. Therefore, the question is whether the observed associated adverse perinatal outcome reflects the sequela of these comorbidities, the medical management, or whether they are a direct result of the reduced AF volume (AFV) itself [15]. In 1999, Chauhan et al. [16] performed a meta-analysis (MA) evaluating the association between AFV and adverse perinatal outcome. The authors confirmed oligohydramnios to be associated with a significant increase in the risk of Cesarean delivery for fetal distress (risk ratio 2.2) and a low 5-min Apgar score (risk ratio 5.2). Fourteen years later, in 2013, Rossi and Prefumo [17] published a systematic review and MA focusing on perinatal outcomes of IO. The authors included 4 studies and concluded that in term and postterm pregnancies, IO was associated with an increased risk of obstetrical interventions but not with adverse neonatal outcome. The American College of Obstetricians and Gynecologists (ACOG) in the 1999 practice bulletin points out the lack of convincing data to support labor induction for IO in the absence of other risk factors for adverse perinatal outcome. Thus, the ACOG does not take a firm stand regarding the optimal timing of delivery in such cases and suggests either delivery or close surveillance [18]. An interesting survey among 632 Society for Maternal-Fetal Medicine members, published in 2009, revealed that approximately 80% of the participants believed that induction of labor, in cases of IO, did not reduce perinatal morbidity, or they did not know whether it did. However, despite being unsure of its benefits, 96% of the practitioners leaned towards intervention in this setting [19].

We sought to systematically re-examine the questionable justification for this common practice of labor induction at term in the presence of IO related to an otherwise low-risk pregnancy. Specifically, we aimed to investigate whether IO at term is associated with increased rates of perinatal morbidity and mortality and whether induction of labor in term pregnancies with IO is superior to conservative management in reducing perinatal morbidity and mortality.

Methods

The study was conducted based on a prospectively prepared protocol and is reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (the PRISMA Statement) [20].

This systematic review and MA is divided into two parts: (1) the investigation of whether true IO at term is associated with increased rates of perinatal morbidity and mortality compared with normal AF at term. (2) The investigation of whether induction of labor in term pregnancies with IO is superior to conservative management in reducing perinatal morbidity and mortality.

Literature Search

We searched Medline, the Cochrane Central Register of Controlled Trials, and Web of Science from inception to May 2015, using the following combination of keywords and text words: ‘isolated oligohydramnios/s’, ‘term pregnancy’, and one of the following: ‘induction of labor’ or ‘conservative management’ or ‘management’ or ‘perinatal outcome’. The search strategy has been supplemented by checking the reference lists of the retrieved articles for additional articles that may not have been revealed by the electronic search. No language restriction was used. An information science specialist supervised the search.

Study Selection

We included randomized control trials (RCTs), nonrandomized controlled clinical trials, prospective and retrospective cohort studies, and case-control studies, all of which evaluated whether IO (defined as AFV ≤5 cm) at term is associated with increased rates of perinatal morbidity and mortality compared with normal AF at term. In addition, we searched for studies that evaluated whether induction of labor in term pregnancies with IO is superior to conservative management in reducing perinatal morbidity and mortality. Case reports, case series, reviews, editorials, and studies published as abstracts only were excluded. Inclusion criteria were: singleton pregnancies at term (37–42 weeks gestation) and diagnosis of oligohydramnios (defined as AFV ≤5 cm). Exclusion criteria were: complicated pregnancies involving maternal systemic illnesses, fetal malformations or growth restriction, and oligohydramnios secondary to ruptured membranes.

Although there is no consensus regarding both the best method of assessment as well as the optimal cutoff for the diagnosis of oligohydramnios and the prediction of perinatal morbidity and mortality, we chose to consider oligohydramnios as an AFV ≤5 cm, because this definition is the one most commonly used in studies evaluating oligohydramnios.

Two investigators (G.S. and A.W.) independently reviewed all potentially relevant articles for eligibility. Titles and abstracts were reviewed for possible exclusion or inclusion. In cases where the reviewer judged the abstract to be potentially eligible, or where the
abstract had insufficient information to make a determination, the full articles were obtained for review. A disagreement between the reviewers was referred to a third reviewer (M.H.) for decision.

