PREDICTING CESAREAN DELIVERY FOR FAILURE TO PROGRESS AS AN OUTCOME OF LABOR INDUCTION IN TERM SINGLETON PREGNANCY

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PREDICTING CESAREAN DELIVERY FOR FAILURE TO PROGRESS AS AN OUTCOME OF LABOR INDUCTION IN TERM SINGLETON PREGNANCY

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Condensation:

To develop and validate an objective and easily applicable model to predict successful induction of labor.

Short title: Prediction model for induction of labor outcome

AJOG at a glance:

A. Why was this study conducted?

To develop a reliable model for prediction of cesarean delivery for failure to progress as an outcome of labor induction in term singleton pregnancies.

B. What are the key findings?

A predictive model comprising maternal age, cervical length, angle of progression at rest and fetal occiput posterior position provided accurate prediction of successful induction of labor (area under the receiver operating characteristic curve (AUC 0.79, 95% confidence interval 0.71-0.87). There was also a good performance in validation of the model with AUC of 0.88, 95% confidence interval 0.79-0.97).

C. What does this study add to what is already known?

A model for prediction of the success of induction of labor, focusing on objective, accessible and acceptable predictors.
ABSTRACT:

Background:
Induction of labor is one of the most common interventions in modern obstetrics and its frequency is expected to continue to increase. There is inconsistency as to how failed induction of labor is defined, however, the majority of studies, define success as the achievement of vaginal delivery. Induction of labor in nulliparous women poses an additional challenge with a 15-20% incidence of failure, ending in emergency operative deliveries. The Bishop score has been traditionally used before decisions for induction of labor. Nonetheless, it is subjective and prone to significant inter-observer variation. Several studies have been conducted to find alternative predictors, yet, a reliable, objective method still remains to be introduced and validated. Hence, there is still a need for the development of new predictive tools to facilitate informed decision making, optimization of resources, and minimization of potential risks of failure. Furthermore, peripartum transperineal ultrasound scan has been proven to provide objective, non-invasive assessment of labor.

Objectives:
To assess the feasibility of developing and validating an objective and reproducible model for the prediction of cesarean delivery for failure to progress as an outcome of labor induction in term singleton pregnancies.

Study Design:
This was a prospective observational cohort study conducted in Cairo University Hospitals and University of Bologna Hospitals between November 2018 and
November 2019. We recruited 382, primigravidae, with singleton term pregnancies in cephalic presentation. All patients had baseline Bishop scoring together with various transabdominal and transperineal ultrasound assessments of the fetus, maternal cervix and pelvic floor. The managing obstetricians were blinded to the ultrasound scan findings. The method and indication of induction of labor, the total duration of stages of labor, mode of birth, and neonatal outcomes were all recorded. Women who had operative delivery for fetal distress or indications other than failure to progress in labor were excluded from the final analysis leaving a total of 344 participants who were randomly divided into 243 and 101 pregnancies that constituted the model development and cross-validation groups, respectively.

Results:

It was possible to perform transabdominal and transperineal scans and assess all the required parameters on all study participants. Univariate and multivariate analyses were used for selection of potential predictors and model fitting. The independent predictive variables for cesarean delivery included maternal age (OR 1.12, P = 0.003), cervical length (OR 1.08, P = 0.04), angle of progression at rest (OR 0.9, P = 0.001), occiput posterior position (OR 5.7, P = 0.006). We tested the performance of the prediction model on our cross-validation group. The calculated areas under the curve for the ability of the model to predict cesarean delivery were 0.7969 (95% confidence interval 0.71-0.87) and 0.88 (95% confidence interval 0.79-0.97) for the developed and validated models, respectively.

Conclusions:
Maternal age and sonographic fetal occiput position angle of progression at rest and cervical length prior to labor induction are very good predictors of induction outcome in nulliparous women at term.

