Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicenter, prospective study

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Corresponding Author:	Andrea Dall'Asta, M.D. University of Parma Parma, ITALY
First Author:	Andrea Dall'Asta, PhD
Order of Authors:	Andrea Dall'Asta, PhD
	Giuseppe Rizzo
	Bianca Masturzo
	Elvira Di Pasquo
	Giovanni Battista Luca Schera
	Giovanni Morganelli
	Ruben Ramirez Zegarra
	Pavjola Maqina
	Ilenia Mappa
	Giulia Parpinel
	Rossella Attini
	Enrica Roletti
	Guido Menato
	Tiziana Frusca
	Tullio Ghi
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Abstract:	Background To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor. Objective To assess the relationship between the transabdominal sonographic indices of fetal head flexion and the mode of delivery in women with protracted active phase of labor. Study design Prospective evaluation of women with protracted active phase of labor recruited across three tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the evaluation of the fetal head position and flexion, which was measured by means of the occiput-spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-chest angle (CCA) in fetuses in OP

position. The OSA and the CCA were compared between women who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention was performed solely based on suspected fetal distress were excluded.

Results

129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery, instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%) cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to those submitted to cesarean delivery due to labor dystocia (126 + 14 vs 115 + 24, p<0.01). At ROC curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), p<0.01, and the optimal OSA cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean delivery was 109 degrees. A narrower CCA was measured in cases who had vaginal delivery compared to those undergoing cesarean delivery (27 + 33 vs 56 + 28 degrees, p<0.01). The AUC of the CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), p<0.01, and the optimal cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

Conclusions

In women with protracted active phase of labor, the sonographic demonstration of fetal head deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

UNIVERSITA' DI PARMA
Dipartimento di Medicina e Chirurgia
Ospedale Maggiore di Parma
Via Gramsci 14
43100 Parma Italia
Tel: +39 0521 702434 - Fax: +39 0521 702434
Email: tullioghi@yahoo.com
andrea.dallasta1@gmail.com

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To the Editor in Chief

American Journal of Obstetrics & Gynecology

Professor Roberto Romero

Dear Professor Romero,

We hereby enclose the revised version of our manuscript entitled "Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study." for consideration for publication in the American Journal of Obstetrics & Gynecology.

In this revised version we have addressed the Reviewers' comments and added a figure (Figure 5) showing the findings of a sub-analysis evaluating the relationship between the OSA and the sonographic indicators of head station in non-OP fetuses with favorable head flexion. Overall, we genuinely believe that the quality of the manuscript has improved and thank the Reviewers for their inputs.

The manuscript has been formatted according to the Journal Guidelines for Original Research articles.

This work is novel, has not been reported elsewhere and is not under consideration by another journal.

All the Authors have contributed significantly and are in agreement with the content of the manuscript.

There are no financial disclosures nor financial support or relationships that may pose potential conflict of interest.

Thank you in advance for your consideration.

Sincerely yours,

Andrea Dall’Asta

Tullio Ghi

TITLE PAGE

Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study.

Authors:

Andrea Dall'Asta[1], Giuseppe Rizzo[2,3], Bianca Masturzo[4], Elvira Di Pasquo[1], Giovanni Battista Luca Schera[1], Giovanni Morganelli[1], Ruben Ramirez Zegarra[1], Pavjola Maqina[2], Ilenia Mappa[2], Giulia Parpinel[4], Rossella Attini[4], Enrica Roletti[1,4], Guido Menato[4], Tiziana Frusca[1], Tullio Ghi[1]

Institution:

[1]Department of Medicine and Surgery, Obstetrics and Gynecology Unit, University of Parma, Parma, Italy

[2]Division of Maternal and Fetal Medicine, Cristo Re Hospital, University of Rome Tor Vergata, Rome, Italy

[3]Department of Obstetrics and Gynecology, The First I.M. Sechenov Moscow State Medical University, Moscow, Russia

[4]Department of Obstetrics and Gynecology, Sant'Anna Hospital, University of Turin, Turin, Italy

Address for correspondence:

Prof Tullio Ghi, MD, PhD

Department of Medicine and Surgery, Obstetrics and Gynaecology Unit, University of Parma

Via Gramsci 14, 43126 Parma, Italy

Email: tullioghi@yahoo.com

Phone: +390521702434

Condensation:

The sonographic indicators of deflexed fetal head are associated with labor dystocia leading to caesarean delivery in women with protracted active phase of labor.

Short title:

Intrapartum US in protracted active phase of labor.

AJOG at a glance

A.Why was the study conducted?

- To evaluate the relationship between the intrapartum sonographic indicators of fetal head flexion and the mode of delivery in women with protracted active phase of labor.

B.What are the key findings?

- A wide occiput-spine angle and a narrow chin-chest angle are associated with an increased incidence of vaginal delivery. A correlation between the occiput-spine angle and the sonographic indicators of fetal head station was also demonstrated.

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

- The sonographic indicators of fetal head flexion are associated with labor dystocia leading to cesarean delivery in women with protracted active phase of labor. The findings from this study suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

Keywords

Ultrasound in labor, labor dystocia, intrapartum care, caesarean delivery, instrumental delivery, occiput-spine angle, chin-chest angle, angle of progression, head-perineum distance**.**

Abstract

Background

To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor.

Objective

To assess the relationship between the transabdominal sonographic indices of fetal head flexion and the mode of delivery in women with protracted active phase of labor.

Study design

Prospective evaluation of women with protracted active phase of labor recruited across three tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the evaluation of the fetal head position and flexion, which was measured by means of the occiput-spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-chest angle (CCA) in fetuses in OP position. The OSA and the CCA were compared between women who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention was performed solely based on suspected fetal distress were excluded.

Results

129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery, instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%) cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to those submitted to cesarean delivery due to labor dystocia (126±14 vs 115±24, $p<0.01$). At ROC curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), $p<0.01$, and the optimal OSA cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean delivery was 109 degrees. A narrower CCA was measured in cases who had vaginal delivery compared to those undergoing cesarean delivery (27±33 vs 56±28 degrees, $p<0.01$). The AUC of the

CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p<0.01$, and the optimal cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

Conclusions

In women with protracted active phase of labor, the sonographic demonstration of fetal head deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

Introduction

Labor dystocia is estimated to account for approximately one third of all caesarean deliveries, the vast majority being primary cesarean deliveries (1,2). Among these, arrest of dilatation in the first-stage of labor is acknowledged to represent the most common indication (3,4). Such condition may result from distinct but potentially coexisting mechanisms which include abnormalities of the uterine contractions, malpositions or malpresentations of the fetal head and cephalopelvic disproportion (5-13).

The progression of the first-stage of labor has been historically assessed by means of the norms of active phase dilatation described by Friedman (14-26) and more recently re-evaluated by Zhang et al. (1,27,28). These latter, which show a slow but progressive first-stage dilatation prior to 6 cm and an overall slower course of labor compared to Friedman's sigmoid curve (14-17,23,25,26), are currently endorsed for labor management by the American College of Obstetricians and Gynecologists and by the Society for Maternal and Fetal Medicine (4,29). The active phase dilatation is positively affected by the descent of the fetal head in the birth canal, and in normal labor a direct correlation between the first-stage dilatation and the descent of the fetal head has been demonstrated (30). The engagement and the progression of the fetal head through the birth canal in the first-stage of labor are known to be to be influenced by the mechanism of head flexion – which allow the shortest cephalic diameters to negotiate the maternal pelvis (5,6).

Available data suggests that ultrasound outweighs the digital examination in the assessment of the fetal head station (31,32), progression and attitude, and ultrasound is currently endorsed as an adjunct to the clinical evaluation in conditions of protracted active phase of labor and arrest of dilatation (31). Under these circumstances, the sonographic indicators of the fetal head station including the head-perineum distance (HPD) and the angle of progression (AoP) have been shown to be more accurate than the digital examination in predicting the occurrence of cesarean delivery

(33-35). In an unselected group of women in the active phase of labor with occiput anterior and occiput transverse fetuses the degree of fetal head flexion measured at transabdominal ultrasound has been shown to be associated with the digital station and the likelihood of operative delivery (36). Other sonographic studies have demonstrated that also in fetuses in occiput posterior (OP) position the qualitative assessment of the fetal head deflexion is related to the chance of vaginal delivery (37,38). To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor. The aim of this study was to evaluate the relationship between the intrapartum ultrasound indicators of malposition and malpresentation and the risk of obstetric intervention within a selected cohort of women diagnosed with a protracted active phase of labor.

Methods

Study design

This was a prospective, observational study conducted between December 2018 and June 2020 and including three maternity units in Italy (University Hospitals of Parma and Rome Tor Vergata and Sant'Anna Hospital of Turin). A non-consecutive series of non-anomalous singleton term pregnancies, with no history of previous uterine scar and with a protracted active phase of labor was included. According to the local protocol of the participating Units, women diagnosed with protracted active phase of labor are submitted to clinical examination by the senior Obstetrician responsible for the patient care. For the present study, following the clinical diagnosis of protracted active phase of labor intrapartum ultrasound was performed for research purposes also by five investigators with dedicated training on ultrasound in labor (AD, TG, EDP, BM and GR) who were not involved in the clinical management. The senior Obstetricians in charge for the labor care were blinded to the ultrasound findings.

According to the protocol for the labor management adopted across the participating Units, protracted active phase of labor was defined based on the ACOG/SMFM recommendations for the safe prevention of the primary cesarean delivery (4). In details, a protracted active phase of labor was defined in women ≥6 cm of dilatation with ruptured membranes who fail to progress despite 4 hours of adequate uterine activity or at least 6 hours of oxytocin administration with inadequate uterine activity and no first-stage dilatation. In such cases, the arrest of dilatation requiring cesarean delivery was defined following two more hours of oxytocin administration with no cervical change. In the case of progression of the first-stage dilatation, obstetric intervention was indicated during the first-stage in the event of the above criteria, while the diagnosis of arrest of labor in the second stage was made in the event of a duration of the active phase of at least two hours in multiparous women or three hours in nulliparous women, in accordance with the ACOG/SMFM

recommendations (4).With regards to instrumental vaginal delivery, the use of forceps is not performed as part of routine clinical practice in the participating Units. Obstetric intervention – i.e. cesarean delivery or vacuum extraction – due to suspected intrapartum fetal compromise represented an exclusion criterion for the study. All the obstetric interventions were performed according to a commonly shared management protocol when the criteria for arrest of dilatation or arrest of labor in the second stage were fulfilled (4).

Clinical data including maternal age, ethnicity, body mass index, gestational at delivery, induced or spontaneous labor, epidural analgesia, augmentation during labor, length of the first and of the second stage of labor, head station and cervical dilatation at diagnosis of protracted active phase of labor as well as mode of delivery, estimated blood loss, birthweight, 5 minutes APGAR and arterial pH was collected from patient case notes.

<u>Intrapartum ultrasound performed for research purposes</u>

Portable ultrasound devices equipped with low frequency transabdominal probe were used for the study purposes. The US measurements were performed on women lying in semirecumbent position with an empty bladder. Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position of the fetal head, while the flexion was evaluated by tilting the probe by 90 degrees to the longitudinal plane. The position was defined from the landmarks depicting fetal occiput and described as a clock face with 12 hourly divisions. Positions >09:30 and <2:30 o’clock were classified as occiput anterior, while occiput transverse and occiput posterior (OP) were defined in the case of occiput ≥02.30 and ≤03.30 o’clock or ≥08.30 h and ≤09.30 o’clock and >03.30 and <08.30 o’clock, respectively (31,39).

Based on our experience no ultrasound parameter has the potential to objectively evaluate the degree of head flexion for all the positions of the fetal occiput. The flexion of the fetal head was quantitatively defined by means of the occiput-spine angle (OSA) for the fetuses in occiput anterior and occiput transverse position and by means of the chin-to-chest angle (CCA) for the fetuses in OP position. In details, the OSA was identified by the angle between a line tangent to the posterior cervical spine and a second line tangent to the fetal occiput, as previously described (36) (Figure 1). The CCA was defined as the angle identified by the intersection between one line through the longest axis of the sternum and a second line through another straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin (Figure 2).

Transperineal ultrasound was performed with the transducer placed in a transverse or longitudinal position between the labia majora or more caudally at the level of the fourchette and allowed the measurement of the sonographic indicators of fetal head station and descent. The head-perineum distance (HPD) was assessed by placing the probe in the posterior fourchette and applying a gentle but firm pressure on the perineum as previously described (40). The angle of progression (AoP) was measured on the midsagittal image by drawing one line between calipers placed at the two points identifying the long axis of the pubic symphysis; a second caliper line was then created on the frozen image that extended from the most inferior portion of the pubic symphysis tangentially to the fetal skull contour (41). All the measurements were obtained in the absence of uterine contractions and/or maternal pushing efforts.

<u>Endpoints</u>

The primary outcome of the study was to evaluate the sonographic indicators of fetal head flexion, i.e. the OSA and the CCA in fetuses in non-OP and in OP position, respectively, as measured at diagnosis of protracted active phase of labor in relation to the mode of delivery and other labor outcomes. Furthermore, we evaluated the relationship between the OSA and the CCA and the transperineal sonographic indicators of fetal head descent.

<u>Ethics approval</u>

Ethics approval for this study was granted by the local Ethics Committee at the University Hospitals of Parma (N 270/2018/OSS/UNIPR on 03/12/2018) and Rome Tor Vergata (N 17/Ob2 on 15/10/2017) and at the Sant'Anna Hospital of Turin (N 0061542 on 21/06/2017).

Statistical analysis

Statistical analysis was performed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Normal or abnormal distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov and the Shapiro-Wilk tests and data were shown as mean ± standard deviation or as median (range) accordingly. Comparison of normally and non-normally distributed continuous variables included the T test for independent sample and 2-tailed t test and the Mann-Whitney U-test, respectively. Categorical variables were reported as number (percentage) and compared using the Chi-square or Fisher exact test. Logistic regression analysis was used to control for potential confounding variables, while the prediction of the mode of delivery by intrapartum sonographic parameters was determined by receiver operating characteristic (ROC) curve analysis. $p < 0.05$ was considered as significant. This study was conducted following the STROBE guidelines (42).