**Outcome Measures**

The primary outcome measure was the Cesarean section rate. Secondary outcome measures were delivery characteristics including induction of labor, rates of Cesarean section due to nonreassuring fetal heart rate monitoring (NRFHR), and fetal outcome characteristics including MSAF, an Apgar score <7 at 1 and 5 min, umbilical cord pH <7.1, and admission to a neonatal intensive care unit (NICU).

**Data Collection**

We collected the pregnancy outcome data from the studies that were eligible for this MA, as presented in the published articles. Not all included studies reported all of the outcomes of interest, and each outcome table summarizes the relevant data reported. Consequently, each outcome includes a variable number of studies. E-mail contact with authors was attempted for articles in which data abstraction required clarification.

**Assessment of Methodological Quality**

We assessed the risk of bias using the criteria outlined in the Newcastle-Ottawa scale for assessing the quality of nonrandomized studies in MA [21].

Three parameters related to risk of bias were assessed in each included study: the selection of the study population, the comparability of the groups, and the measured outcome. Each parameter consists of subcategorized questions: selection (n = 4), comparability (n = 2), and outcome (n = 3). Stars awarded for each item serve as a quick visual assessment for the methodological quality of the studies. A study can be awarded a maximum of 9 stars, indicating the highest quality. Studies were classified as 'low risk' of bias when scoring ≥6 stars, while 'high risk' of bias received <6 stars.

The risk of bias in each study included was assessed individually by two reviewers (G.S. and S.S.N.). Any differences in opinion regarding the assessment of the risk of bias were resolved by discussion. Quality assessment was not used as an exclusion criterion.

The risk of bias of RCTs was assessed using the Cochrane Collaboration’s tool for evaluating the risk of bias in randomized trials [22]. Six parameters related to the risk of bias were assessed: (1) selection bias, (2) performance bias, (3) detection bias, (4) attrition bias, (5) reporting bias, and (6) other bias. Each parameter was graded as high or low risk of bias. The risk of bias was measured individually by two reviewers (G.S. and A.W.). Any differences in opinion were resolved by discussion. The risk of publication bias was assessed using funnel plots as appropriate.

**Statistical Analysis and Data Synthesis**

Extracted relevant data were tabulated in a 2 by 2 contingency table. MA was performed with MetaXL software version 1.31 (EpiGear International Pty Ltd.). We analyzed each outcome separately, performing a comparative analysis between the study and control groups.Homogeneity across studies was calculated with the I² test, which defined the percentage of total variation across studies due to heterogeneity rather than chance [23, 24]; Cochran’s Q and I² statistics were used for measuring heterogeneity and the percentage of variation across studies, respectively. A random effect model and a fixed effect model were used appropriately according to the significance of the heterogeneity test. When I² was ≤25%, studies were regarded as homogeneous, and the fixed effect model was used. When I² was ≥75% (as in outcomes 'induction of labor' and 'meconium-stained amniotic fluid'), a random effect model was used. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to ascertain a standardized difference between the IO group and the control group. Forest plots were used to portray the effect estimates for each study with their CIs. p < 0.05 was considered statistically significant.

Post hoc sensitivity analyses were conducted to investigate the potential sources of heterogeneity from specific studies that may have biased the analyses. We conducted sensitivity analyses to explore the effects of study quality and effect size on the results.

**Ethical Issues**

This study is a best evidence review of previously published data and, as such, does not require ethics approval. The data were not used for any purpose other than those of the original study, and no new data were collected. Moreover, no patient identifiers were provided by any investigator.

**Results**

**Study Selection, Details, and Quality**

The searches yielded 905 citations and 178 additional records identified through other resources. Among them, 36 were considered for potential inclusion (fig. 1). Following the exclusion of an additional 24 studies after full text review, 12 studies (35,999 cases) met the inclusion criteria.

![Fig. 1. PRISMA flow chart.](https://example.com/PRISMA.png)
Table 1. Characteristics of included studies