Keywords:

Angle of progression; biomarkers; cervical length; cesarean delivery; maternal age; occiput posterior position; parturition; prediction; replication; successful induction of labor; transperineal ultrasound; ultrasound in labor; vaginal birth.
INTRODUCTION

Induction of labor (IOL), is one of the most common exercised and studied interventions in obstetrics. Its frequency has been increasing, with reports of 1 in 5 pregnant women undergoing IOL\(^1,2\) and is expected to continue to rise given the increase in the evidence-based, recommended indications for IOL, whether for obstetric, fetal, maternal, or medical reasons.\(^3–5\) There is inconsistency in defining failed IOL: some authors define failure of IOL based on the duration of the latent phase, using 15 hours as a cut-off value\(^6\) and others consider an inability to achieve cervical dilatation > 4 cm within 12 hours of oxytocin administration as an indicator of failed IOL.\(^7\) Another study suggested that the simple achievement of active labor should be considered a measure of successful IOL.\(^8\) Nonetheless, the majority of authors, find it pertinent to consider the outcome, rather than the process, and propose vaginal delivery as the main IOL outcome. After all, for the expectant woman, when embarking on IOL, the outcome sought is vaginal delivery; otherwise she would opt for cesarean delivery from the start. Induction of labor in nulliparous women at term does not always lead to a normal spontaneous vaginal delivery; some cases, especially primigravidae of advanced age, need assistance with an instrumental delivery or require cesarean delivery.\(^5,9\) It is estimated that 15-20% of IOLs fail to result in vaginal birth, ending in intrapartum operative deliveries.\(^10\)

Numerous investigators have evaluated several clinical and ultrasonographic parameters as predictors of IOL outcome and reported varying results.\(^11–18\) The Bishop score has traditionally been used as the standard test prior
to IOL determination. Nonetheless, it is a subjective assessment associated with poor predictive value, reproducibility and high degrees of inter- and intra-observer disagreement.\textsuperscript{18–20} Moreover, studies that compared the predictive value of ultrasonographic indices to the Bishop score have generated contradictory results.\textsuperscript{21–23} The negative impacts of failed IOL range from the stress of enduring a futile, prolonged trial of labor; an increased economic burden and misuse of healthcare resources due to prolonged hospital stay; excessive use of medications; vigilant maternal/fetal monitoring; and an increased rate of interventions to the increased prevalence of maternal, fetal, and neonatal complications of an emergency cesarean delivery.\textsuperscript{24} Therefore, to enable obstetricians to individualize the care offered to patients, it is important to identify women at high risk of IOL failure, improve clinical outcomes, and optimize the cost-effectiveness of healthcare interventions. In an attempt to identify methods of assessment more objective than digital examination, ultrasound has been shown to be suitable to assess labor progression. Transabdominal and transperineal ultrasound have been shown to provide reproducible, objective and non-invasive assessment of labor progression.\textsuperscript{16,25–32} Nevertheless, a reliable, objective method to predict the likelihood of vaginal delivery still remains to be introduced and validated. This calls for the development of new predictive tools for the success of IOL to allow for informed decision making, optimization of resources, and minimization of potential risks of failure. The objective of this study was to assess the feasibility of developing and validating an objective and reproducible model for the prediction of cesarean delivery for failure to progress as an outcome of labor induction in term singleton pregnancies.
METHODS

Design and setting

This was a prospective observational cohort study conducted between November 2018 and November 2019 in two tertiary-level university-affiliated maternity units: Kasr Al-Ainy University Hospital, Cairo University, Egypt, and Sant’Orsola Malpighi University Hospital, University of Bologna, Bologna, Italy. The local research ethics committees of both participating units approved the study protocol prior to study commencement (Kasr Al-Ainy University Hospital reference number O18005 and Sant’Orsola Malpighi University Hospital, reference number 139/2016/U/Oss). All study participants provided written informed consent prior to enrollment.

Participants

Women were considered eligible for inclusion in this study if they met the following requirements: ≥ 18 years of age, nulliparous, singleton, term pregnancy (37-42 weeks of gestation) planned for induction of labor for any indication, and a fetus in a cephalic presentation. Women presenting in labor or with a history of uterine surgery or scarring were excluded from the study. Recruitment into the study was non-consecutive, depending on the availability of a member of the study team trained to undertake the a priori set of ultrasound parameters under consideration.