Results

Overall, 129 women were included (Figure 3). The transabdominal and transperineal ultrasound examination was successfully performed in all the eligible cases. Baseline and obstetrical features of our cohort population are shown in Table 1. Spontaneous vaginal delivery occurred in 66 (51.2%) women, while instrumental vaginal delivery and cesarean delivery were recorded in 17 (13.1%) and 46 (35.7%), cases, respectively. The mean length of the first and second stage of labor was 495 ± 171 minutes and 107 ± 52 minutes, respectively. No case of failed instrumental delivery requiring emergency cesarean delivery was recorded. At diagnosis of protracted active phase of labor occiput anterior, occiput transverse and OP positions accounted for 59 (45.8%), 27 (20.9%) and 43 (33.3%) of the included cases.

Clinical and sonographic findings in fetuses in non-occiput posterior position are shown in Table 2a. A wider OSA (126±14 vs 115±24 degrees, p=0.006) and AoP (118±13 vs 104±11 degrees, p<0.001) and a shorter HPD (40±5 vs 49±9 mm, p<0.001) were measured in women who had vaginal delivery, however only the OSA and the HPD proved to be independently associated with the mode of delivery at logistic regression analysis (p=0.007 and p=0.001, respectively) (Table 3a). At ROC curve the OSA was found to be associated with an area-under-the-curve (AUC) of 0.675, 95%CI (0.538-0.812), p<0.01. The optimal cut-off value of the OSA discriminating between cases of VD vs those delivered by CS was 109 degrees, and was associated with a 56.7% sensitivity, 87.5% specificity, 70.8% PPV and 79.0% NPV. When addressing the correlation between the OSA and the sonographic indicators of fetal head station, the OSA showed a direct correlation with the AoP (Pearson's correlation 0.449, p<0.01) but no correlation with the HPD (p=0.15). At visual analysis of the scatter/dot charts (Figure 4), 9 cases in which the AoP of progression was not positively correlated with the OSA were noted and labelled as outliers. Such cases showing a narrow AoP and a wide OSA were all submitted to cesarean delivery and characterized by a lower maternal height (157±7 vs

163±6 cm, p<0.01) and a higher ratio between the birthweight and the maternal height (22.6±1.6 vs 20.7±2.6, p=0.04) compared to the non-outlier cases.

When considering only the 62 non-OP fetuses with OSA width above 109 degrees – i.e. with favorable head flexion –, such outlier cases accounted for 9/13 cesarean deliveries. Outlier cases showed a higher ratio between the OSA and the AoP (1.45±0.19 vs 1.09±0.10, p<0.001) and a lower ratio between the OSA and the HPD (2.60±0.46 vs 3.40±0.50, p<0.001) compared to non-outliers. The distribution of the OSA/AoP ratio in relation to the mode of delivery showed a trend towards an increased rate of CS with increasing OSA/AoP ratio (Figure 5a), while a trend towards an increased rate of CS was noted with decreasing OSA/HPD ratio (Figure 5b). At ROC curve the OSA/AoP ratio was found to be associated with an AUC for the prediction of cesarean delivery of 0.769, 95%CI (0.586-0.952), p=0.003, while the OSA/HPD ratio was associated with an AUC of 0.778, 95%CI (0.631-0.925), p=0.002. The optimal cut-off value of the OSA/AoP ratio discriminating between cases of VD vs those delivered by CS was 1.20, and was associated with a 69.2% sensitivity, 87.8% specificity, 60.0% PPV and 91.5% NPV; the optimal cut-off value of the OSA/HPD ratio discriminating between cases of VD vs those delivered by CS was 3.05, and was associated with a 69.2% sensitivity, 77.6% specificity, 45.0% PPV and 90.5% NPV.

The clinical and the sonographic findings in fetuses in OP position are shown in Table 2b. A narrower CCA (27±33 vs 56±28 degrees, p=0.005) and a lower rate of induction of labor (22.2% vs 62.5%, p=0.008) were found in women who had vaginal delivery. At logistic regression analysis CCA and labor induction proved to be independently associated with the mode of delivery (p=0.008 and p=0.007, respectively, Table 3b). At ROC curve the CCA was associated with an area-under-the-curve (AUC) for the mode of delivery of 0.758, 95%CI (0.612-0.904), p<0.01. The optimal cut-off value of the CCA discriminating between cases of VD vs those delivered by CS was 33.0 degrees, which was associated with a 93.8% sensitivity, 63.0% specificity, 60.0% PPV and 94.4% NPV. No correlation was found between the CCA and the AoP (p=0.48) nor the HPD (p=0.98).

Discussion

Principal findings

The results from this study conducted on a selected cohort of women with protracted active phase of labor demonstrate that the degree of flexion of the fetal head as measured at transabdominal ultrasound is related to the mode of delivery in OP as well as in non-OP fetuses, being head deflexion associated with an increased risk of cesarean delivery due to labor dystocia. Furthermore, fetal head station as measured at transperineal ultrasound by means of the HPD is independently associated with the likelihood of vaginal delivery in non-OP fetuses. Finally, in non-OP fetuses the degree of fetal head flexion correlates with the transperineal sonographic indicators of fetal head station.

Results in the context of what is known

The relationship of fetal head to spine – also referred to as "fetal attitude" – in the first-stage of labor has traditionally been considered to impact on fetal head descent and ultimately on labor outcome. Deflexed cephalic presentations are acknowledged to represent major determinants of obstructed labor (7,8,36). According to the mechanics of the human labor the descent of the presenting part through the birth canal is associated with a progressive flexion of the fetal head on the chest (5). On this basis, previous data from an unselected population of non-OP fetuses suggested that cephalic malpresentations in terms of deflexed fetal head are associated with a higher clinical station and an increased likelihood of obstetric intervention secondary to intrapartum dystocia (36). Consistently, a recent research conducted on 200 women found an increased incidence of cesarean delivery in fetuses showing sonographic features of head deflexion (43). In this study the degree of fetal head flexion was measured by means of the OSA in non-OP fetuses, while in OP fetuses a qualitative assessment of the fetal attitude was performed. However, this research did not include cases of labor dystocia, and the participating women were recruited at full cervical dilatation and not during the first-stage of labor (43).

Some studies previously evaluated the risk of obstetric intervention secondary to labor dystocia in relation to the position and the station of the fetal head at diagnosis of protracted active phase of labor (33-35,44-47). Under these circumstances, an increased likelihood of cesarean delivery due to labor dystocia was reported in fetuses with OP position and a high fetal station at transperineal ultrasound as demonstrated by a long HPD and a narrow AoP. Our study has confirmed a similar relationship between the sonographic indicators of fetal head station and the mode of delivery in fetuses in non-OP position but not in those in OP position, among whom labor induction proved to be independently associated with the likelihood of cesarean delivery.

Clinical implications

According to the recommendations of the International Society on Ultrasound in Obstetrics and Gynecology, intrapartum ultrasound is indicated in conditions of first-stage dystocia (31). Based on the findings from this study, the evaluation of the degree of flexion of the fetal head might be incorporated in the sonographic evaluation of cases of protracted active phase of labor. However, it is uncertain whether in such conditions the use of ultrasound can lead to an individualized management in terms of increased augmentation in the case of favorable conditions in terms of good head flexion and, conversely, anticipated caesarean delivery in the case of malpresentation with or without malposition of the presenting part.

Research implications

Based on our results, we believe that also subtle degrees of deflexion of the fetal head may preclude its descent through the birth canal by impairing the most favorable (suboccipito-bregmatic) diameter of the fetal head to negotiate the pelvic inlet, thus leading to dystocia requiring cesarean delivery (5,6).

Furthermore, this present study suggests that our ability in understanding the underlying cause of protracted active phase of labor may be improved thanks to the use of ultrasound. The finding of

outlier cases requiring cesarean delivery due to labor dystocia and characterized by a high head station (as witnessed by the narrow AoP and the long HPD) and no evidence of malposition and malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic disproportion. This hypothesis is supported by the fact that such cases were characterized by a lower maternal height and by a higher birthweight-to-maternal height ratio in comparison to “non-outliers”. We do envisage that in these conditions any attempt to perform an instrumental vaginal delivery should be balanced against the risks of “true” obstructed labor. However, more research is required in order to clarify whether the head circumference (48,49), the maternal height (50-53) or other sonographic indices may be considered in the individualized management of the laboring woman diagnosed with protracted active phase of labor in cases characterized by non-OP position, wide OSA, narrow AoP and long HPD.

With regards to the degree of flexion of the fetal head in OP fetuses, ours is the first study describing a quantitative parameter – i.e. the CCA – for the assessment of the degree of flexion of the fetal head, which we show to be associated with a fair sensitivity and NPV in the prediction of CS due to labor dystocia. The low specificity and positive predictive value of the CCA suggest that the degree of flexion of the fetal head may vary across labor and may not represent the only determinant of labor arrest in OP fetuses.

While we first describe the CCA as a sonographic indicator of flexion in OP fetuses, no correlation could be demonstrated between the CCA and the AoP nor the HPD. This is likely to be dependent on the different – and thus far unexplored – mechanics of the fetal head descent in OP compared to the non-OP fetuses.

Strengths and limitations

This is the first study evaluating the sonographic indices of fetal head flexion which can be measured on transabdominal ultrasound in women with protracted active phase of labor. Another strength is

that this study was prospectively conducted at three Units with dedicated expertise in intrapartum ultrasound, which has allowed the collection of several ultrasound parameters within a selected population of women at risk of cesarean delivery due to protracted active phase of labor.

With regards to the limitations, we acknowledge that our cohort was not powered for adverse maternal and perinatal outcomes. Therefore, more research is warranted in order to understand whether the deflexion of the fetal head in conditions of protracted active phase of labor impacts on maternal and fetal outcomes other than on the mode of delivery. Another limitation is represented by the fact that the measurement of the CCA may be challenging, and its intra- and inter-observer reproducibility was not preliminary tested. However, it is important to note that all the research scans were performed by a small number of investigators with expertise on ultrasound in labor, therefore we believe that in such context a variability in the CCA measurements is highly unlikely. Therefore, it is uncertain whether the use of such sonographic parameter can be easily implemented outside the context of Units with expertise on ultrasound in labor such as those participating to this present study. We acknowledge that additional malpresentations such as asynclitism, which are known to impact the labor course (54-60), were not evaluated in this study. Such limitation needs to be taken into account in a clinical context where different types of malpresentation may coexist and contribute in determining a protracted active phase of labor.

Finally, the "non-consecutive" enrolment may be accounted as a potential source of bias, even though we believe that the wide number of the enrolled patients together with the strict inclusion criteria allow to overcome such potential limitation.

Conclusions

In conclusion, this work shows that within a selected cohort of women with protracted active phase of labor, the evaluation of the sonographic indices of fetal head flexion is associated with the incidence of labor dystocia leading to cesarean delivery in OP as well as in non-OP fetuses, while the head station is related to the mode of delivery in non-OP but not in OP fetuses. This research supports the sonographic assessment of the degree of flexion of the presenting part in conditions of protracted active phase of labor, and suggest that intrapartum ultrasound may contribute in the categorization of the etiology of the dystocia and support the individualized management of conditions of protracted active phase of labor.

Conflict of interest statement

The Authors state no financial disclosures nor conflict of interest related to the content of this research.

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Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study.

Reply to the Reviewers:

Reviewer #1: The manuscript has improved, and the authors have responded adequately to most comments.

Reviewer #1, POINT 1

A.I have some concerns related to line 221 to 231. Nine outliers (red spots indicating cesarean delivers) in the scatter plots in figure 4 have been subjectively removed. In all 30 cesarean deliveries occurred in non-OP positions. Subjective removal of 30% and thereafter calculate prediction is not appropriate. The removed cases had only a modest difference in maternal height. The birth weight was not known at the time of decision of delivery mode, and should not be part of explaining why these cases were removed.

B.We thank the Reviewer for the comment. It is true that the "subjective removal" of outiler cases is not appropriate, however such attempt was made following on of the previous Reviewers' comments, which we herein report:

"The authors may be the first to quantitate the sonographic angle of flexion, but the positive and negative predictive values (PPV and NPV) are not high enough to seem of much help to the clinician. For example, 30/86 = 35% of fetuses in OA/OT position in this study were delivered by cesarean, whereas if the OSA was at least 108.5 degrees, the 70.8% PPV for vaginal delivery lowered this to about 29%. Not a big difference. The authors do acknowledge this in the Discussion, but it would help if they could provide insight as to why their findings nonetheless are of clinical importance. Is there anything to suggest that measuring these angles is an improvement over standard digital exams in managing labor?

Reply: we thank again the Reviewer for this comment, which allows to further explain the main findings of the study. The Reviewer is correct in pointing out that the performance of the OSA cut-off is poor in discriminating fetuses who are likely to be delivered vaginally compared to those requiring cesarean delivery. However, when looking at the relationship between the OSA and the sonographic indicators of fetal head station (i.e. HPD and AoP, please see Figure 4) we demonstrate the existence of outlier cases characterized by a wide OSA – i.e. a good flexion of the fetal head – and a high station – i.e. narrow AoP and long HPD – and all delivered by cesarean. As

we state in the manuscript, by demonstrating a lower maternal height and a higher birthweight/maternal height ratio, we hypothesize that such discrepancy represents an indicator of cephalo-pelvic disproportion. On this basis, such outlier cases characterized by a wide OSA BUT a high station (narrow AoP, long HPD) do impact in reducing the AUC as well as the PPV for vaginal delivery of the cases with OSA >108.5 degrees. In the results section of the amended version of the manuscript we report a secondary analysis of the sensitivity, specificity, PPV and NPV for vaginal delivery in relation to the OSA cut-off value following the removal of the 9 outlier cases. In the analysis we demonstrate that a OSA >108.5° is associated with a 80.9% sensitivity, 87.5% specificity, 70.8% PPV and 92.5% NPV for vaginal delivery, with an overall rate of cesarean delivery as low as 7.5%. Therefore, we believe that the evaluation of the sonographic indicators of fetal head flexion and station does add an improvement in managing labor as this may allow to identify the etiology of the labor dystocia, ultimately leading to optimized management."