<table>
<thead>
<tr>
<th>First author [Ref.], year</th>
<th>Study design</th>
<th>Objective</th>
<th>Inclusion/exclusion criteria</th>
<th>Sample size and characteristics</th>
<th>Outcomes assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chauhan [25], 1996</td>
<td>Prospective cohort</td>
<td>Determine if an intrapartum AFI ≤5 cm is associated with CS for fetal intolerance to labor or an Apgar score &lt;7 at 1 and 5 min</td>
<td>Inclusion: singleton gestation in vertex presentation and no known chromosomal or structural abnormalities Exclusion: NRFRH upon admission, prophylactic amnioinfusion, cervical dilatation &gt;5 cm upon admission, gestational age &gt;26 weeks</td>
<td>161 IO 187 controls only noncomplicated</td>
<td>CS due to NRFRH, Apgar score &lt;7 at 1 and 5 min</td>
</tr>
<tr>
<td>Chauhan [26], 1997</td>
<td>Prospective cohort</td>
<td>Determine whether AFI ≤5 cm or 2-diameter pocket volume &lt;15 cm is a predictor of abdominal delivery due to fetal distress or an Apgar score &lt;7 at 1 or 5 min</td>
<td>Inclusion: singleton gestation in vertex presentation with intact membrane, normal fetal heart rate tracing on admission, and no known chromosomal or structural abnormalities</td>
<td>209 IO 209 controls</td>
<td>CS due to NRFRH, Apgar score &lt;7 at 1 and 5 min</td>
</tr>
<tr>
<td>Conway [27], 1998</td>
<td>Retrospective cohort</td>
<td>Evaluate the outcome of labor induction in cases of IO term gestations</td>
<td>Exclusion: pregnancies complicated by hypertension, diabetes, fetal anomalies, suspected fetal growth restriction, ruptured membrane, or oligohydramnios that existed prior to 37 weeks gestation</td>
<td>183 IO 183 controls</td>
<td>Route of delivery, neonatal morbidity/mortality</td>
</tr>
<tr>
<td>Kreiner [29], 2001</td>
<td>Retrospective cohort</td>
<td>Evaluate perinatal outcomes of pregnancies complicated by IO at ≥30 weeks gestation</td>
<td>Exclusion: gestational age &gt;30 weeks Exclusion: complicated pregnancies: PROM, diabetes requiring insulin, pre-eclampsia, confirmed fetal growth restriction (&lt;10th percentile on ultrasound examination confirmed by birth weight)</td>
<td>57 IO 93 controls</td>
<td>Abnormal NST, CS due to NRFRH, MSAF, Apgar score &lt;7 at 5 min</td>
</tr>
<tr>
<td>Rainford [28], 2001</td>
<td>Prospective cohort</td>
<td>Establish whether an association between oligohydramnios and pregnancy outcome is present in IO term pregnancies</td>
<td>Inclusion: term pregnancies (37–42 weeks gestation), singleton in cephalic presentation, reactive NST within 4 days of delivery Exclusion: maternal or fetal complication or unavailable data</td>
<td>44 IO 188 controls</td>
<td>Adverse perinatal outcome, rates of operative vaginal or CS due to NRFRH</td>
</tr>
<tr>
<td>Locatelli [30], 2003</td>
<td>Prospective cohort</td>
<td>Evaluate the effect of oligohydramnios on perinatal outcome in uncomplicated pregnancies between 40 + 0 and 41 + 6 weeks gestation</td>
<td>Inclusion: gestational age between 40 + 0 and 41 + 6 weeks of gestation with singleton fetus and reliable dating (menstrual history confirmed by ultrasound examination before 20 weeks gestation) who underwent monitoring with the protocol Exclusion: PROM, multiple gestation, indications for monitoring of fetal well-being other than gestational age ≥40 weeks, and fetal anomalies</td>
<td>341 IO 2,708 controls</td>
<td>CS due to NRFRH, MSAF, 5-min Apgar score &lt;7, umbilical artery pH &lt;7.0, SGA</td>
</tr>
<tr>
<td>Zhang [15], 2004</td>
<td>Prospective cohort</td>
<td>Examine fetal growth and perinatal outcomes in pregnancies with IO</td>