A total of 382 nulliparous women were enrolled into the study, including 268 of a total of 1440 (18.6%) pregnancies during the study period at Kasr Al-Ainy University Hospital and 114 of a total of 983 (11.6%) at Sant’Orsola Malpighi
University Hospital. All participants had a baseline clinical cervical assessment using the modified Bishop score\textsuperscript{33}; the attending obstetricians managed the labor in line with the unit’s protocol and were blinded to the ultrasound scan findings (supplementary appendix). In addition to demographic details, data were collected as follows: the method and indication of induction of labor, the total duration of labor (onset of induction to delivery), duration of first and second stages including length of the pushing phase, mode of birth, and neonatal outcomes. As the aim of our study was to develop and validate a prediction model for successful induction of labor, women who had a cesarean delivery for fetal distress or indications other than failure to progress in labor were excluded from the final analysis.

**Ultrasound parameters**

Once enrolled, study participants underwent a transabdominal scan to evaluate fetal biometry and fetal occiput position, and a transperineal ultrasound examination was conducted to measure the cervical length, angle of progression (AoP), antero-posterior diameter of the levator hiatus, head-to-perineum distance, and head-to-symphysis distance; the last four parameters were assessed both at rest and at maximum Valsalva \textsuperscript{34} (Figures 1 and 2). Scans were performed using a convex 3.5-5 MHz transducer (Voluson 730 Expert, Voluson P8 or Voluson E10, GE Medical Systems, Zipf, Austria) by one of two operators with more than three years of experience in obstetric and transperineal ultrasound (R.K. and A.Y.) who were blind to clinical examination findings. Fetal biometry was conducted in accordance with published ISUOG guidelines.\textsuperscript{35} Occiput position determination was made by transabdominal ultrasound as previously published.\textsuperscript{36–38} This was
performed by looking for the following landmarks: the fetal occiput, the fetal orbits, the midline of the fetal brain, and cerebellum. According to these landmarks, the fetal occiput position was described in relation to a clockface.\textsuperscript{39} Occiput position was described as anterior if the occiput was between 09:30 and 02:30 h, transverse (OT) if between 02:30 and 03:30 h, or 08:30 and 09:30 h, and posterior (OP) if between 03:30 and 08:30 h.

For transperineal ultrasound examination, the transducer was covered with a sterile surgical glove. The transducer was placed between the labia majora in a mid-sagittal plane, aligning the acquisition plane with the long axis of the pubic symphysis. Cervical length was measured along the length of the endocervical canal with simultaneous visualization of the internal os and external os, using a straight line drawn between internal os and external os for the measurement.

Transvaginal ultrasound was used in cases of non-optimal visualization with care not to compress and distort the cervix by the probe.\textsuperscript{40} The antero-posterior diameter of the levator hiatus was measured in mid-sagittal view as the distance between the inferior border of the symphysis pubis to the anterior border of the puborectalis muscle.\textsuperscript{41} The AoP was measured as the angle between a line running along the long axis of the pubic symphysis and another line extending from the most inferior portion of the pubic symphysis tangentially to the fetal skull contour.\textsuperscript{16} Head-symphyisis distance is the distance along the infrapubic line between the caudal end of the pubic symphysis and the fetal skull.\textsuperscript{42} For head-to-perineum distance, the transducer was rotated into a transperineal transverse plane at the level of the posterior commissure and pressed against the pubic
Head-perineum distance is defined as the shortest distance between the perineum and the outer-most part of the bony skull.

**Statistical analysis**

Simulation studies examining predictor variables for inclusion in logistic regression models suggest that 5 - 10 events are necessary for each candidate predictor to avoid overfitting. Based on 7 events per predictor and the assumption that we will examine 10 candidate predictors, it was estimated that 70 women with the primary outcome of interest (cesarean delivery following IOL due to failure to progress) would be required. Based on a cesarean delivery rate of 22% following IOL a sample size of 318 women would be required. Applying the methodology proposed by Riley et al, a global shrinkage factor and adjusted $R^2$ ($R^2_{\text{adjust}}$) are required to estimate the minimum number of events per predictor. In view of the absence of any information regarding these two parameters we assumed that ($R^2_{\text{adjust}}$) and shrinkage factor values would be 0.25 and 0.9, respectively. To develop our logistic regression model based on up to 10 predictors and assuming a cesarean delivery rate of 22% a sample size of 307 would be needed and the events per predictor would be 7 per predictor (supplementary appendix).