It is also true that "The removed cases had only a modest difference in maternal height. The birth weight was not known at the time of decision of delivery mode, and should not be part of explaining why these cases were removed", however we believe that the maternal height, the birthweight and their ratio can assist in supporting our hypothesis that those identified as outliers on the basis of the discrepancy between these usually paired sonographic findings (flexion and station) are delivered by cesarean because of cephalopelvic disproportion. Indeed, such cases all showed favorable degree of head flexion but unexpectedly the station was high and, interestingly, an increased mean birthweight and birthweight/maternal height ratio was eventually found. The paragraph was inserted in the amended version as we believe that such explanation can help the readers to better understand our point, but we are of course happy to amend the results section and remove it as requested. We e have added to the results section a further paragraph detailing the findings of the analysis evaluating the relationship between the sonographic indicators of head station (AoP and HPD) and the OSA in non-occiput posterior fetuses with favorable head flexion (i.e. with OSA wider than 109 degrees) in relation to the mode of delivery in outlier and non-outlier cases. As stated in the paragraph, the sub-analysis evaluating the ratios between the OSA and the sonographic indicators of head station allows to identify 9/13 (sensitivity 69%) cesarean deliveries performed within a selected cohort of fetuses with protracted active phase of labor but no apparent malpresentation, and in Figure 5 we clearly show a trend towards an increased frequency of cesarean delivery with increasing OSA/AoP ratio and with decreasing OSA/HPD ratio. Based on our hypothesis, such findings support the concept that outlier cases represent a population characterized by a mismatch between the size of the birth canal and that of the fetus.

C. Lines 229-242

D. Paragraph removed: “An inverse correlation between the OSA and the HPD (Pearson’s correlation -0.566, p<0.01) and a stronger correlation between the OSA and the AoP (Pearson’s correlation 0.693, p<0.01) were demonstrated following the removal of the 9 outliers from the non-OP dataset. Furthermore, following the removal of the 9 outlier cases a OSA width >108.5 degrees showed 80.9% sensitivity, 87.5% specificity, 70.8% PPV and 92.5% NPV for the mode of delivery and an overall 7.5% rate of cesarean delivery.”

Paragraph added: “When considering only the 62 non-OP fetuses with OSA width above 109 degrees – i.e. with favorable head flexion –, such outlier cases accounted for 9/13 cesarean deliveries. The distribution of the OSA/AoP ratio in relation to the mode of delivery showed a trend towards an increased rate of CS with increasing OSA/AoP ratio (Figure 5a), while a trend towards an increased rate of CS was noted with decreasing OSA/HPD ratio (Figure 5b). At ROC curve the OSA/AoP ratio was found to be associated with an AUC for the prediction of cesarean delivery of 0.769, 95%CI (0.586-0.952), p=0.003, while the OSA/HPD ratio was associated with an AUC of 0.778, 95%CI (0.631-0.925), p=0.002. The optimal cut-off value of the OSA/AoP ratio discriminating between cases of VD vs those delivered by CS was 1.20, and was associated with a 69.2% sensitivity, 87.8% specificity, 60.0% PPV and 91.5% NPV; the optimal cut-off value of the OSA/HPD ratio discriminating between cases of VD vs those delivered by CS was 3.05, and was associated with a 69.2% sensitivity, 77.6% specificity, 45.0% PPV and 90.5% NPV.”

Reviewer #1, POINT 2

A.The authors say that cases showing a narrow AoP and a wide OSA were all submitted to cesarean delivery. Were the responsible clinicians aware of the ultrasound findings when deciding delivery mode? I suppose that they were blinded to the ultrasound findings.

B.As stated in the methods section (lines 127-128), “The senior Obstetricians in charge for the labor care were blinded to the ultrasound findings.” Thank you.

C.No change has been made to the manuscript.

D.No change has been made to the manuscript.

Reviewer #1, POINT 3

A.Predictive calculation should be based on all cases. Revise the discussion part accordingly.

B.Please see our Reply to the POINT 1. The results section has been amended.

C.No change has been made to the manuscript.

D.No change has been made to the manuscript.

Reviewer #1, POINT 4

A.In accordance with table 2, 30 women were delivered by cesarean, but I can only count 27 red spots in figure 4. Please explain.

B.We thank the Reviewer for this very smart comment. The Reviewer is correct in pointing out this, however there is no mistake. We have gone through our dataset again, and have concluded that the apparent absence of some dots in the scatter/dot chart can be explained by the overlapping of some cases among the non-outliers. We have of course happy to share our dataset should you have any further concern. Thank you.

C.No change has been made to the manuscript.

D.No change has been made to the manuscript.

Reviewer #1, POINT 5

A. The authors explain much better how the angles were measured. The authors say "It is important to acknowledge that a straight plane can identify only one tangent line". To my best knowledge, this is not correct or at least a very uncommon use of the word tangent. A tangent line is defined as a line which locally touches a CURVE at one and only one point. This could easily be corrected in the manuscript by saying that the chin-chest angle was defined as the angle identified by a line through the sternum and a second line through the straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin.

B.The Reviewer is correct in pointing out the actual definition of tangent line. The methods section has been amended consistently with the Reviewer's suggestion.

C.Lines 166-169

D.” The CCA was defined as the angle identified by the intersection between one line through the longest axis of the sternum and a second line through another straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin”

Reviewer #1, POINT 6

A.Line 212-213; Too many decimals are used. The angles and distances cannot be measured as OSA (126.2+14.4 vs 114.5+23.6 degrees, p=0.006) and AoP (117.5+12.7 vs 104.0+10.7 degrees, p<0.001) and a shorter HPD (39.7+5.2 vs 49.0+9.4 mm, p<0.001). Please remove the imprecise decimals throughout the manuscript.

B.This has been done as requested. Thank you.

C.See decimals changes in the results section and in the tables. Thank you.

D. See decimals changes in the results section and in the tables. Thank you.

Reviewer #2: This is an paper is original in its conception: namely defining the degree of head extension (non OP) and flexion (OP) deliveries and the relationship with vaginal, assisted vaginal or Cesarean delivery. Indices OSA (non OP) and CCA (OP) appear to be related to Cesarean where they denote fetal head extension. It seems that intrapartum ultrasound was undertaken in the late first and second stages of labour, based on a diagnosis of prolonged labour. This does introduce a potential difficulty as the timing or stage of ultrasound assessment in relation to delivery was not standardized, that said studies of this type in a delivery ward are notoriously difficult to undertake so this should be kept in mind.

Reply: we thank the reviewer for such comment. It is true that that we standardized the timing of the US assessment at the diagnosis of protracted active phase of labor but not at delivery, which could represent a potential limitation of the study, however it has to be acknowledged that this sort studies are difficult to be conducted in a clinical setting.

Reviewer #2, POINT 1

A.The authors report predictive value cut-offs and AUCs for OSA and CCA however I wonder how robust these are in the context of a selected, non consecutive population? The authors might wish to comment on this.

B.We thank the Reviewer for this comment. It is true that the “non-consecutive” enrolment may represent a limitation of the study, therefore this has been listed among the limitations in the revised version of the manuscript. The “non-consecutive” enrolment was dependent upon the fact that the study investigators were not always available to perform the ultrasound examination at the time of the diagnosis of protracted active phase of labor, which may be accounted as a source of bias also for randomized trials. On balance, we believe that the wide number of the enrolled patients and the strict inclusion criteria allow to overcome such potential limitation, therefore we believe that the “non-consecutive” enrolment does not impact on the robustness of our findings.

C.Lines 348-350

D.Finally, the “non-consecutive” enrolment may be accounted as a potential source of bias, even though we believe that the wide number of the enrolled patients together with the strict inclusion criteria allow to overcome such potential limitation.

Reviewer #2, POINT 2

A.Furthermore, while the OSA has been previously described, as far as I can see, the CCA hasn't, so there is little known about the reproduciblity and variability of the technique: this knowledge is normally a pre-requisite before developing predictive models.
B.The Reviewer is correct in pointing out that the reproducibility of the measurement of the CCA was not tested, as we have acknowledged in the limitations section. However, it is important to note that all the research scans were performed by a small number of study investigators with expertise in ultrasound in labor, therefore we believe that in such context a variability in the CCA measurements is highly unlikely.
C.Lines 337-339
D.However, it is important to note that all the research scans were performed by a small number of investigators with expertise on ultrasound in labor, therefore we believe that in such context a variability in the CCA measurements is highly unlikely.

Reviewer #2, POINT 3
A.Figure 2(b) shows CCA being measured, however the fetal head appears either oblique or asynclitic: would the authors comment on the variability of the measurement in these circumstances? Furthermore, I am not clear if the posterior or anterior sternal aspect should be used to lay the chest line.
B.Thank you for this comment. As we state in the discussion ("Additionally, we acknowledge that complex malpresentations such as asynclitism, among whom some are known to impact on the labor outcome regardless of the additional sonographic parameters (54-60), were not evaluated"), we agree that the asynclitism of the fetal head may impact on the measurement of the sonographic indicators of fetal head flexion, however in a clinical context of protracted active phase of labor different types of malpresentation may coexist and impact on the fetal head descent. The variability of the measurement of the CCA in OP fetuses with co-existent asynclitism was not evaluated in this present study, and it is not clear how this may further affect the labor course. We have further commented on this in the limitation section, and we have amended Figure 2 by providing a new US picture of an OP fetus with synclitic head.
With regards to the technique for the measurement of the CCA, we now state in the methods section that "…The CCA was defined as the angle identified by the intersection between one line through the longest axis of the sternum and a second line through another straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin". One line

only can be identified through the longest axis of the sternum, and lines parallel to such line can be used to lay the chest line either on the anterior or the posterior sternal aspect, with no difference in the measurement of the CCA. Thank you.

C.Lines 367-374

D.Such limitation needs to be taken into account in a clinical context where different types of malpresentation may coexist and contribute in determining a protracted active phase of labor.

Reviewer #2, POINT 4

A.On page 19, line 154-155: "Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position and the flexion of the fetal head." but I guess that for the OSA and CCA measurements, the probe was placed in plane with the long axis of the fetus (longitudinally?).

B.Yes, the reviewer is correct in pointing out that the sonographic indicators can be measured on a longitudinal axis and not on a transverse plane. The methods section was amended accordingly. Thank you.

C.Lines 154-156

D.”Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position of the fetal head, while the flexion was evaluated by tilting the probe by 90 degrees to the longitudinal plane.”

Table 1 – Features of the included cases.

Maternal age, years ***Mean + SD***	32.9 + 4.9
Ethnicity ***n (%)***	Caucasian 107 (82.9%) African 7 (5.4%) Asian 15 (11.6%)
Parity ***n (%)***	Nulliparous 116 (89.9%)
Maternal height, cm ***Mean + SD***	164 + 11
Booking BMI, kg/m² ***Mean + SD***	23.6 + 3.5
Term pregnancy BMI, kg/m² ***Mean + SD***	28.3 + 4.3
Gestational age at delivery, weeks+days ***Mean + SD***	40^{+1} + 1^{+0}
Occiput position at diagnosis ***n (%)***	OA 59 (45.7%) OT 29 (22.5%) OP 41 (31.8%)
Digital station at diagnosis, cm ***Median (range)***	-2 (-4 – +1)
Cervical dilatation at diagnosis, cm ***Median (range)***	8 (6 – 9)
Occiput-spine angle, degrees ***Mean + SD***	122 + 19
Chin-chest angle, degrees ***Mean + SD***	38 + 34
Angle of progression, degrees ***Mean + SD***	111 + 14
Head-perineum distance, mm ***Mean + SD***	43 + 8
Mode of delivery ***n (%)***	SVD 66 (51.2%) VE 17 (13.1%) CS 46 (35.7%)
Birthweight, grams ***Mean + SD***	3492 + 411
Umbilical artery pH ***Mean + SD***	7.24 + 0.09
Apgar at 5 minutes ***Median (range)***	9 (7 – 10)
Estimated blood loss, mls ***Mean + SD***	500 (50 – 2000)
Labor induction ***n (%)***	Yes 34 (26.4%)
Epidural in labor ***n (%)***	Yes 117 (90.7%)
Length of first stage of labor, minutes ***Mean + SD***	495 + 171
Length of second stage of labor, minutes ***Mean + SD***	107 + 52

Length of labor, minutes ***Mean ± SD***	587 ± 193

Table 2 – Demographic features, transperineal and transabdominal ultrasound parameters at diagnosis of protracted active phase of labor and outcomes in the vaginal delivery and in the cesarean delivery group in fetuses a) in non-occiput posterior (n=86) and b) in occiput posterior (n=43) position.

a)

	Vaginal delivery ***N 56 (65.1%)***	***Cesarean delivery*** ***N 30 (34.9%)***	***p value***
Maternal age, years ***Mean + SD***	32.4 + 4.2	33.7 + 5.2	0.20
Ethnicity ***N (%)***	Caucasian 47 (83.9%) African 2 (3.96%) Asian 7 (12.5%)	Caucasian 21 (70.0%) African 3 (10.0%) Asian 6 (20.0%)	0.27
Parity ***N (%)***	Nulliparous 53 (94.6%)	Nulliparous 29 (96.7%)	0.67
Maternal height, cm ***Mean + SD***	164 + 6	161 + 7	0.03
Booking BMI, kg/m² ***Mean + SD***	22.8 + 3.8	24.8 + 3.4	0.02
Term pregnancy BMI, kg/m² ***Mean + SD***	27.3 + 4.6	29.6 + 4.2	0.03
Gestational age at delivery, weeks $^{+days}$ ***Mean + SD***	40^{+0} + 1^{+0}	40^{+0} + 0^{+6}	0.72
Digital station at diagnosis, cm ***Median (range)***	-2 (-3 – -1)	-2 (-4 – +1)	0.29
Cervical dilatation at diagnosis, cm ***Median (range)***	8 (6 – 9)	8 (6 – 9)	0.57
Occiput-spine angle, degrees ***Mean + SD***	126 + 14	115 + 24	0.006
Angle of progression, degrees ***Mean + SD***	118 + 13	104 + 11	<0.001
Head-perineum distance, mm ***Mean + SD***	40 + 5	49 + 9	<0.001
Birthweight, grams ***Mean + SD***	3476 + 397	3503 + 311	0.74
Labor induction ***N (%)***	Yes 12 (21.4%)	Yes 6 (20.0%)	0.88
Epidural in labor ***N (%)***	Yes 54 (96.4%)	Yes 27 (90.0%)	0.23

b)