<td>Inclusion: pregnant women &gt;18 years, speaking English, where the last menstrual period was known within 1 week, and gestational age was &lt;18 weeks at recruitment Exclusion: previous still birth, prior SGA, irregular menstrual cycles, fetal anomalies, discrepancy between uterine size and dates of &gt;3 weeks, diabetes, chronic hypertension, or chronic renal failure</td>
<td>86 IO 6,571 controls only noncomplicated</td>
<td>Total CS and due to NRFRH, birth weight &lt;10th percentile, arterial umbilical cord pH &lt;7.10, Apgar score at 1 and 5 min, MSAF, NICU admissions, perinatal morbidity and mortality</td>
</tr>
<tr>
<td>Manzanares [31], 2007</td>
<td>Retrospective cohort</td>
<td>Evaluate the outcome of induction of labor for IO in low-risk term gestations</td>
<td>Inclusion: singleton cephalic presentation pregnancies between 37 and 42 weeks gestation Exclusion: fetal abnormalities, PROM, SGA, IUGR, other fetal or maternal disorders</td>
<td>206 IO 206 controls</td>
<td>Rate of operative delivery birth weight, birth weight &lt;10th percentile, arterial umbilical cord pH &lt;7.10, Apgar score at 1 and 5 min, MSAF, NICU admissions</td>
</tr>
<tr>
<td>Donon [32], 2007</td>
<td>Retrospective cohort</td>
<td>Evaluate maternal and neonatal outcomes in pregnancies complicated by IO at term, managed by induction of labor</td>
<td>Exclusion: multifetal gestation, noncephalic presentation, uterine scars, placenta previa or any contraindication for vaginal delivery, patients with hypertensive disorders, diabetes, and autoimmune diseases</td>
<td>67 IO 276 controls</td>
<td>Mode of delivery, indications for operative delivery, Apgar score at 1 and 5 min, birth weight, gestational age at birth</td>
</tr>
<tr>
<td>Ahmad [33], 2009</td>
<td>Prospective cohort</td>
<td>Assess the impact of IO on perinatal outcomes</td>
<td>Exclusion: patients with medical disorders like diabetes, PET, and multiple pregnancies; fetal growth restriction, congenital anomalies, and PROM</td>
<td>71 IO 350 controls</td>
<td>Induction of labor and CS rates, birth weight, perinatal mortality and morbidity, Apgar scores</td>
</tr>
<tr>
<td>Ashwal [34], 2014</td>
<td>Retrospective cohort</td>
<td>Assess the association between IO and pregnancy outcome in low-risk pregnancies at term</td>
<td>Inclusion: IO pregnancies – AFI ≤5 cm, between 37 + 0 and 41 + 6 weeks gestation Exclusion: known chromosomal or structural anomalies, hypertensive disorders, diabetes, polyhydramnios (AFI &gt;25), suspected fetal growth restriction (fetal weight &lt;10th percentile), suspected choioamnionitis, or ruptured amniotic membrane</td>
<td>987 IO 22,280 controls</td>
<td>CS or operative delivery due to NRFRH, Apgar score &lt;5 at 5 min, umbilical artery pH &lt;7.1, NICU admission, need for intubation, meconium aspiration syndrome, or hyponotic ischemic encephalopathy</td>
</tr>
<tr>
<td>Lakshmi [35], 2015</td>
<td>Prospective cohort</td>
<td>Study the correlation of AFI on fetal outcome at term gestation</td>
<td>Inclusion: singleton pregnancy, gestational age between 37 and 42 weeks, gestational age confirmed by history of regular menstrual cycle or ultrasonography done in the early trimester, no fetal anomalies detected on initial screening Exclusion: history of irregular menstrual cycle, patients with uncertain and unreliable dates, history of contraceptive use before the last menstrual period, multiple pregnancies, hydramnios, all high-risk pregnancies</td>
<td>100 IO 100 controls</td>
<td>MSAF, mode of delivery and indication for CS, Apgar score at 1 min, birth weight, and admission to NICU</td>
</tr>
</tbody>
</table>