The study sample ($n = 344$) was randomly divided into 243 and 101 pregnancies that constituted the model development and cross-validation groups, respectively. For model development, the differences of the maternal and ultrasonographic data between the vaginal delivery and cesarean delivery groups were calculated by a Student’s t-test (for continuous variables) and the $\chi^2$ test (for categorical variables). All variables in the bivariate analysis with $P<0.2$ were
evaluated further using multiple logistic regression analysis by computing odds ratios (OR) and their 95% confidence intervals (CI). Variables with a P value > 0.2 were removed from the model. The reduced model was then successively refitted, and the model with the lowest Akaike’s information criteria value was considered the best. Akaike’s information criteria represents the ratio between the number of parameters in the numerator and log likelihood in the denominator (supplementary appendix). Akaike’s information criteria score of the model will increase in proportion to the growth in the value of the numerator, which contains the number of parameters in the model (i.e. a measure of model complexity). And the Akaike’s information criteria score will decrease in proportion to the growth in the denominator which contains the maximized log likelihood. Thus, Lower value of Akaike’s information criteria suggests "better" model.48

Only significant objective variables that predicted the risk of cesarean delivery after IOL were included in the final model. We constructed a receiver operating characteristic (ROC) curve to assess the prognostic accuracy of the devised model. The predicted probability of cesarean delivery was used as the predictive variable with the actual occurrence of cesarean delivery as the tested outcome. The area under the ROC curve (AUC), expressing the prognostic performance of the model, was calculated and compared for statistically significant differences.

We applied bootstrap resampling methodology of AUC as previously described.49 This method was used to implement 10-fold cross-validation for the AUC for a dependent variable after fitting a logistic regression model and provides
the cross-validated fitted probabilities for the dependent variable. Then bootstrap
resampling for AUC and 95% CI were generated. Bootstrap resampling
methodology was done using Stata Corp. 2013 (Stata Statistical Software Release
13. College station, TX: StataCorp LP) with the command of CVAUROC

The final model was then applied to the cross-validation group by using the
holdout sample validation method, and a ROC curve was constructed to assess
the accuracy of the cross-validated model.

We conducted all data analyses by using statistical software programs
(MedCalc version 12.1.4.0 (MedCalc Software byba, Mariakerke, Belgium) SPSS
for Windows version 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 382 women who fulfilled the inclusion criteria were enrolled into the study.
Of these participants, 38 women underwent a cesarean delivery for unpredictable
indications (e.g. fetal distress) and were excluded from the study herein, leaving a
total of 344 pregnancies contributing to the analysis (Figure 3). It was possible to
perform ultrasound scans and assess all the required parameters on all study
participants who found it quite acceptable. The characteristics of the study
population are shown in Table 1.

We aimed to study variables that are objective, easily assessed, and
reproducible to minimize inter- and intra-observer variability and to establish a
reliable model Multivariate logistic regression analysis (Table 2) revealed the
independent predictive variables for cesarean delivery to be maternal age (OR 1.12, 95% CI 1.03-1.2; P value = 0.003), cervical length (OR 1.08, 95% CI 1.002-1.17; P = 0.04), AoP at rest (OR 0.9, CI 0.85-0.96; P = 0.001), occiput posterior (OP) position, where OA is the reference position, (OR 5.7, 95% 1.6-19; P = 0.006).

The following equation can calculate the probability of cesarean delivery:

\[
P(CS) = \frac{e^{1.62+0.11X_{age}+0.08X \text{cervical length}+0.09X_{AOP_{rest}}+0.009X_{HSD-val}+(0[OA]|-0.28[OT]|+1.75[OP]}{1+ e^{1.62+0.11X_{age}+0.08X \text{cervical length}+0.09X_{AOP_{rest}}+0.009X_{HSD-val}+(0[OA]|-0.28[OT]|+1.75[OP]}}
\]

The calculated AUC for the ability of the model to predict cesarean delivery was 0.79 (95%CI 0.71-0.87).

Applying bootstrap resampling methodology, the AUC calculated using CVAUROC was 0.73 (95%CI 0.58-0.78).

We internally validated our model where it was applied to the cross-validation group by using the holdout sample validation method, and a ROC curve was constructed to assess the accuracy of the cross-validated model. Table 3 shows the characteristics of the cross-validation group. The calculated AUC for the model to predict cesarean delivery as an outcome of IOL in the validation cohort was 0.88 (95%CI 0.79-0.97) (Figure 4).