	Vaginal delivery ***N 27 (62.8%)***	***Cesarean delivery*** ***N 16 (37.2%)***	***p value***
Maternal age, years ***Mean ± SD***	31.6 ± 5.4	33.3 ± 5.7	0.34
Ethnicity ***N (%)***	Caucasian 23 (85.2%) African 2 (7.4%) Asian 2 (7.4%)	Caucasian 16 (100.0%) African 0 (0.0%) Asian 0 (0.0%)	0.27
Parity ***N (%)***	Nulliparous 8 (29.6%)	Nulliparous 1 (6.2%)	0.07
Maternal height, cm ***Mean ± SD***	163 ± 5	162 ± 6	0.47
Booking BMI, kg/m² ***Mean ± SD***	24.4 ± 0.9	24.0 ± 1.0	0.55
Term pregnancy BMI, kg/m² ***Mean ± SD***	29.5 ± 2.1	29.5 ± 2.0	0.99
Gestational age at delivery, weeks^{+days} ***Mean ± SD***	40^{+1} ± 1^{+3}	40^{+3} ± 0^{+6}	0.52
Digital station at diagnosis, cm ***Median (range)***	-2 (-3 – -1)	-3 (-3 – -2)	0.15
Cervical dilatation at diagnosis, cm ***Median (range)***	8 (6 – 9)	7 (6 – 9)	0.29
Chin-chest angle, degrees ***Mean ± SD***	27 ± 33	56 ± 28	0.005
Angle of progression, degrees ***Mean ± SD***	108 ± 16	92 ± 14	0.06
Head-perineum distance, mm ***Mean ± SD***	42 ± 6	43 ± 4	0.68
Birthweight, grams ***Mean ± SD***	3537 ± 524	3493 ± 446	0.78
Labor induction ***N (%)***	Yes 6 (22.2%)	Yes 10 (62.5%)	0.008
Epidural in labor ***N (%)***	Yes 21 (77.8%)	Yes 15 (93.8%)	0.17

Table 3 – Logistic regression analysis for intrapartum clinical, transperineal and transabdominal ultrasound parameters at diagnosis of protracted active phase of labor and mode of delivery (vaginal delivery vs cesarean delivery) a) for fetuses in non-occiput posterior position and b) for fetuses in occiput posterior position.

a)

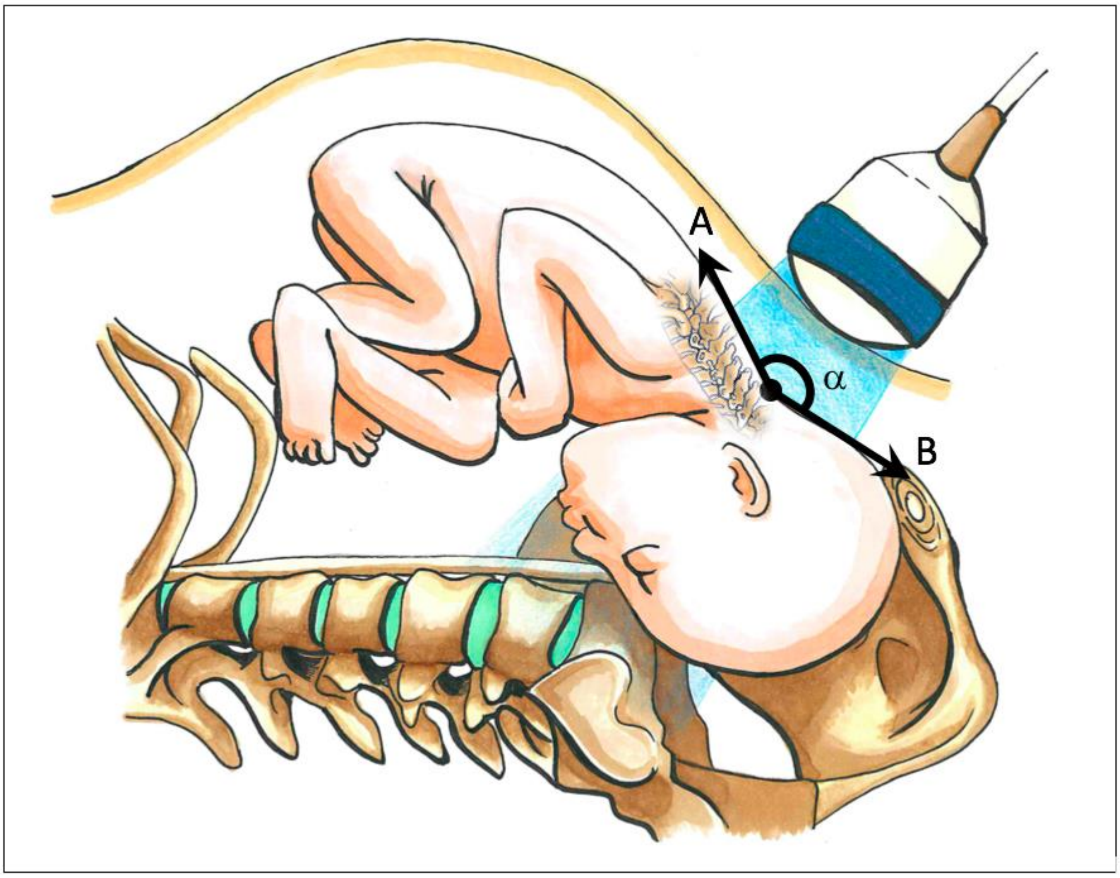
Variable	***Adjusted OR***	***(95%CI)***	***p***
Maternal heigth	1.020	0.897-1.158	0.766
Booking BMI	0.997	0.567-1.752	0.992
Term pregnancy BMI	1.418	0.877-2.293	0.155
OSA	0.921	0.868-0.977	0.007
AoP	1.052	0.962-1.150	0.266
HPD	1.305	1.116-1.525	0.001

b)

Variable	***Adjusted OR***	***(95%CI)***	***p***
Induction of labor	9.316	1.800-48.198	0.008
CCA	1.035	1.010-1.062	0.007

Figure 1 – Attitude in fetuses in non-occiput posterior position as measured by means of the occiput-spine angle (OSA): a) graphic representation of the OSA and b) sonographic view of a flexed fetal head showing a wide OSA.

a)



b)

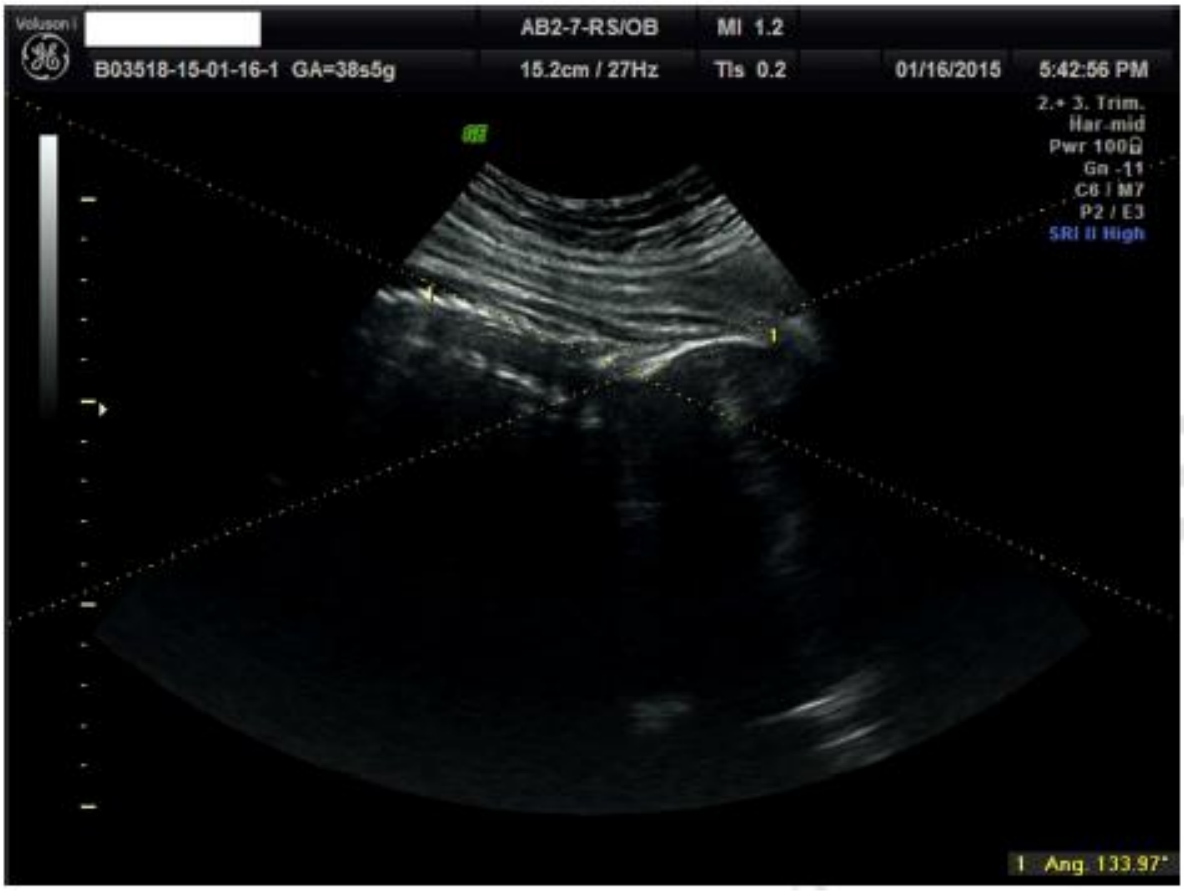
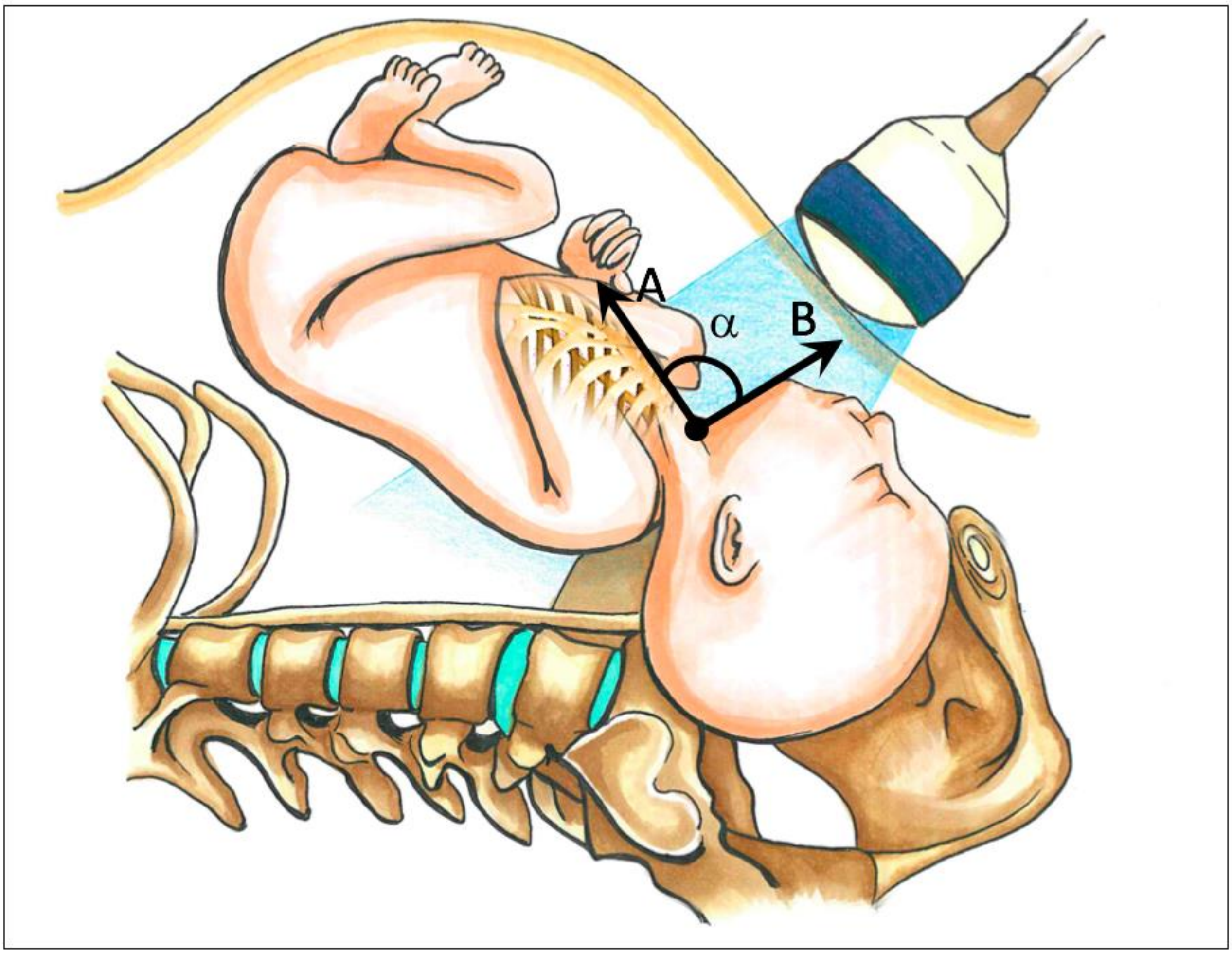

Voluson
AB2-7-RS/OB
MI 1.2
B03518-15-01-16-1 GA=38s5g
15.2cm / 27Hz
TIs 0.2
01/16/2015
5:42:56 PM
2.+ 3. Trim.
Har-mid
Pwr 100
Gn -11
C6 / M7
P2 / E3
SRI II High
1 Ang. 133.97°

Figure 2 – Attitude in fetuses in occiput posterior position as measured by means of the chin-to-chest angle (CCA): a) graphic representation of the CCA and b) sonographic view of a deflexed fetal head showing a CCA between 45 and 90 degrees (A: line tangent to the longest axis of the sternum; 2: line tangent to the skin covering the inferior boundary of the oral cavity up to the chin).

a)



b)