CS = Cesarean section; NST = nonstress test; PROM = premature rupture of membranes; SGA = small for gestational age; IUGR = intrauterine growth retardation; PET = pre-eclampsia.
criterion and were used in the final analyses [15, 25–35]. IO was diagnosed in 2,414 cases (6.7%, study group) and 33,585 cases (93.29%) had normal AFI (control group).

The main characteristics of the studies included in the MA are shown in tables 1 and 2. All studies were cohort studies. Some of the admitted studies investigated oligohydramnios in general, but data on IO was available for extraction and included in our analysis [25, 26]. Three of the studies focused specifically on women with IO managed by induction of labor [27, 31, 32], and 6 studies measured induction rates among IO pregnancies [28–30, 33–35].

We were able to identify a single RCT eligible for inclusion. In this pilot trial, which compared induction of labor versus conservative management in term pregnancies with IO, perinatal morbidity and mortality were compared between the two study arms [36]. This study’s results and the risk of bias are presented separately and are not included in the MA.

We contacted several corresponding authors of the studies analyzed and were able to get access to some additional data required for the analysis. Table 3 presents the risk of bias in each included study using the Newcastle-Ottawa scale [21]. Eleven of the 12 studies included in the MA were judged to be of medium-high quality with a low risk of bias (table 3).

The single RCT by Ek et al. [36] was graded with ‘high risk of bias’ in several categories due to several methodological flaws, including lack of blinding and small study groups (table 3).

**Primary Outcome**

Total Cesarean section rates were significantly higher in the IO group compared with the normal AF group (13.77 vs. 6.31%; OR 2.07; CI 1.77–2.41; I² 46%) (fig. 2). In particular, a separate analysis for Cesarean section rates due to NRFHR demonstrated significantly higher rates in the IO group compared with controls (5.9 vs. 1.85%; OR 2.17; CI 1.73–2.73; I² 0%) (fig. 3).

In the single, small RCT by Ek et al. [36], patients with NRFHR were excluded. The total Cesarean section rate was not significantly different between the two groups.

**Secondary Outcomes**

IO was associated with a significantly higher rate of labor induction compared with the control group (43 vs. 6.53%; OR 7.56; CI 4.58–12.48; I² 88%) (fig. 4). Similar significant associations were found with the Apgar score <7 at 1 min (OR 1.53; CI 1.03–2.26; I² 0%) and 5 min (OR 2.01; CI 1.3–3.09) as well as with admission to the NICU (OR 1.47; CI 1.17–1.84; I² 8%) (fig. 5).

We performed a sensitivity analysis in which studies with extreme results were omitted (Manzanares et al. [31], Apgar score <7 at 1 min; Manzanares et al. [31] and Kreiser et al. [29], admission to NICU). The results were sustained (fig. 6).
Blood cord pH <7.1 and MSAF were not found to be significantly different between the groups (fig. 7).

A second sensitivity analysis was performed in which data extracted from studies with a high risk of bias were excluded (Ahmad and Munim [33]). These analyses did not demonstrate any significant changes in the results.

In the single RCT published by Ek et al. [36], no significant differences were found in mean birth weight and NICU admission.

The risk of publication bias is presented as 7 funnel plots for the different outcomes assessed (fig. 8).

### Discussion

**Oligohydramnios and Perinatal Outcomes: Study Results and Supporting Data**

In this MA, we found that IO in term pregnancies is significantly associated with higher rates of induction of labor and Cesarean section (both in general and due to NRFHR). Similar associations were found between IO term pregnancies and low Apgar scores (1 and 5 min) and NICU admissions. Although the Apgar score at 5 min is considered a better predictor of neonatal long-term outcome [37, 38], cord pH showed no significant association.
First author [Ref.], year | CS rate OR (95% CI) | Weight, %
--- | --- | ---
Conway [27], 1998 | 2.68 (1.32–5.44) | 5.19
Rainford [28], 2001 | 2.12 (1.00–4.51) | 4.26
Locatelli [30], 2003 | 1.40 (1.02–1.92) | 30.11
Zhang [15], 2004 | 1.40 (0.81–2.43) | 9.94
Manzanares [31], 2007 | 2.97 (1.48–5.95) | 5.21
Danon [32], 2007 | 3.42 (1.75–6.68) | 4.53
Ahmad [33], 2009 | 3.33 (1.93–5.74) | 6.31
Ashwal [34], 2014 | 2.16 (1.66–2.81) | 28.30
Lakshmi [35], 2015 | 2.50 (1.32–4.77) | 6.15
Overall | 2.07 (1.78–2.42) | 100.00

Q = 14.90, p = 0.06, I² = 46%

First author [Ref.], year | CS d/t NRFHR OR (95% CI) | Weight, %
--- | --- | ---
Chauhan [25], 1996 | 1.56 (0.71–3.43) | 10.77
Chauhan [26], 1997 | 2.75 (0.98–7.68) | 1.40
Conway [27], 1998 | 3.10 (0.83–11.65) | 3.36
Kreiser [29], 2001 | 0.93 (0.26–3.32) | 5.83
Locatelli [30], 2003 | 2.20 (1.42–3.38) | 25.65
Zhang [15], 2004 | 0.38 (0.05–2.75) | 5.93
Manzanares [31], 2007 | 4.25 (1.40–12.95) | 4.35
Danon [32], 2007 | 3.52 (1.25–9.88) | 4.37
Ashwal [34], 2014 | 2.11 (1.37–3.25) | 24.32
Lakshmi [35], 2015 | 2.60 (1.26–5.39) | 11.03
Overall | 2.17 (1.73–2.73) | 100.00