We aimed to assess the prediction model on a clean sample of women who failed to progress in labor without diluting the sample with women who had cesarean delivery for fetal distress since this can result from other factors such as
placental insufficiency and oligohydramnios induced cord compression, nonetheless we appreciate the possible overlap between various causes. Therefore, we calculated the AUC including women who had cesarean delivery for fetal distress for, both, model development and validation cohorts and these were 0.73 (95% CI 0.65-0.81) and 0.87 (95% CI 0.79-0.96) respectively.

DISCUSSION

**Principal findings of the study**

A prediction model was devised utilizing a combination of patient characteristics and pre-induction clinical and ultrasonographic variables; maternal age, cervical length, AoP at rest and fetal occiput position. We provided a calculator for the probability of cesarean delivery. Based on the calculated AUC of 0.79, this model performed well as a predictor of women whose IOL failed and who required cesarean delivery. This finding was also confirmed when the model was tested on our validation cohort with an AUC of 0.88.

**Results in the context of what is known**

Several groups have attempted to predict IOL outcome and it is anticipated that these attempts will continue due to the increasing prevalence of IOL and hence the need to alleviate maternal, fetal and neonatal complications as well as optimise the cost effectiveness of the procedure. A predictive model proposed by Kawakita *et al.*, reported independent significant predictors for successful vaginal delivery in nulliparous women who underwent IOL: maternal age, gestational age at delivery,
race, maternal height, pre-pregnancy weight, gestational weight gain, cervical examination on admission (dilation, effacement, and station), chronic hypertension, gestational diabetes, pre-gestational diabetes, and abruption. Their study, a retrospective analysis, included a large number of patients (10591), yet the predictors it introduced are largely demographic and rely on clinical assessment of the cervix, which is subjective.

Tolcher et al., devised a nomogram for predicting cesarean delivery after IOL in nulliparous women. This nomogram identified advanced maternal age, short maternal stature, high body mass index, increased weight gain during pregnancy, advanced gestational age, hypertension, diabetes mellitus, and initial cervical dilatation < 3 cm as independent risk factors associated with an increased risk for cesarean delivery. This study also included a relatively large number of patients (785), and introduced parameters representing subjective assessment of the cervix as well as maternal medical and demographic factors.

Our findings are concordant with these two studies in that maternal age is a strong predictor of successful IOL, with advanced maternal age increasing the likelihood of cesarean delivery; nonetheless, we opted to use cervical length assessed by ultrasound rather than clinically assessed cervical dilatation, used in the two studies cited above, to provide a more objective, reproducible means of assessment. Cervical length was mostly assessed transperineally, not transvaginally, as there were other transperineal parameters to measure. We found that this method avoids risk of cervical distortion due to pressure by the transvaginal probe, and is more acceptable to patients.
Previously Rane et al., and Peregrine et al., also found cervical assessments to be highly predictive and incorporated this in their IOL outcome predictive models. The model of Peregrine et al, included body mass index and height, both parameters were not identified as significant enough to be selected during our model development.\textsuperscript{51} Rane et al., added posterior cervical angle measurement and occiput position to the cervical length measurement.\textsuperscript{52} We also added the occiput position as a significant predictor in our model, which is of interest as in a previous study conducted by our group, we found that pre-induction assessment of the fetal occiput and spinal position did not associate well with the likelihood of cesarean delivery in 136 nulliparous women undergoing IOL at term.\textsuperscript{53} The difference in the number of the study population might account for this discrepancy. It has been previously suggested that the exclusion of estimated fetal weight or information on maternal pelvic adequacy was a shortcoming of a web-based calculator devised for the prediction of success of IOL.\textsuperscript{54,55} In our study, both parameters were identified as strong predictors of IOL outcome, but more so when combined, because the process of labor involves the synergistic relationship between these two factors, which was represented in our study by the AoP, but not as single isolated parameters. AoP has been previously identified as a useful sonographic predictor for successful vaginal delivery among nulliparous women at term undergoing IOL.\textsuperscript{56} Levy et al., found that a narrow AoP in nulliparous women, not in labor at term is associated with a high rate of CS.\textsuperscript{57} We found that the AoP was a strong predictor for cesarean delivery as an outcome for IOL in nulliparous women, and its inclusion improved the performance of our model.
In contrast, Pereira *et al.*, when attempting to include the AoP in a predictive model with cervical elastography and pre-induction cervical length in women undergoing IOL found that the AoP and an internal os elastographic score were unlikely to be useful.\(^{58}\) The variation between the findings of Pereira *et al* and ours could be due to our larger sample size (344 vs 99) or the non-inclusion of cervical elastography in our pre-IOL variables, given its limited availability in regular ultrasound machines commonly used in labor units.