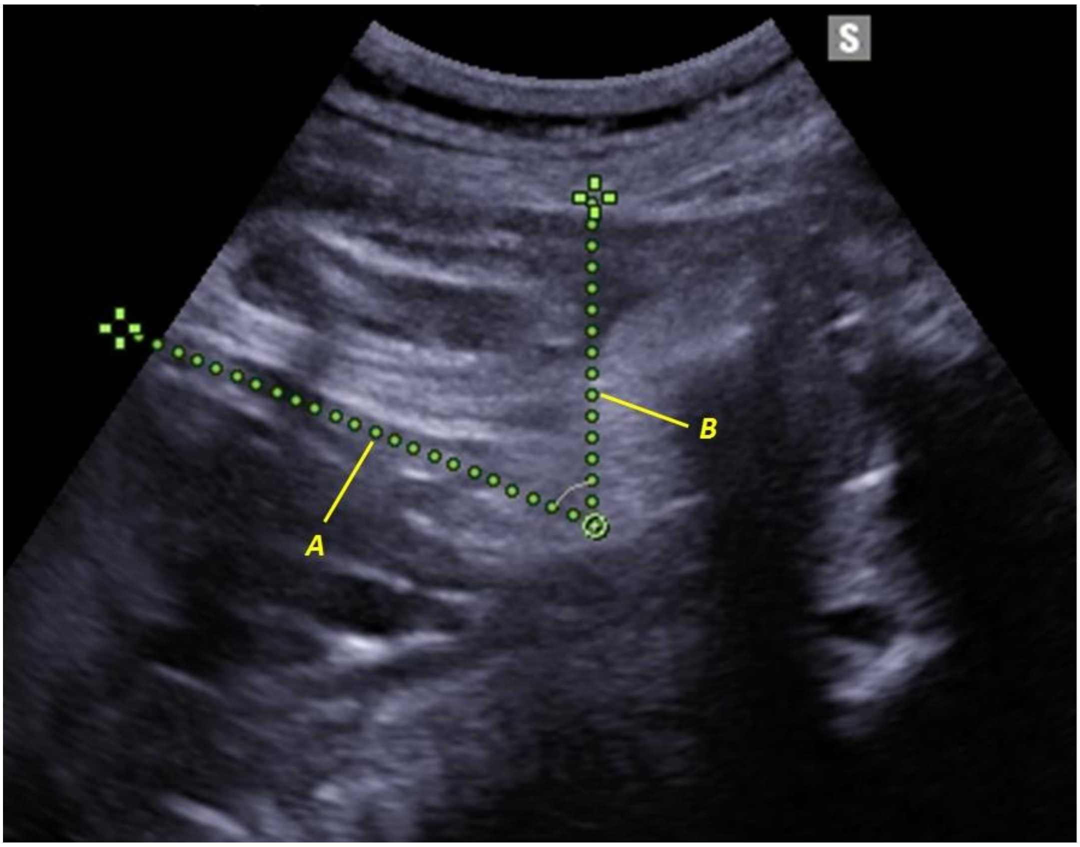
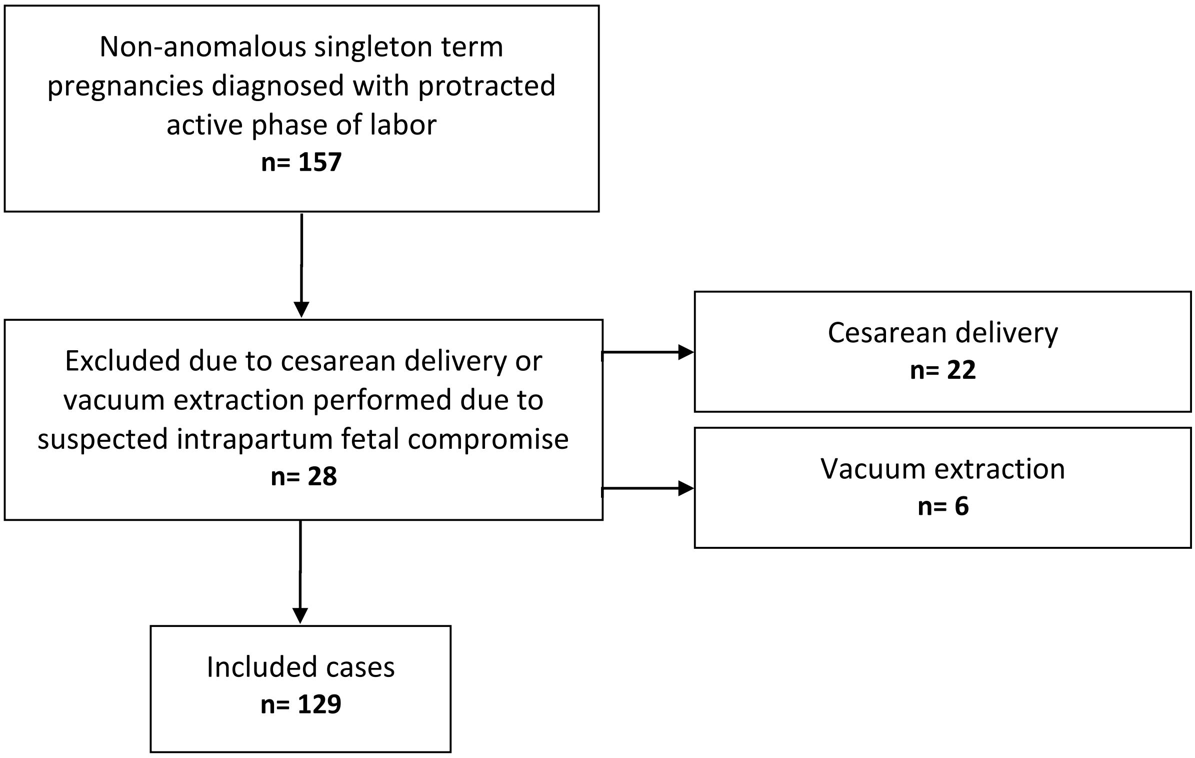


Figure 3 – Flow chart (according to STROBE guidelines) (33) for inclusion of cases.



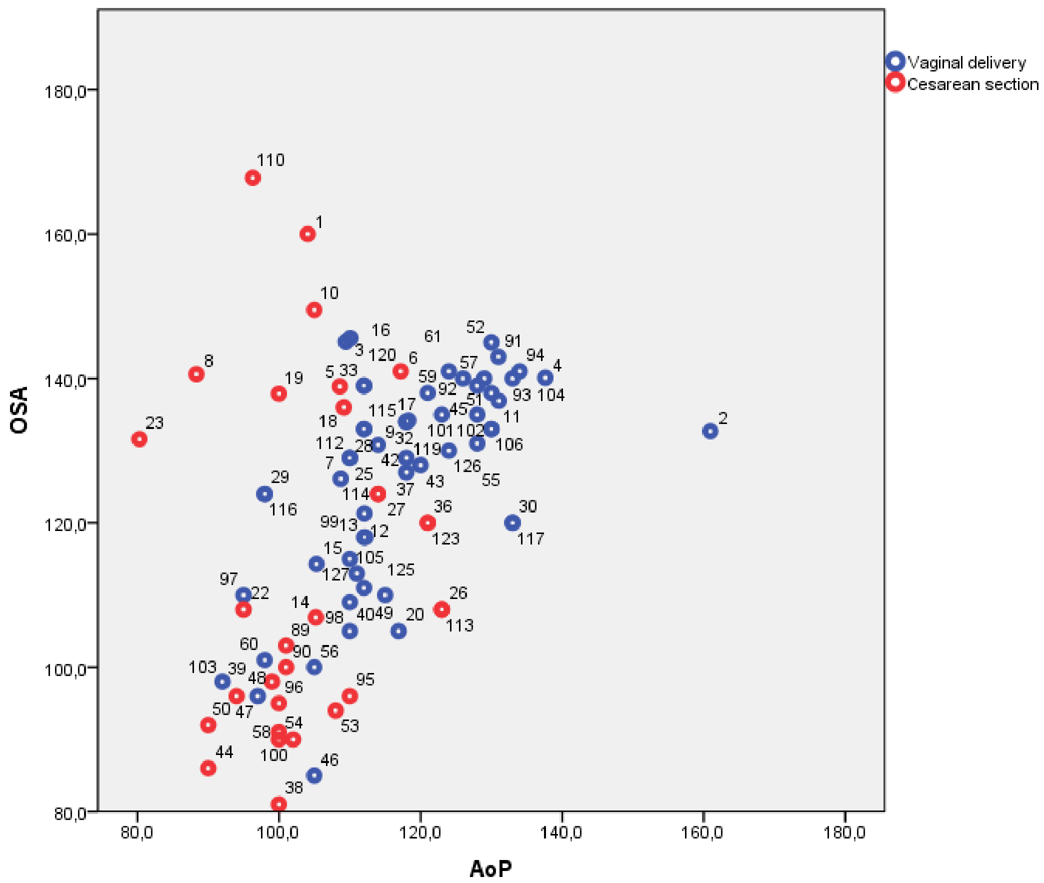
Figure(s)

Click here to access/download;Figure(s);Figure 4 23.11.2020.docx

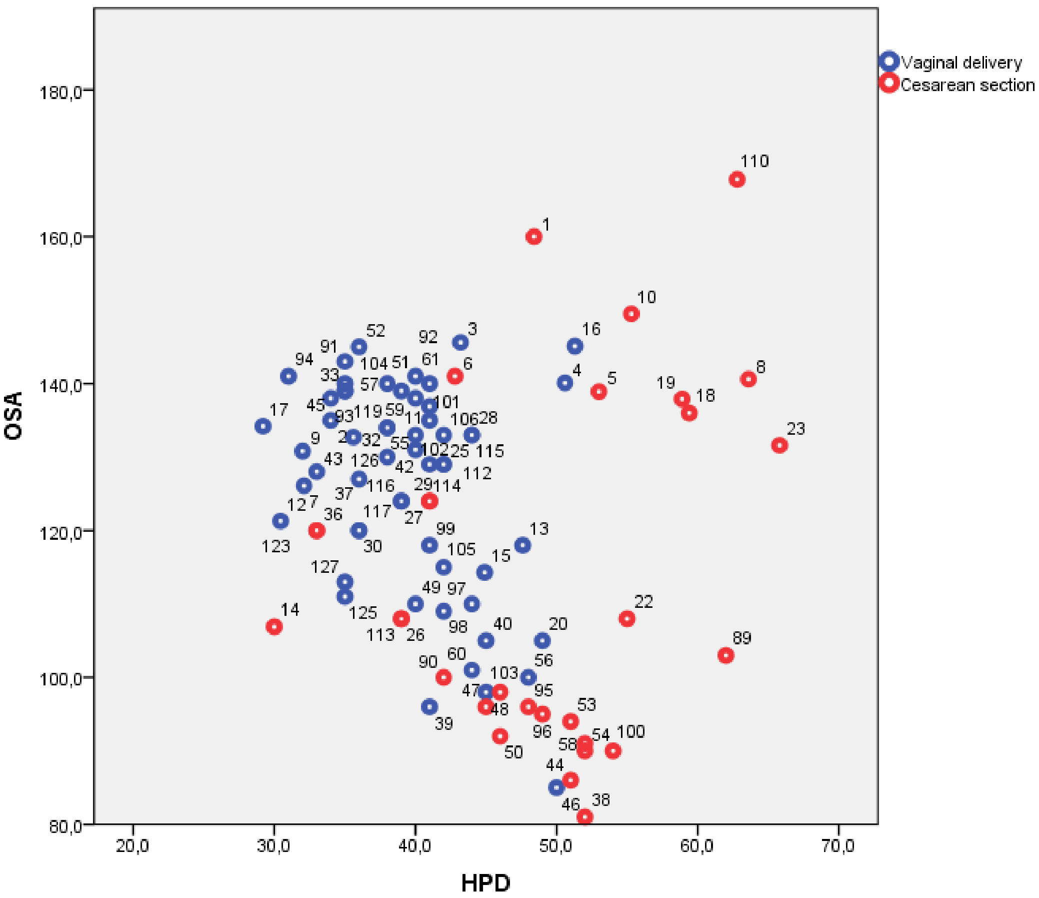
Figure 4 – Scatter/dot charts demonstrating the correlations a) between the occiput-spine angle (OSA) and the angle of progression (AoP) and b) between the OSA and the head-perineum distance (HPD) in fetuses in non-occiput posterior position.

Outliers corresponding to the case numbers 1, 5, 6, 8, 10, 18, 19, 23 and 110.

a)



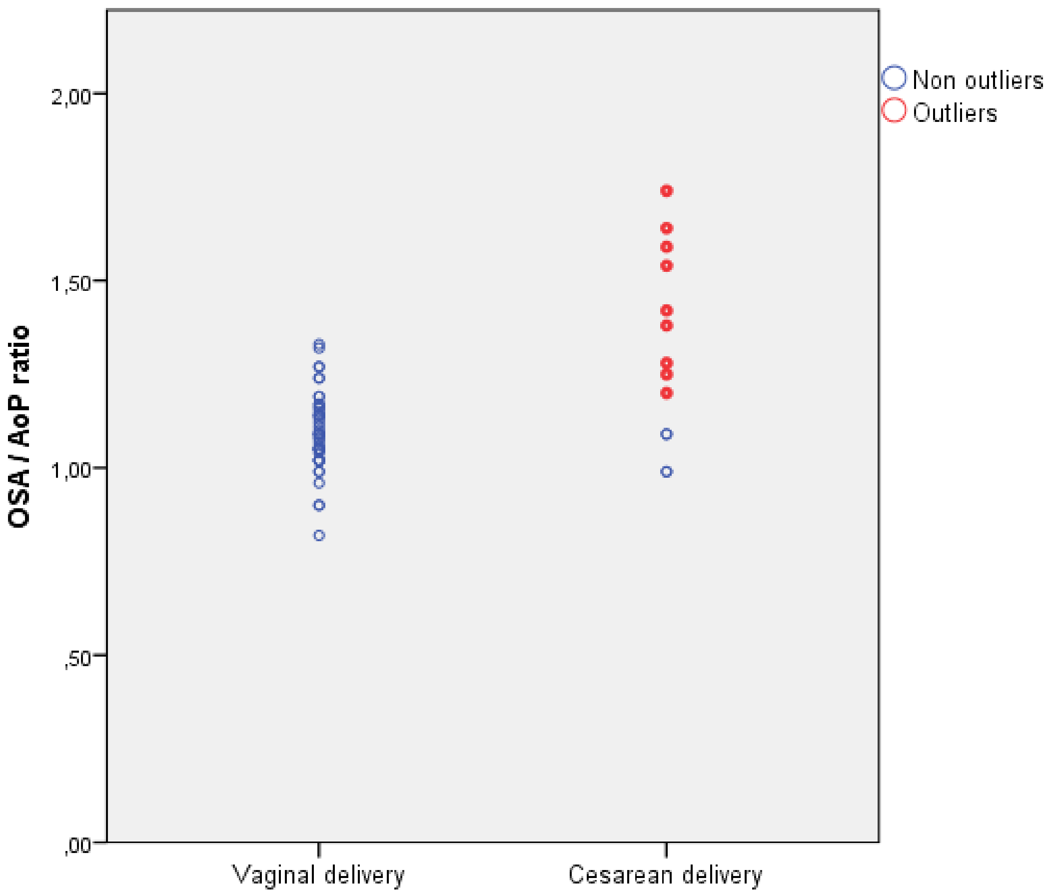
b)