Q = 8.34, p = 0.50, I² = 0%

First author [Ref.], year | Induction rate OR (95% CI) | Weight, %
--- | --- | ---
Kreiser [29], 2001 | 0.93 (0.26–3.32) | 9.48
Rainford [28], 2001 | 20.12 (4.73–85.54) | 8.06
Locatelli [30], 2003 | 14.66 (10.89–19.73) | 22.55
Ahmad [33], 2009 | 10.63 (6.02–18.79) | 18.61
Ashwal [34], 2014 | 9.96 (8.52–11.64) | 23.93
Lakshmi [35], 2015 | 3.04 (1.59–5.81) | 17.38
Overall | 7.56 (4.58–12.48) | 100.00

Q = 33.63, p = 0.00, I² = 85%
While both NRFHR and the 1-min Apgar score have poor sensitivity for fetal status and outcome, cord pH is a direct measure of the fetal oxygenation status. Thus, our results are not entirely conclusive.

Our findings are partially corroborated with a previous smaller MA performed by Rossi and Prefumo [17], in which prospective and retrospective cohort studies published between 2000 and 2012 were included. The authors concluded that IO in uncomplicated term pregnancies is associated with an approximately 2-fold increase in operative delivery because of NRFHR. However, the authors could not find a significant association of IO at term with low Apgar scores, low umbilical artery pH, and NICU admissions. The reason for the difference in the results is
probably due to different selection criteria (Rossi and Prefumo [17] included high-risk pregnancies) and the inclusion of several more recent studies in our MA (4 studies and 3,873 total cases in Rossi and Prefumo vs. 12 studies and 35,999 total cases in the present MA).

Therefore, we conclude that IO at term is associated with both high intervention rates and several fetal and neonatal parameters that may indicate compromise. This is true even when a rigorous attempt was done to exclude all high-risk cases and cases in which placental insufficiency was evident. Nevertheless, the long-term significance of these findings is yet to be determined, especially in the absence (in all 3 MAs) of a clear association with arterial cord pH.

It is essential to point out that, with the available data, we cannot evaluate the effect of the widely used iatrogenic interventions on perinatal outcomes. There is no clear evidence to support the benefits of labor induction on short- and long-term neonatal outcome in this setting. It is also possible that the intervention itself (i.e. the induction of labor) worsens outcome parameters (as a result, for example, of early term induction consequences).

The widely studied issue of labor induction and Cesarean section rates is now approaching resolution. Older studies have shown conflicting results with a trend towards higher Cesarean section rates when labor induction is attempted [39–41]. However, more recent data indicate that this is probably not the case when appropriate control groups are selected. Most recent reviews show that there is no increase in Cesarean section rates with labor induction among term pregnancies and, in fact, there may even be a reduction [42–45]. Thus, high labor induction rates for IO pregnancies cannot entirely explain the high Cesarean section rate and specifically those performed due to NRFHR.

Another aspect that should be mentioned while discussing the necessity of labor induction among IO pregnancies is the accuracy of AFI as a true measure of AFV. The gold standard for the estimation of AFV is the dye dilution test [46]. This method, however, is invasive and rarely required or used. There are many noninvasive methods for AFV assessment, and their number reflects the inherent inaccuracies and weaknesses in each of these methods. Although no superiority was ever proven to any of these indirect assessments, when the AFI is used, significantly more cases of oligohydramnios are diagnosed, and more women undergo interventions [47]. The challenge in oligohydramnios diagnosis is composed of two

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**Fig. 6.** Sensitivity analyses excluding studies with extreme results: for Apgar score <7 at 1 min (a) and for NICU admission (b).
The first relates to the questionable accuracy of ultrasonography in assessing the actual AFV. The second being that no consensus exists on optimal AFI cutoff values which accurately predict perinatal morbidity or mortality. However, according to our results, it does appear that a cutoff of 5 is significantly associated with both medical interventions and several adverse outcomes.