In the present study, we measured indices of the fetal head descent and the anteroposterior diameter of the levator ani muscle hiatus at rest and under Valsalva. There is growing evidence on the relationship between the pelvic floor and labor outcome. Some authors suggested that larger anteroposterior diameters measured before the onset of labor were associated with an increased likelihood of vaginal delivery and with lower fetal head descent in the birth canal, whereas others found an association exclusively with the duration of the second stage of labor.\(^{41,59–63}\) In the present study we did not demonstrate an association between anteroposterior diameters and Cesarean delivery. However, some studies demonstrated an association between the angle of progression under Valsalva and the mode of delivery.\(^{64}\) Although this was confirmed in the present study, the angle of progression under Valsalva did not add any predictive value to our model, reflecting a more important role to the static rather than the dynamic ultrasound indices of the fetal head descent in the birth canal in the prediction of Cesarean delivery.

**Clinical Implications**
Prediction models and calculators are means of providing patients with an individualized risk assessment to help them decide their management. IOL is one of the most common interventions in current obstetric practice. However, at present, women make decisions about IOL based on a non-specific background risk of cesarean delivery. Upon external validation, this prediction model has the potential to be a useful tool for clinicians and women to make management plans and informed healthcare choices by providing them with the individualized risk of cesarean delivery. Moreover, it will be helpful to transfer this model to a user-friendly platform e.g., a computer software or a mobile application. An additional benefit is perhaps the possibility of optimizing the timing of IOL till a more favorable failure risk assessment is achieved, given that some of the parameters assessed are dynamic. This is particularly relevant to the increasing indications for early IOL to improve maternal and fetal outcomes.\textsuperscript{65}

**Research Implications**

We were able to develop and validate our prediction model on two different cohorts which increases the internal validity of our work. Further external validation of our findings by in larger unselected population will be useful to substantiate their generalizability, particularly in view of our higher than previously reported cesarean delivery rates. Based on the methodology previously proposed by Riley et al,\textsuperscript{47} a shrinkage factor of 0.9, $R^2$adjust of 0.05 and a cesarean delivery incidence of 29\% as calculated from our model development cohort, the total number of patients required for external validation is 1050 and the number of events per predictor is 50 (supplementary appendix).
Strengths and limitations

Strengths of the study include: first, relatively large sample size, second, prospective enrolment of women, third, random stratification of the study cohort into model development and model validation groups, fourth, the managing obstetricians were blinded to the pre-induction assessment and ultrasound parameters. This study provides an applicable, objective prediction model for the success of IOL in nulliparous women, thus providing patients with useful information that can empower them to make informed choices about their respective birth plans. The model performed well upon cross validation, adding to the overall strength of this study.

The limitations of the study include: first, ultrasound measurements were obtained by experienced maternal-fetal medical consultans. This issue can potentially have implications on the external validity of our findings. Nonetheless, transperineal measurements are expected to be performed at the time of counselling about IOL rather than as an “out of hours” procedure. Hence, it is feasible that such assessment could be conducted by a clinician trained in performing transperineal scans. Second, we factored in a model validation component within our study on a cohort different from our model development group; however, these groups were recruited from our unit at the same time. It would be prudent to validate our model on independent cohorts to further test its predictive performance.
Conclusions

Maternal age, ultrasound assessments of occiput position, angle of progression at rest and cervical length prior to labor induction are good predictors of induction outcome in nulliparous women at term.
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REFERENCES


55. Levine LD, Downes KL, Parry S, Elovitz MA, Sammel MD, Srinivas SK. A validated calculator to estimate risk of cesarean after an induction of labor...


62. Brunelli E, Del Prete B, Casadio P, Pilu G, Youssef A. The dynamic change of the anteroposterior diameter of the levator hiatus under Valsalva


FIGURE LEGENDS

Figure 1: Transabdominal ultrasound assessment of the fetal occiput position.