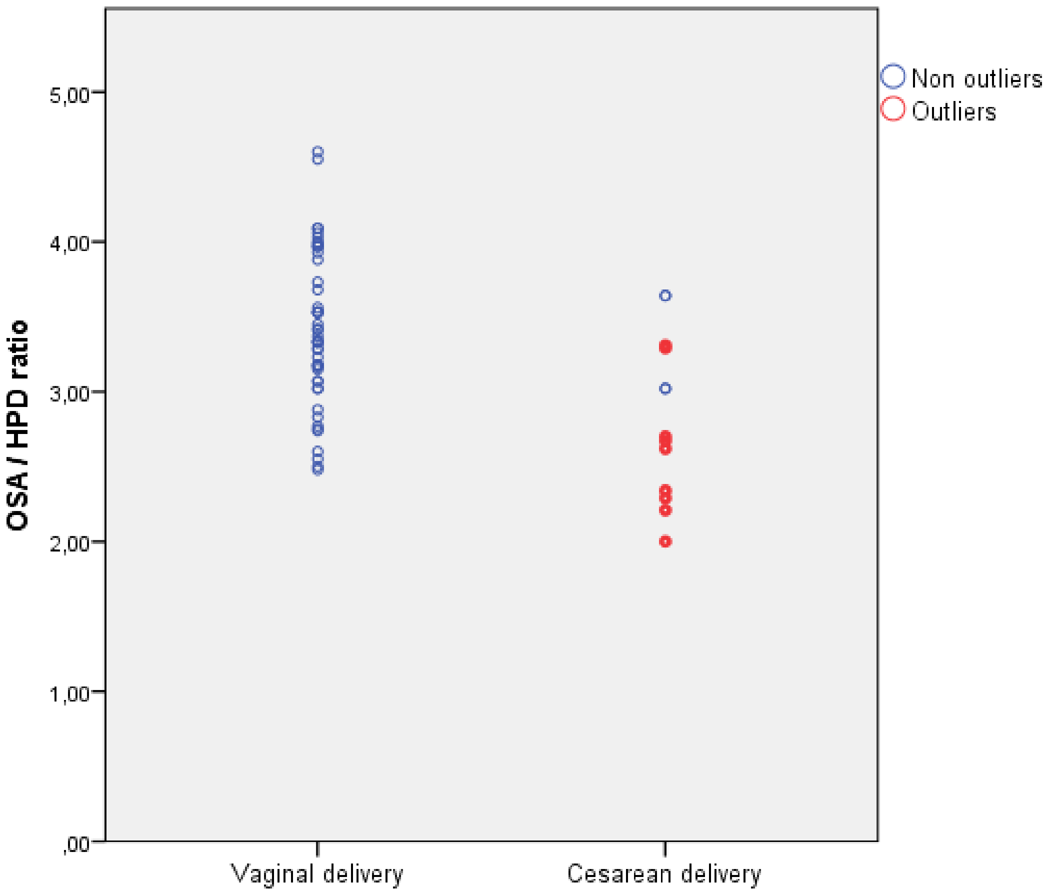
Vaginal delivery
Cesarean section
OSA
HPD
180,0
160,0
140,0
120,0
100,0
80,0
20,0
30,0
40,0
50,0
60,0
70,0

Figure 5 – Distribution of the occiput-spine angle (OSA)-to-angle of progression (AoP) ratio (Figure 5a) and of the OSA-to-head perineum distance (HPD) ratio (Figure 5b) in relation to the mode of delivery in outlier and non-outlier cases in cases with OSA >109 degrees.

a)



b)



Non outliers
Outliers
OSA / HPD ratio
5,00
4,00
3,00
2,00
1,00
,00
Vaginal delivery
Cesarean delivery

AJOG American Journal of Obstetrics & Gynecology

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Corresponding author: Prof Tullio Ghi

Authors may either sign the same form or submit individually

I am an author on this submission, have adhered to all editorial policies for submission as described in the Information for Authors, attest to having met all authorship criteria, and all potential conflicts of interest / financial disclosures appears on the title page of the submission.

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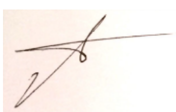
Typed or CLEARLY Printed Name: **Andrea Dall'Asta**

Signature: 

Typed or CLEARLY Printed Name: **Giuseppe Rizzo**

Signature: 

Typed or CLEARLY Printed Name: **Bianca Masturzo**

Signature: 

Typed or CLEARLY Printed Name: **Elvira Di Pasquo**

Signature:

Typed or CLEARLY Printed Name: **Giovanni Battista Luca Schera**

Signature:

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Signature:

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Signature:

Typed or CLEARLY Printed Name: **Rossella Attini**

Signature:

Typed or CLEARLY Printed Name: **Guido Menato**

Signature:

Typed or CLEARLY Printed Name: **Tiziana Frusca**

Signature:

Typed or CLEARLY Printed Name: **Tullio Ghi**

Signature: ____________________

TITLE PAGE

Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study.

Authors:

Andrea Dall'Asta[1], Giuseppe Rizzo[2,3], Bianca Masturzo[4], Elvira Di Pasquo[1], Giovanni Battista Luca Schera[1], Giovanni Morganelli[1], Ruben Ramirez Zegarra[1], Pavjola Maqina[2], Ilenia Mappa[2], Giulia Parpinel[4], Rossella Attini[4], Enrica Roletti[1,4], Guido Menato[4], Tiziana Frusca[1], Tullio Ghi[1]

Institution:

[1]Department of Medicine and Surgery, Obstetrics and Gynecology Unit, University of Parma, Parma, Italy

[2]Division of Maternal and Fetal Medicine, Cristo Re Hospital, University of Rome Tor Vergata, Rome, Italy

[3]Department of Obstetrics and Gynecology, The First I.M. Sechenov Moscow State Medical University, Moscow, Russia

[4]Department of Obstetrics and Gynecology, Sant'Anna Hospital, University of Turin, Turin, Italy

Address for correspondence:

Prof Tullio Ghi, MD, PhD

Department of Medicine and Surgery, Obstetrics and Gynaecology Unit, University of Parma

Via Gramsci 14, 43126 Parma, Italy

Email: tullioghi@yahoo.com

Phone: +390521702434

Condensation:

The sonographic indicators of deflexed fetal head are associated with labor dystocia leading to caesarean delivery in women with protracted active phase of labor.

Short title:

Intrapartum US in protracted active phase of labor.

AJOG at a glance

A.Why was the study conducted?

- To evaluate the relationship between the intrapartum sonographic indicators of fetal head flexion and the mode of delivery in women with protracted active phase of labor.

B.What are the key findings?

- A wide occiput-spine angle and a narrow chin-chest angle are associated with an increased incidence of vaginal delivery. A correlation between the occiput-spine angle and the sonographic indicators of fetal head station was also demonstrated.

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

- The sonographic indicators of fetal head flexion are associated with labor dystocia leading to cesarean delivery in women with protracted active phase of labor. The findings from this study suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

Keywords

Ultrasound in labor, labor dystocia, intrapartum care, caesarean delivery, instrumental delivery, occiput-spine angle, chin-chest angle, angle of progression, head-perineum distance**.**

Abstract

Background

To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor.

Objective

To assess the relationship between the transabdominal sonographic indices of fetal head flexion and the mode of delivery in women with protracted active phase of labor.

Study design

Prospective evaluation of women with protracted active phase of labor recruited across three tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the evaluation of the fetal head position and flexion, which was measured by means of the occiput-spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-chest angle (CCA) in fetuses in OP position. The OSA and the CCA were compared between women who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention was performed solely based on suspected fetal distress were excluded.

Results

129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery, instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%) cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to those submitted to cesarean delivery due to labor dystocia (126.2±14.4 vs 114.5±23.6, $p<0.01$). At ROC curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), $p<0.01$, and the optimal OSA cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean delivery was 108.5 degrees. A narrower CCA was measured in cases who had vaginal delivery compared to those undergoing cesarean delivery (27.2±32.9 vs 56.2±27.7 degrees, $p<0.01$). The AUC

of the CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p<0.01$, and the optimal cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

Conclusions

In women with protracted active phase of labor, the sonographic demonstration of fetal head deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

Introduction

Labor dystocia is estimated to account for approximately one third of all caesarean deliveries, the vast majority being primary cesarean deliveries (1,2). Among these, arrest of dilatation in the first-stage of labor is acknowledged to represent the most common indication (3,4). Such condition may result from distinct but potentially coexisting mechanisms which include abnormalities of the uterine contractions, malpositions or malpresentations of the fetal head and cephalopelvic disproportion (5-13).

The progression of the first-stage of labor has been historically assessed by means of the norms of active phase dilatation described by Friedman (14-26) and more recently re-evaluated by Zhang et al. (1,27,28). These latter, which show a slow but progressive first-stage dilatation prior to 6 cm and an overall slower course of labor compared to Friedman's sigmoid curve (14-17,23,25,26), are currently endorsed for labor management by the American College of Obstetricians and Gynecologists and by the Society for Maternal and Fetal Medicine (4,29). The active phase dilatation is positively affected by the descent of the fetal head in the birth canal, and in normal labor a direct correlation between the first-stage dilatation and the descent of the fetal head has been demonstrated (30). The engagement and the progression of the fetal head through the birth canal in the first-stage of labor are known to be to be influenced by the mechanism of head flexion – which allow the shortest cephalic diameters to negotiate the maternal pelvis (5,6).

Available data suggests that ultrasound outweighs the digital examination in the assessment of the fetal head station (31,32), progression and attitude, and ultrasound is currently endorsed as an adjunct to the clinical evaluation in conditions of protracted active phase of labor and arrest of dilatation (31). Under these circumstances, the sonographic indicators of the fetal head station including the head-perineum distance (HPD) and the angle of progression (AoP) have been shown to be more accurate than the digital examination in predicting the occurrence of cesarean delivery

(33-35). In an unselected group of women in the active phase of labor with occiput anterior and occiput transverse fetuses the degree of fetal head flexion measured at transabdominal ultrasound has been shown to be associated with the digital station and the likelihood of operative delivery (36). Other sonographic studies have demonstrated that also in fetuses in occiput posterior (OP) position the qualitative assessment of the fetal head deflexion is related to the chance of vaginal delivery (37,38). To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor. The aim of this study was to evaluate the relationship between the intrapartum ultrasound indicators of malposition and malpresentation and the risk of obstetric intervention within a selected cohort of women diagnosed with a protracted active phase of labor.

Methods

Study design

This was a prospective, observational study conducted between December 2018 and June 2020 and including three maternity units in Italy (University Hospitals of Parma and Rome Tor Vergata and Sant'Anna Hospital of Turin). A non-consecutive series of non-anomalous singleton term pregnancies, with no history of previous uterine scar and with a protracted active phase of labor was included. According to the local protocol of the participating Units, women diagnosed with protracted active phase of labor are submitted to clinical examination by the senior Obstetrician responsible for the patient care. For the present study, following the clinical diagnosis of protracted active phase of labor intrapartum ultrasound was performed for research purposes also by five investigators with dedicated training on ultrasound in labor (AD, TG, EDP, BM and GR) who were not involved in the clinical management. The senior Obstetricians in charge for the labor care were blinded to the ultrasound findings.

According to the protocol for the labor management adopted across the participating Units, protracted active phase of labor was defined based on the ACOG/SMFM recommendations for the safe prevention of the primary cesarean delivery (4). In details, a protracted active phase of labor was defined in women ≥6 cm of dilatation with ruptured membranes who fail to progress despite 4 hours of adequate uterine activity or at least 6 hours of oxytocin administration with inadequate uterine activity and no first-stage dilatation. In such cases, the arrest of dilatation requiring cesarean delivery was defined following two more hours of oxytocin administration with no cervical change. In the case of progression of the first-stage dilatation, obstetric intervention was indicated during the first-stage in the event of the above criteria, while the diagnosis of arrest of labor in the second stage was made in the event of a duration of the active phase of at least two hours in multiparous women or three hours in nulliparous women, in accordance with the ACOG/SMFM

recommendations (4).With regards to instrumental vaginal delivery, the use of forceps is not performed as part of routine clinical practice in the participating Units. Obstetric intervention – i.e. cesarean delivery or vacuum extraction – due to suspected intrapartum fetal compromise represented an exclusion criterion for the study. All the obstetric interventions were performed according to a commonly shared management protocol when the criteria for arrest of dilatation or arrest of labor in the second stage were fulfilled (4).

Clinical data including maternal age, ethnicity, body mass index, gestational at delivery, induced or spontaneous labor, epidural analgesia, augmentation during labor, length of the first and of the second stage of labor, head station and cervical dilatation at diagnosis of protracted active phase of labor as well as mode of delivery, estimated blood loss, birthweight, 5 minutes APGAR and arterial pH was collected from patient case notes.

<u>Intrapartum ultrasound performed for research purposes</u>

Portable ultrasound devices equipped with low frequency transabdominal probe were used for the study purposes. The US measurements were performed on women lying in semirecumbent position with an empty bladder. Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position and the flexion of the fetal head. The position was defined from the landmarks depicting fetal occiput and described as a clock face with 12 hourly divisions. Positions >09:30 and <2:30 o'clock were classified as occiput anterior, while occiput transverse and occiput posterior (OP) were defined in the case of occiput ≥02.30 and ≤03.30 o'clock or ≥08.30 h and ≤09.30 o'clock and >03.30 and <08.30 o'clock, respectively (31,39).

Based on our experience no ultrasound parameter has the potential to objectively evaluate the degree of head flexion for all the positions of the fetal occiput. The flexion of the fetal head was quantitatively defined by means of the occiput-spine angle (OSA) for the fetuses in occiput anterior and occiput transverse position and by means of the chin-to-chest angle (CCA) for the fetuses in OP position. In details, the OSA was identified by the angle between a line tangent to the posterior cervical spine and a second line tangent to the fetal occiput, as previously described (36) (Figure 1). The CCA was defined as the angle identified by the intersection between one line tangent to one straight structure represented by the longest axis of the sternum and a second line tangent to another straight structure represented the skin covering the inferior boundary of the oral cavity up to the chin (Figure 2).