To date, only one, small, prospective randomized trial evaluated maternal and neonatal outcomes in uncomplicated pregnancies with oligohydramnios at term [36]. This pilot trial compared maternal and neonatal outcomes in cases of IO, randomized to either induction of labor or expectant management. Twenty-six women beyond 40 completed weeks of gestation were randomized to expectant management and 28 women to induction of labor. The primary maternal outcome was the mode of delivery, and the primary neonatal outcomes were cord blood pH and Apgar score. No significant differences were found in any important maternal or neonatal outcomes. Although this study raises the awareness to IO pregnancies and questions the current active management protocols, no real conclusions are to be drawn, as the study suffers from multiple methodological flaws, primarily, its small sample size. We feel that similar larger and more rigorous studies are urgently needed.

**Limitation**

Our analysis (similar to previous ones) demonstrates an unbalanced sample size: 6.7% of the entire data set comprised the study group and 93.29% the control group. This inevitable gap is due to the actual percentage of IO in the pregnant population and the lack of prospective randomized trials.

Another methodological issue refers to the high heterogeneity demonstrated in the analysis of labor induction rates (unlike other outcomes analyzed). This heterogeneity is due to the extreme results presented in the different studies. Due to different management protocols, several studies showed an almost 100% induction rate in the IO group [28], while others presented equal rates in both groups [29]. Although high heterogeneity requires cautious interpretation of the results, we acknowledge that presently, IO is a strong indication for labor induction in most institutions.

![Forest plot of blood cord pH of <7.1](a) and MSAF (b).
Another possible limitation is our choice of the definition of oligohydramnios as previously discussed. We did not analyze perinatal outcomes associated with IO pregnancies diagnosed by alternative methods (such as deepest vertical pocket or percentiles for gestational age). Recent data are now arguing that the deepest vertical pocket is perhaps a better choice carrying lower false-positive rates and, thus, less interventions [48].

The two research questions raised in this MA refer to adverse perinatal outcome. Yet, the primary outcome
measure of the study was chosen to be the overall Cesarean section rate. Our primary concern was unwarranted iatrogenic intervention in the case of IO, which may result in higher rates of labor induction and/or Cesarean section without a clear benefit to the fetus/newborn. Evidently, all included studies provided data on both maternal and perinatal outcome, and no study was excluded due to the lack of data on delivery mode. Thus, the choice of the primary outcome did not affect the extent of included studies. Yet, the most problematic issue in this analysis is the studies included. A systematic and exhaustive search of the literature did not identify RCTs except for 1 study [36], and we were forced to use observational cohort studies. Although the risk of bias assessment reached relatively high scores (table 3), the inherent multiple weaknesses of such studies are well documented [49]. The reasons for this include potential biases in the original studies (as compared with randomized controlled trials) and the diversity of study designs and populations, which make the interpretation of simple summaries problematic. Most importantly, nonrandomized cohorts may have major differences among study groups, unrelated to the AFV.

In addition, methodological issues specifically related to MA, such as publication bias, could have a particular impact when combining results of observational studies. With regard to publication bias, the selective publication of studies based on the magnitude and direction of their findings represents a particular threat to the validity of MAs of observational studies [50–52]. We have used funnel plots to assess a possible publication bias of the different outcomes assessed (fig. 8). Although publication bias techniques have been mainly developed for clinical trials, we found publication bias probable in several outcomes assessed.

Conclusions and Summery

When considering IO at term, one encounters multiple challenges. Primarily, a definitive diagnosis can only be made with an invasive procedure. All methods of ultrasonographic AFV assessment are inaccurate, and the cutoff of AFI, which is the most commonly used method, is poorly defined.

Since oligohydramnios is often associated with maternal and fetal comorbidities affecting the pregnancy outcome, induction of labor in term pregnancies with IO is common (although by definition IO is isolated). We have shown that IO at term is associated with significantly higher rates of medical interventions including labor induction and Cesarean sections. It is also associated with several important adverse neonatal outcomes including low Apgar scores and NICU admissions, even in the absence of other ‘high-risk’ characteristics. There is simply no evidence to support or defy routine labor induction in this setting, and high-quality data are urgently needed. We cannot determine whether our findings represent the benefits of common management protocols or actually their possibly harmful implications. The desired reduction in perinatal morbidity is lacking solid scientific support. Only randomized controlled trials evaluating optimal management protocols in cases of IO term pregnancies will resolve this issue.

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Disclosure Statement

The authors report no conflicts of interest.

References

Isolated Oligohydramnios