Figure 2: Transperineal ultrasound assessment of cervical length, head to symphysis distance and angle of progression.

Figure 3: Flowchart of the study participants.

Figure 4: Calculated area under the curve for the ability of the model to predict cesarean delivery (left) and results from the validation cohort (right).
**Table 1:** Variables studied for the development of the prediction model grouped by mode of birth.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vaginal delivery (n=172)</th>
<th>Cesarean delivery (n=71)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>26.6 (6)</td>
<td>28.5 (6.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29 (4)</td>
<td>31 (5.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>39 (1.5)</td>
<td>39 (1.5)</td>
<td>0.80</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1 (0.5)</td>
<td>3 (4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fetal sex: Male</td>
<td>85 (49)</td>
<td>38 (53)</td>
<td>0.30</td>
</tr>
<tr>
<td>Epidural</td>
<td>30 (18)</td>
<td>15 (23)</td>
<td>0.30</td>
</tr>
<tr>
<td>Prepidil®Dinoprostine gel</td>
<td>17 (9.9)</td>
<td>10 (14)</td>
<td>0.416</td>
</tr>
<tr>
<td>Propess®Dinoprostine vaginal insert</td>
<td>27 (15.7)</td>
<td>14 (20)</td>
<td></td>
</tr>
<tr>
<td>Misoprostol</td>
<td>128 (74.4)</td>
<td>47 (66)</td>
<td></td>
</tr>
<tr>
<td>Occiput anterior</td>
<td>48 (28)</td>
<td>15 (21)</td>
<td>0.30</td>
</tr>
<tr>
<td>Occiput transverse</td>
<td>93 (54)</td>
<td>39 (55)</td>
<td></td>
</tr>
<tr>
<td>Occiput posterior</td>
<td>31 (18)</td>
<td>17 (24)</td>
<td></td>
</tr>
<tr>
<td>Head circumference (mm)</td>
<td>333 (15)</td>
<td>334 (15)</td>
<td>0.40</td>
</tr>
<tr>
<td>Biparietal diameter (mm)</td>
<td>92 (4)</td>
<td>93 (4)</td>
<td>0.27</td>
</tr>
<tr>
<td>Femur length (mm)</td>
<td>72 (4)</td>
<td>72 (4)</td>
<td>0.34</td>
</tr>
<tr>
<td>Abdominal circumference (mm)</td>
<td>337 (21)</td>
<td>344 (22)</td>
<td>0.017</td>
</tr>
<tr>
<td>Estimated fetal weight (gm)</td>
<td>3244 (447)</td>
<td>3405 (503)</td>
<td>0.01</td>
</tr>
<tr>
<td>Angle of progression at rest (degrees)</td>
<td>92.7 (10.8)</td>
<td>86 (10.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Angle of progression at Valsalva (degrees)</td>
<td>100.8 (12.2)</td>
<td>95.6 (11.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Head-to-symphysis distance at rest (mm)</td>
<td>46.3 (9.8)</td>
<td>50.6 (11)</td>
<td>0.015</td>
</tr>
<tr>
<td>Head-to-symphysis distance at Valsalva (mm)</td>
<td>38.4 (9.8)</td>
<td>43.2 (11.9)</td>
<td>0.006</td>
</tr>
<tr>
<td>Head-to-perineum distance at rest (mm)</td>
<td>51.1 (8.5)</td>
<td>55.7 (10.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Head-to-perineum distance at Valsalva (mm)</td>
<td>45.3 (7.9)</td>
<td>49.8 (9.5)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Antero-posterior diameter of the levator hiatus at rest (mm)</td>
<td>53.8 (8.7)</td>
<td>54.9 (8.7)</td>
<td>0.39</td>
</tr>
<tr>
<td>Antero-posterior diameter of the levator hiatus at Valsalva (mm)</td>
<td>59.5 (10.4)</td>
<td>59.6 (11)</td>
<td>0.90</td>
</tr>
<tr>
<td>Cervical length (mm)</td>
<td>27.7 (5)</td>
<td>29.9 (6.8)</td>
<td>0.016</td>
</tr>
<tr>
<td>Bishop score</td>
<td>3.6 (1.7)</td>
<td>3.4 (1.4)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Values are mean (standard deviation) or n (%).
Table 2: Antepartum independent variables significantly associated with cesarean delivery as an outcome of induction of labor.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.12</td>