Transperineal ultrasound was performed with the transducer placed in a transverse or longitudinal position between the labia majora or more caudally at the level of the fourchette and allowed the measurement of the sonographic indicators of fetal head station and descent. The head-perineum distance (HPD) was assessed by placing the probe in the posterior fourchette and applying a gentle but firm pressure on the perineum as previously described (40). The angle of progression (AoP) was measured on the midsagittal image by drawing one line between calipers placed at the two points identifying the long axis of the pubic symphysis; a second caliper line was then created on the frozen image that extended from the most inferior portion of the pubic symphysis tangentially to the fetal skull contour (41). All the measurements were obtained in the absence of uterine contractions and/or maternal pushing efforts.

Endpoints

The primary outcome of the study was to evaluate the sonographic indicators of fetal head flexion, i.e. the OSA and the CCA in fetuses in non-OP and in OP position, respectively, as measured at diagnosis of protracted active phase of labor in relation to the mode of delivery and other labor outcomes. Furthermore, we evaluated the relationship between the OSA and the CCA and the transperineal sonographic indicators of fetal head descent.

Ethics approval

Ethics approval for this study was granted by the local Ethics Committee at the University Hospitals of Parma (N 270/2018/OSS/UNIPR on 03/12/2018) and Rome Tor Vergata (N 17/Ob2 on 15/10/2017) and at the Sant'Anna Hospital of Turin (N 0061542 on 21/06/2017).

Statistical analysis

Statistical analysis was performed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Normal or abnormal distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov and the Shapiro-Wilk tests and data were shown as mean ± standard deviation or as median (range) accordingly. Comparison of normally and non-normally distributed continuous variables included the T test for independent sample and 2-tailed t test and the Mann-Whitney U-test, respectively. Categorical variables were reported as number (percentage) and compared using the Chi-square or Fisher exact test. Logistic regression analysis was used to control for potential confounding variables, while the prediction of the mode of delivery by intrapartum sonographic parameters was determined by receiver operating characteristic (ROC) curve analysis. $p < 0.05$ was considered as significant. This study was conducted following the STROBE guidelines (42).

Results

Overall, 129 women were included (Figure 3). The transabdominal and transperineal ultrasound examination was successfully performed in all the eligible cases. Baseline and obstetrical features of our cohort population are shown in Table 1. Spontaneous vaginal delivery occurred in 66 (51.2%) women, while instrumental vaginal delivery and cesarean delivery were recorded in 17 (13.1%) and 46 (35.7%), cases, respectively. The mean length of the first and second stage of labor was 495 ± 171 minutes and 107 ± 52 minutes, respectively. No case of failed instrumental delivery requiring emergency cesarean delivery was recorded. At diagnosis of protracted active phase of labor occiput anterior, occiput transverse and OP positions accounted for 59 (45.8%), 27 (20.9%) and 43 (33.3%) of the included cases.

Clinical and sonographic findings in fetuses in non-occiput posterior position are shown in Table 2a. A wider OSA (126.2±14.4 vs 114.5±23.6 degrees, p=0.006) and AoP (117.5±12.7 vs 104.0±10.7 degrees, p<0.001) and a shorter HPD (39.7±5.2 vs 49.0±9.4 mm, p<0.001) were measured in women who had vaginal delivery, however only the OSA and the HPD proved to be independently associated with the mode of delivery at logistic regression analysis (p=0.007 and p=0.001, respectively)(Table 3a). At ROC curve the OSA was found to be associated with an area-under-the-curve (AUC) of 0.675, 95%CI (0.538-0.812), p<0.01. The optimal cut-off value of the OSA discriminating between cases of VD vs those delivered by CS was 108.5 degrees, and was associated with a 56.7% sensitivity, 87.5% specificity, 70.8% PPV and 79.0% NPV. When addressing the correlation between the OSA and the sonographic indicators of fetal head station, the OSA showed a direct correlation with the AoP (Pearson's correlation 0.449, p<0.01) but no correlation with the HPD (p=0.15). At visual analysis of the scatter/dot charts (Figure 4), 9 cases in which the AoP of progression was not positively correlated with the OSA were noted and labelled as outliers. Such cases showing a narrow AoP and a wide OSA were all submitted to cesarean delivery and characterized by a lower maternal height

(157±7 vs 163±6 cm, p<0.01) and a higher ratio between the birthweight and the maternal height (22.6±1.6 vs 20.7±2.6, p=0.04) compared to the non-outlier cases. An inverse correlation between the OSA and the HPD (Pearson’s correlation -0.566, p<0.01) and a stronger correlation between the OSA and the AoP (Pearson’s correlation 0.693, p<0.01) were demonstrated following the removal of the 9 outliers from the non-OP dataset. Furthermore, following the removal of the 9 outlier cases a OSA width >108.5 degrees showed 80.9% sensitivity, 87.5% specificity, 70.8% PPV and 92.5% NPV for the mode of delivery and an overall 7.5% rate of cesarean delivery.

The clinical and the sonographic findings in fetuses in OP position are shown in Table 2b. A narrower CCA (27.2±32.9 vs 56.2±27.7 degrees, p=0.005) and a lower rate of induction of labor (22.2% vs 62.5%, p=0.008) were found in women who had vaginal delivery. At logistic regression analysis CCA and labor induction proved to be independently associated with the mode of delivery (p=0.008 and p=0.007, respectively, Table 3b). At ROC curve the CCA was associated with an area-under-the-curve (AUC) for the mode of delivery of 0.758, 95%CI (0.612-0.904), p<0.01. The optimal cut-off value of the CCA discriminating between cases of VD vs those delivered by CS was 33.0 degrees, which was associated with a 93.8% sensitivity, 63.0% specificity, 60.0% PPV and 94.4% NPV. No correlation was found between the CCA and the AoP (p=0.48) nor the HPD (p=0.98).

Discussion

Principal findings

The results from this study conducted on a selected cohort of women with protracted active phase of labor demonstrate that the degree of flexion of the fetal head as measured at transabdominal ultrasound is related to the mode of delivery in OP as well as in non-OP fetuses, being head deflexion associated with an increased risk of cesarean delivery due to labor dystocia. Furthermore, fetal head station as measured at transperineal ultrasound by means of the HPD is independently associated with the likelihood of vaginal delivery in non-OP fetuses. Finally, in non-OP fetuses the degree of fetal head flexion correlates with the transperineal sonographic indicators of fetal head station.

Results in the context of what is known

The relationship of fetal head to spine – also referred to as “fetal attitude” – in the first-stage of labor has traditionally been considered to impact on fetal head descent and ultimately on labor outcome. Deflexed cephalic presentations are acknowledged to represent major determinants of obstructed labor (7,8,36). According to the mechanics of the human labor the descent of the presenting part through the birth canal is associated with a progressive flexion of the fetal head on the chest (5). On this basis, previous data from an unselected population of non-OP fetuses suggested that cephalic malpresentations in terms of deflexed fetal head are associated with a higher clinical station and an increased likelihood of obstetric intervention secondary to intrapartum dystocia (36). Consistently, a recent research conducted on 200 women found an increased incidence of cesarean delivery in fetuses showing sonographic features of head deflexion (43). In this study the degree of fetal head flexion was measured by means of the OSA in non-OP fetuses, while in OP fetuses a qualitative assessment of the fetal attitude was performed. However, this research did not include cases of labor dystocia, and the participating women were recruited at full cervical dilatation and not during the first-stage of labor (43).

Some studies previously evaluated the risk of obstetric intervention secondary to labor dystocia in relation to the position and the station of the fetal head at diagnosis of protracted active phase of labor (33-35,44-47). Under these circumstances, an increased likelihood of cesarean delivery due to labor dystocia was reported in fetuses with OP position and a high fetal station at transperineal ultrasound as demonstrated by a long HPD and a narrow AoP. Our study has confirmed a similar relationship between the sonographic indicators of fetal head station and the mode of delivery in fetuses in non-OP position but not in those in OP position, among whom labor induction proved to be independently associated with the likelihood of cesarean delivery.

Clinical implications

According to the recommendations of the International Society on Ultrasound in Obstetrics and Gynecology, intrapartum ultrasound is indicated in conditions of first-stage dystocia (31). Based on the findings from this study, the evaluation of the degree of flexion of the fetal head might be incorporated in the sonographic evaluation of cases of protracted active phase of labor. However, it is uncertain whether in such conditions the use of ultrasound can lead to an individualized management in terms of increased augmentation in the case of favorable conditions in terms of good head flexion and, conversely, anticipated caesarean delivery in the case of malpresentation with or without malposition of the presenting part.

Research implications

Based on our results, we believe that also subtle degrees of deflexion of the fetal head may preclude its descent through the birth canal by impairing the most favorable (suboccipito-bregmatic) diameter of the fetal head to negotiate the pelvic inlet, thus leading to dystocia requiring cesarean delivery (5,6).

Furthermore, this present study suggests that our ability in understanding the underlying cause of protracted active phase of labor may be improved thanks to the use of ultrasound. The finding of

outlier cases requiring cesarean delivery due to labor dystocia and characterized by a high head station (as witnessed by the narrow AoP and the long HPD) and no evidence of malposition and malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic disproportion. This hypothesis is supported by the fact that such cases were characterized by a lower maternal height and by a higher birthweight-to-maternal height ratio in comparison to “non-outliers”. We do envisage that in these conditions any attempt to perform an instrumental vaginal delivery should be balanced against the risks of “true” obstructed labor. However, more research is required in order to clarify whether the head circumference (48,49), the maternal height (50-53) or other sonographic indices may be considered in the individualized management of the laboring woman diagnosed with protracted active phase of labor in cases characterized by non-OP position, wide OSA, narrow AoP and long HPD.

With regards to the degree of flexion of the fetal head in OP fetuses, ours is the first study describing a quantitative parameter – i.e. the CCA – for the assessment of the degree of flexion of the fetal head, which we show to be associated with a fair sensitivity and NPV in the prediction of CS due to labor dystocia. The low specificity and positive predictive value of the CCA suggest that the degree of flexion of the fetal head may vary across labor and may not represent the only determinant of labor arrest in OP fetuses.

While we first describe the CCA as a sonographic indicator of flexion in OP fetuses, no correlation could be demonstrated between the CCA and the AoP nor the HPD. This is likely to be dependent on the different – and thus far unexplored – mechanics of the fetal head descent in OP compared to the non-OP fetuses.

Strengths and limitations

This is the first study evaluating the sonographic indices of fetal head flexion which can be measured on transabdominal ultrasound in women with protracted active phase of labor. Another strength is

that this study was prospectively conducted at three Units with dedicated expertise in intrapartum ultrasound, which has allowed the collection of several ultrasound parameters within a selected population of women at risk of cesarean delivery due to protracted active phase of labor.

With regards to the limitations, we acknowledge that our cohort was not powered for adverse maternal and perinatal outcomes. Therefore, more research is warranted in order to understand whether the deflexion of the fetal head in conditions of protracted active phase of labor impacts on maternal and fetal outcomes other than on the mode of delivery. Another limitation is represented by the fact that the measurement of the CCA may be challenging, and its intra- and inter-observer reproducibility was not preliminary tested. Therefore, it is uncertain whether the use of such sonographic parameter can be easily implemented outside the context of Units with expertise on ultrasound in labor such as those participating to this present study. Additionally, we acknowledge that complex malpresentations such as asynclitism, among whom some are known to impact on the labor outcome regardless of the additional sonographic parameters (54-60), were not evaluated.

Conclusions

In conclusion, this work shows that within a selected cohort of women with protracted active phase of labor, the evaluation of the sonographic indices of fetal head flexion is associated with the incidence of labor dystocia leading to cesarean delivery in OP as well as in non-OP fetuses, while the head station is related to the mode of delivery in non-OP but not in OP fetuses. This research supports the sonographic assessment of the degree of flexion of the presenting part in conditions of protracted active phase of labor, and suggest that intrapartum ultrasound may contribute in the categorization of the etiology of the dystocia and support the individualized management of conditions of protracted active phase of labor.

Conflict of interest statement

The Authors state no financial disclosures nor conflict of interest related to the content of this research.

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TITLE PAGE

Intrapartum sonographic assessment of the fetal head flexion in protracted active phase of labor and association with labor outcome: a multicentre, prospective study.

Authors:

Andrea Dall'Asta[1], Giuseppe Rizzo[2,3], Bianca Masturzo[4], Elvira Di Pasquo[1], Giovanni Battista Luca Schera[1], Giovanni Morganelli[1], Ruben Ramirez Zegarra[1], Pavjola Maqina[2], Ilenia Mappa[2], Giulia Parpinel[4], Rossella Attini[4], Enrica Roletti[1,4], Guido Menato[4], Tiziana Frusca[1], Tullio Ghi[1]

Institution:

[1]Department of Medicine and Surgery, Obstetrics and Gynecology Unit, University of Parma, Parma, Italy

[2]Division of Maternal and Fetal Medicine, Cristo Re Hospital, University of Rome Tor Vergata, Rome, Italy

[3]Department of Obstetrics and Gynecology, The First I.M. Sechenov Moscow State Medical University, Moscow, Russia

[4]Department of Obstetrics and Gynecology, Sant'Anna Hospital, University of Turin, Turin, Italy

Address for correspondence:

Prof Tullio Ghi, MD, PhD

Department of Medicine and Surgery, Obstetrics and Gynaecology Unit, University of Parma

Via Gramsci 14, 43126 Parma, Italy

Email: tullioghi@yahoo.com

Phone: +390521702434

Condensation:

The sonographic indicators of deflexed fetal head are associated with labor dystocia leading to caesarean delivery in women with protracted active phase of labor.

Short title:

Intrapartum US in protracted active phase of labor.

AJOG at a glance

A.Why was the study conducted?

- To evaluate the relationship between the intrapartum sonographic indicators of fetal head flexion and the mode of delivery in women with protracted active phase of labor.

B.What are the key findings?

- A wide occiput-spine angle and a narrow chin-chest angle are associated with an increased incidence of vaginal delivery. A correlation between the occiput-spine angle and the sonographic indicators of fetal head station was also demonstrated.

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

- The sonographic indicators of fetal head flexion are associated with labor dystocia leading to cesarean delivery in women with protracted active phase of labor. The findings from this study suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

Keywords

Ultrasound in labor, labor dystocia, intrapartum care, caesarean delivery, instrumental delivery, occiput-spine angle, chin-chest angle, angle of progression, head-perineum distance.

Abstract

Background

To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor.

Objective

To assess the relationship between the transabdominal sonographic indices of fetal head flexion and the mode of delivery in women with protracted active phase of labor.

