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Caesarean Section Rates and Adverse Neonatal Outcomes After Induction of Labour Versus Expectant Management in Women With an Unripe Cervix: A Secondary Analysis of the HYPITAT and DIGITAT Trials

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ABSTRACT

Between 20% and 25% of pregnancies require induction of labor (IOL), especially in situations that indicate better outcomes for mother and child if the pregnancy is not further prolonged. However, the effectiveness of IOL is subject to considerable debate because of concerns regarding the associated high rates of cesarean deliveries in women with an unripe cervix. The objective of this study was to evaluate the risk of cesarean delivery (CD) and adverse neonatal outcome rates after IOL or expectant management in women with an unripe cervix at or near term. This study used combined data from the multicenter, open-label, randomized controlled trials (RCTs) HYPITAT and DIGITAT. The inclusion criteria were women with hypertensive disease (HYPITAT trial) or suspected fetal growth restriction (DIGITAT trial) and a Bishop score of 6 or less. The study compared the outcomes after IOL and expectant management. The primary outcomes of this study were CD and a composite adverse neonatal outcome (defined as 5-minute Apgar score ≤6 and/or arterial umbilical cord pH <7.05 and/or neonatal intensive care unit admission and/or seizures and/or perinatal death).

Results of the study revealed that of 1172 women with an unripe cervix 572 women had IOL and 600 women had expectant management. It was noted that there was no significant difference in the overall CD rate (difference, −1.1%; 95% CI, −5.4 to 3.2). Also, IOL did not increase CD rates in women with Bishop scores from 3 to 6 (difference, −2.7%; 95% CI, −7.6 to 2.2) or adverse neonatal outcome rates (difference, −1.5%; 95% CI, −4.3 to 1.3). Results, however, noted that there was a significant difference in the rates of arterial umbilical cord pH less than 7.05 favoring IOL (difference, −3.2%; 95% CI, −5.6 to −0.9). The study concludes that there is no evidence that IOL increases the CD rate or compromises neonatal outcome as compared with expectant management in term or near-term pregnancies complicated by intrauterine growth restriction (IUGR), gestational hypertension, or preeclampsia. In addition, it was noted that there is no basis for concern regarding any increase in risk of failed induction in women with a Bishop score from 3 to 6.

EDITORIAL COMMENT

(Anyone who has spent time on labor and delivery has seen that the risk of cesarean delivery is higher in women who are induced as compared with those who experience spontaneous labor. This, however, does not mean that inducing labor increases the risk of cesarean delivery. Why not? Because when making the decision to induce labor, the comparison group is not spontaneous labor, but expectant management, which leads to a greater gestational age and the potential concomitant complications of increasing gestation such as macrosomia, IUGR, preeclampsia, and the need

for IOL. Thus, while spontaneous labor does occur with expectant management, sometimes it leads to an IOL at a greater gestational age in the setting of complications. Thus, methodologically, a proper comparison group to IOL is those women who were expectantly managed, not only those in spontaneous labor (*Am J Obstet Gynecol* 2006;195:700–705).

In the first study to retrospectively compare IOL to expectant management, women who were induced at 38, 39, or 40 weeks were found to have a lower risk of cesarean delivery when compared with women who were managed expectantly (*Am J Obstet Gynecol* 2006;195:700–705). These findings have been duplicated (*Obstet Gynecol* 2013;122:761–769; *BMJ* 2012;344:e2838), and in other studies, even if a reduction in cesarean delivery has not been found, no increased risk of cesarean delivery with IOL has been demonstrated (*Obstet Gynecol* 2011;117:583–587). However, although this methodological improvement is better than comparing women induced to spontaneous labor, it still has problems of confounding bias that could be improved by a prospective RCT.

These findings of a reduction in cesarean delivery from IOL as compared with expectant management have been demonstrated in the late term and postterm pregnancy in prospective RCTs (*N Engl J Med* 1992;326:1587–1592). In a meta-analysis, IOL in the term period was also demonstrated to have a reduction in cesarean delivery as compared with expectant management, but the studies were small and all were conducted prior to 1990 (*Cochrane Database Syst Rev* 2012;6: CD004945). Most recently, another small randomized trial did not identify a statistically significant difference between induction and expectant management in cesarean delivery (*Obstet Gynecol* 2015;126:1258–1264).

What about prospective RCTs in other settings? In a large RCT of women with large for gestational age fetuses, IOL was not found to increase the risk of cesarean delivery (*Lancet* 2015;385:2600–2605). In addition, in a prospective RCT that examined IOL versus expectant management in the setting of gestational hypertension or preeclampsia (HYPITAT), there was no difference in rates of cesarean delivery between women induced and those managed expectantly (*Lancet* 2009;374:979–988).

One subgroup that investigators disagree about are women with an unfavorable cervix. The issue is that whereas women with a favorable cervix are easier to induce, those with an unfavorable cervix have higher rates of cesarean delivery. However, this does not mean that such women would necessarily have a higher risk of cesarean delivery from IOL as compared with expectant management as they may have a higher risk of cesarean delivery regardless of management. The authors in the study abstracted above sought to address the issue of the effect of IOL women with an unfavorable cervix. They combined subjects from 2 prior randomized trials, HYPITAT and DIGITAT, which were studies of induction versus expectant management of hypertension and IUGR, respectively. They restricted their analysis to women with an unfavorable cervix and demonstrated no statistically significant difference in cesarean delivery between the 2 groups (IOL: 15.4% vs expectant management: 16.5%).

This study joins a small but increasing literature that suggests that IOL itself does not necessarily increase the risk of cesarean delivery. Currently, there is a large, prospective RCT being conducted by the Maternal Fetal Medicine Units Network that will address whether elective IOL at 39 or 40 weeks' gestation will affect the risk of cesarean delivery. Because the neonatal outcomes at 39 and 40 weeks' gestation are better than gestational ages before or after, the ultimate question will be whether it will be reasonable to induce all women at one of these thresholds on a routine basis. If the findings from these recent studies hold out that there is no difference in cesarean delivery, although such an intervention may be reasonable, it may not be cost-effective to routinely induce labor, which is generally a more labor-intensive and costly management than awaiting spontaneous labor. However, if such a study found even a slightly lower risk of cesarean delivery of IOL, it would be hard not to routinely offer induction to all women at 39 weeks' gestation.—ABC)