<td>1.03-1.20</td>
<td>0.003</td>
</tr>
<tr>
<td>Cervical length</td>
<td>1.08</td>
<td>1.002-1.17</td>
<td>0.04</td>
</tr>
<tr>
<td>Angle of progression at rest</td>
<td>0.9</td>
<td>0.85-0.96</td>
<td>0.001</td>
</tr>
<tr>
<td>Head-to-symphysis distance at Valsalva</td>
<td>1.009</td>
<td>0.96-1.05</td>
<td>0.60</td>
</tr>
<tr>
<td>Occiput position</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occiput anterior (ref)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occiput transverse.</td>
<td>0.7</td>
<td>0.2-2</td>
<td>0.60</td>
</tr>
<tr>
<td>Occiput posterior</td>
<td>5.7</td>
<td>1.6-19</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Table 3. Characteristics of the cross-validation group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD) or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>24.8 (5.2)</td>
</tr>
<tr>
<td>Body mass index (Kg/m²)</td>
<td>28.5 (3.4)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>38.9 (1.5)</td>
</tr>
<tr>
<td>Head circumference (mm)</td>
<td>330.8 (28.2)</td>
</tr>
<tr>
<td>Biparietal diameter (mm)</td>
<td>93.0 (4.2)</td>
</tr>
<tr>
<td>Femur length (mm)</td>
<td>70.6 (9.8)</td>
</tr>
<tr>
<td>Abdominal circumference (mm)</td>
<td>335.7 (37.1)</td>
</tr>
<tr>
<td>Estimated fetal weight (gm)</td>
<td>3267 (499)</td>
</tr>
<tr>
<td>Angle of progression at rest (degrees)</td>
<td>91.3 (11.5)</td>
</tr>
<tr>
<td>Angle of progression at Valsalva (degrees)</td>
<td>98.5 (12.7)</td>
</tr>
<tr>
<td>Head-to-symphysis distance at rest (mm)</td>
<td>41.7 (9.7)</td>
</tr>
<tr>
<td>Head-to-symphysis distance at Valsalva (mm)</td>
<td>39.9 (9.0)</td>
</tr>
<tr>
<td>Head-to-perineum distance at rest (mm)</td>
<td>55.8 (6.7)</td>
</tr>
<tr>
<td>Head-to-perineum distance at Valsalva (mm)</td>
<td>52.4 (7.7)</td>
</tr>
<tr>
<td>Antero-posterior diameter of the levator hiatus at rest (mm)</td>
<td>52.1 (5.6)</td>
</tr>
<tr>
<td>Antero-posterior diameter of the levator hiatus at Valsalva (mm)</td>
<td>56.3 (7.1)</td>
</tr>
<tr>
<td>Cervical length (mm)</td>
<td>25.3 (4.1)</td>
</tr>
<tr>
<td>Occiput anterior</td>
<td>38 (37)</td>
</tr>
<tr>
<td>Occiput transverse</td>
<td>47 (46)</td>
</tr>
<tr>
<td>Occiput posterior</td>
<td>16 (15.7)</td>
</tr>
</tbody>
</table>
Figure 1: Illustrated figure (left) with the corresponding ultrasound image (right) demonstrating the transabdominal ultrasound assessment of the fetal posterior occiput position.
Figure 2: Illustrated figure (left) with the corresponding ultrasound image (right) for transperineal assessment of angle of progression (yellow dotted line), head to symphysis distance (blue dotted line) and cervical length (green dotted line).
382 women
Undergoing induction of labor

38 women were excluded
- 31 had cesarean delivery for fetal distress
- 2 had cesarean delivery for anhydramnios
- 1 had cesarean delivery for placental abruption
- 1 had cesarean delivery for antepartum hemorrhage
- 1 had cesarean delivery for malpresentation
- 1 had cesarean delivery for accidental discovery of vaginal HPV
- 1 had cesarean delivery for uncontrolled hypertension

344 women

243 women
Prediction model group
- 172 women had vaginal delivery
- 71 women had cesarean delivery

101 women
Cross validation group
- 77 women had vaginal delivery
- 24 women had cesarean delivery
Figure 4

Area under the curve 0.7969

Area under the curve 0.8821