Study design

Prospective evaluation of women with protracted active phase of labor recruited across three tertiary maternity units. Eligible cases were submitted to transabdominal ultrasound for the evaluation of the fetal head position and flexion, which was measured by means of the occiput-spine angle (OSA) in fetuses in non-occiput posterior (OP) position and by means of the chin-to-chest angle (CCA) in fetuses in OP position. The OSA and the CCA were compared between women who had vaginal delivery vs those who had cesarean delivery. Cases where obstetric intervention was performed solely based on suspected fetal distress were excluded.

Results

129 women were included, of whom 43 (33.3%) had OP position. Spontaneous vaginal delivery, instrumental delivery and cesarean delivery were recorded in 66 (51.2%), 17 (13.1%) and 46 (35.7%) cases, respectively. A wider OSA was measured in women who had vaginal delivery compared to those submitted to cesarean delivery due to labor dystocia (126±14 vs 115±24, p<0.01). At ROC curve the area-under-the-curve (AUC) was 0.675, 95%CI (0.538-0.812), p<0.01, and the optimal OSA cut-off value discriminating between cases of vaginal delivery vs those delivered by cesarean delivery was 109 degrees. A narrower CCA was measured in cases who had vaginal delivery compared to those undergoing cesarean delivery (27±33 vs 56±28 degrees, p<0.01). The AUC of the

CCA in relation to the mode of delivery was 0.758, 95%CI (0.612-0.904), $p<0.01$, and the optimal cut-off value discriminating between vaginal delivery and cesarean delivery was 33.0 degrees.

Conclusions

In women with protracted active phase of labor, the sonographic demonstration of fetal head deflexion in OP and in non-OP fetuses is associated with an increased incidence of cesarean delivery due to labor dystocia. Such findings suggest that intrapartum ultrasound may contribute in the categorization of the etiology of labor dystocia.

Introduction

Labor dystocia is estimated to account for approximately one third of all caesarean deliveries, the vast majority being primary cesarean deliveries (1,2). Among these, arrest of dilatation in the first-stage of labor is acknowledged to represent the most common indication (3,4). Such condition may result from distinct but potentially coexisting mechanisms which include abnormalities of the uterine contractions, malpositions or malpresentations of the fetal head and cephalopelvic disproportion (5-13).

The progression of the first-stage of labor has been historically assessed by means of the norms of active phase dilatation described by Friedman (14-26) and more recently re-evaluated by Zhang et al. (1,27,28). These latter, which show a slow but progressive first-stage dilatation prior to 6 cm and an overall slower course of labor compared to Friedman's sigmoid curve (14-17,23,25,26), are currently endorsed for labor management by the American College of Obstetricians and Gynecologists and by the Society for Maternal and Fetal Medicine (4,29). The active phase dilatation is positively affected by the descent of the fetal head in the birth canal, and in normal labor a direct correlation between the first-stage dilatation and the descent of the fetal head has been demonstrated (30). The engagement and the progression of the fetal head through the birth canal in the first-stage of labor are known to be to be influenced by the mechanism of head flexion – which allow the shortest cephalic diameters to negotiate the maternal pelvis (5,6).

Available data suggests that ultrasound outweighs the digital examination in the assessment of the fetal head station (31,32), progression and attitude, and ultrasound is currently endorsed as an adjunct to the clinical evaluation in conditions of protracted active phase of labor and arrest of dilatation (31). Under these circumstances, the sonographic indicators of the fetal head station including the head-perineum distance (HPD) and the angle of progression (AoP) have been shown to be more accurate than the digital examination in predicting the occurrence of cesarean delivery

(33-35). In an unselected group of women in the active phase of labor with occiput anterior and occiput transverse fetuses the degree of fetal head flexion measured at transabdominal ultrasound has been shown to be associated with the digital station and the likelihood of operative delivery (36). Other sonographic studies have demonstrated that also in fetuses in occiput posterior (OP) position the qualitative assessment of the fetal head deflexion is related to the chance of vaginal delivery (37,38). To date no research has focused on the sonographic quantification of the degree of flexion of the fetal head in relation to the labor outcome in women with protracted active phase of labor. The aim of this study was to evaluate the relationship between the intrapartum ultrasound indicators of malposition and malpresentation and the risk of obstetric intervention within a selected cohort of women diagnosed with a protracted active phase of labor.

Methods

Study design

This was a prospective, observational study conducted between December 2018 and June 2020 and including three maternity units in Italy (University Hospitals of Parma and Rome Tor Vergata and Sant'Anna Hospital of Turin). A non-consecutive series of non-anomalous singleton term pregnancies, with no history of previous uterine scar and with a protracted active phase of labor was included. According to the local protocol of the participating Units, women diagnosed with protracted active phase of labor are submitted to clinical examination by the senior Obstetrician responsible for the patient care. For the present study, following the clinical diagnosis of protracted active phase of labor intrapartum ultrasound was performed for research purposes also by five investigators with dedicated training on ultrasound in labor (AD, TG, EDP, BM and GR) who were not involved in the clinical management. The senior Obstetricians in charge for the labor care were blinded to the ultrasound findings.

According to the protocol for the labor management adopted across the participating Units, protracted active phase of labor was defined based on the ACOG/SMFM recommendations for the safe prevention of the primary cesarean delivery (4). In details, a protracted active phase of labor was defined in women $\geq$6 cm of dilatation with ruptured membranes who fail to progress despite 4 hours of adequate uterine activity or at least 6 hours of oxytocin administration with inadequate uterine activity and no first-stage dilatation. In such cases, the arrest of dilatation requiring cesarean delivery was defined following two more hours of oxytocin administration with no cervical change. In the case of progression of the first-stage dilatation, obstetric intervention was indicated during the first-stage in the event of the above criteria, while the diagnosis of arrest of labor in the second stage was made in the event of a duration of the active phase of at least two hours in multiparous women or three hours in nulliparous women, in accordance with the ACOG/SMFM

recommendations (4).With regards to instrumental vaginal delivery, the use of forceps is not performed as part of routine clinical practice in the participating Units. Obstetric intervention – i.e. cesarean delivery or vacuum extraction – due to suspected intrapartum fetal compromise represented an exclusion criterion for the study. All the obstetric interventions were performed according to a commonly shared management protocol when the criteria for arrest of dilatation or arrest of labor in the second stage were fulfilled (4).

Clinical data including maternal age, ethnicity, body mass index, gestational at delivery, induced or spontaneous labor, epidural analgesia, augmentation during labor, length of the first and of the second stage of labor, head station and cervical dilatation at diagnosis of protracted active phase of labor as well as mode of delivery, estimated blood loss, birthweight, 5 minutes APGAR and arterial pH was collected from patient case notes.

Intrapartum ultrasound performed for research purposes

Portable ultrasound devices equipped with low frequency transabdominal probe were used for the study purposes. The US measurements were performed on women lying in semirecumbent position with an empty bladder. Transabdominal US was performed by placing the probe transversely over the maternal suprapubic region to assess the position of the fetal head, while the flexion was evaluated by tilting the probe by 90 degrees to the longitudinal plane. The position was defined from the landmarks depicting fetal occiput and described as a clock face with 12 hourly divisions. Positions >09:30 and <2:30 o'clock were classified as occiput anterior, while occiput transverse and occiput posterior (OP) were defined in the case of occiput ≥02.30 and ≤03.30 o'clock or ≥08.30 h and ≤09.30 o'clock and >03.30 and <08.30 o'clock, respectively (31,39).

Based on our experience no ultrasound parameter has the potential to objectively evaluate the degree of head flexion for all the positions of the fetal occiput. The flexion of the fetal head was quantitatively defined by means of the occiput-spine angle (OSA) for the fetuses in occiput anterior and occiput transverse position and by means of the chin-to-chest angle (CCA) for the fetuses in OP position. In details, the OSA was identified by the angle between a line tangent to the posterior cervical spine and a second line tangent to the fetal occiput, as previously described (36) (Figure 1). The CCA was defined as the angle identified by the intersection between one line through the longest axis of the sternum and a second line through another straight structure represented by the skin covering the inferior boundary of the oral cavity up to the chin (Figure 2).

Transperineal ultrasound was performed with the transducer placed in a transverse or longitudinal position between the labia majora or more caudally at the level of the fourchette and allowed the measurement of the sonographic indicators of fetal head station and descent. The head-perineum distance (HPD) was assessed by placing the probe in the posterior fourchette and applying a gentle but firm pressure on the perineum as previously described (40). The angle of progression (AoP) was measured on the midsagittal image by drawing one line between calipers placed at the two points identifying the long axis of the pubic symphysis; a second caliper line was then created on the frozen image that extended from the most inferior portion of the pubic symphysis tangentially to the fetal skull contour (41). All the measurements were obtained in the absence of uterine contractions and/or maternal pushing efforts.

Endpoints

The primary outcome of the study was to evaluate the sonographic indicators of fetal head flexion, i.e. the OSA and the CCA in fetuses in non-OP and in OP position, respectively, as measured at diagnosis of protracted active phase of labor in relation to the mode of delivery and other labor outcomes. Furthermore, we evaluated the relationship between the OSA and the CCA and the transperineal sonographic indicators of fetal head descent.

Ethics approval

Ethics approval for this study was granted by the local Ethics Committee at the University Hospitals of Parma (N 270/2018/OSS/UNIPR on 03/12/2018) and Rome Tor Vergata (N 17/Ob2 on 15/10/2017) and at the Sant'Anna Hospital of Turin (N 0061542 on 21/06/2017).

Statistical analysis

Statistical analysis was performed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Normal or abnormal distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov and the Shapiro-Wilk tests and data were shown as mean ± standard deviation or as median (range) accordingly. Comparison of normally and non-normally distributed continuous variables included the T test for independent sample and 2-tailed t test and the Mann-Whitney U-test, respectively. Categorical variables were reported as number (percentage) and compared using the Chi-square or Fisher exact test. Logistic regression analysis was used to control for potential confounding variables, while the prediction of the mode of delivery by intrapartum sonographic parameters was determined by receiver operating characteristic (ROC) curve analysis. $p < 0.05$ was considered as significant. This study was conducted following the STROBE guidelines (42).

Results

Overall, 129 women were included (Figure 3). The transabdominal and transperineal ultrasound examination was successfully performed in all the eligible cases. Baseline and obstetrical features of our cohort population are shown in Table 1. Spontaneous vaginal delivery occurred in 66 (51.2%) women, while instrumental vaginal delivery and cesarean delivery were recorded in 17 (13.1%) and 46 (35.7%), cases, respectively. The mean length of the first and second stage of labor was 495 ± 171 minutes and 107 ± 52 minutes, respectively. No case of failed instrumental delivery requiring emergency cesarean delivery was recorded. At diagnosis of protracted active phase of labor occiput anterior, occiput transverse and OP positions accounted for 59 (45.8%), 27 (20.9%) and 43 (33.3%) of the included cases.

Clinical and sonographic findings in fetuses in non-occiput posterior position are shown in Table 2a. A wider OSA (126±14 vs 115±24 degrees, p=0.006) and AoP (118±13 vs 104±11 degrees, p<0.001) and a shorter HPD (40±5 vs 49±9 mm, p<0.001) were measured in women who had vaginal delivery, however only the OSA and the HPD proved to be independently associated with the mode of delivery at logistic regression analysis (p=0.007 and p=0.001, respectively) (Table 3a). At ROC curve the OSA was found to be associated with an area-under-the-curve (AUC) of 0.675, 95%CI (0.538-0.812), p<0.01. The optimal cut-off value of the OSA discriminating between cases of VD vs those delivered by CS was 109 degrees, and was associated with a 56.7% sensitivity, 87.5% specificity, 70.8% PPV and 79.0% NPV. When addressing the correlation between the OSA and the sonographic indicators of fetal head station, the OSA showed a direct correlation with the AoP (Pearson's correlation 0.449, p<0.01) but no correlation with the HPD (p=0.15). At visual analysis of the scatter/dot charts (Figure 4), 9 cases in which the AoP of progression was not positively correlated with the OSA were noted and labelled as outliers. Such cases showing a narrow AoP and a wide OSA were all submitted to cesarean delivery and characterized by a lower maternal height (157±7 vs

163±6 cm, p<0.01) and a higher ratio between the birthweight and the maternal height (22.6±1.6 vs 20.7±2.6, p=0.04) compared to the non-outlier cases.

When considering only the 62 non-OP fetuses with OSA width above 109 degrees – i.e. with favorable head flexion –, such outlier cases accounted for 9/13 cesarean deliveries. Outlier cases showed a higher ratio between the OSA and the AoP (1.45±0.19 vs 1.09±0.10, p<0.001) and a lower ratio between the OSA and the HPD (2.60±0.46 vs 3.40±0.50, p<0.001) compared to non-outliers. The distribution of the OSA/AoP ratio in relation to the mode of delivery showed a trend towards an increased rate of CS with increasing OSA/AoP ratio (Figure 5a), while a trend towards an increased rate of CS was noted with decreasing OSA/HPD ratio (Figure 5b). At ROC curve the OSA/AoP ratio was found to be associated with an AUC for the prediction of cesarean delivery of 0.769, 95%CI (0.586-0.952), p=0.003, while the OSA/HPD ratio was associated with an AUC of 0.778, 95%CI (0.631-0.925), p=0.002. The optimal cut-off value of the OSA/AoP ratio discriminating between cases of VD vs those delivered by CS was 1.20, and was associated with a 69.2% sensitivity, 87.8% specificity, 60.0% PPV and 91.5% NPV; the optimal cut-off value of the OSA/HPD ratio discriminating between cases of VD vs those delivered by CS was 3.05, and was associated with a 69.2% sensitivity, 77.6% specificity, 45.0% PPV and 90.5% NPV.

The clinical and the sonographic findings in fetuses in OP position are shown in Table 2b. A narrower CCA (27±33 vs 56±28 degrees, p=0.005) and a lower rate of induction of labor (22.2% vs 62.5%, p=0.008) were found in women who had vaginal delivery. At logistic regression analysis CCA and labor induction proved to be independently associated with the mode of delivery (p=0.008 and p=0.007, respectively, Table 3b). At ROC curve the CCA was associated with an area-under-the-curve (AUC) for the mode of delivery of 0.758, 95%CI (0.612-0.904), p<0.01. The optimal cut-off value of the CCA discriminating between cases of VD vs those delivered by CS was 33.0 degrees, which was associated with a 93.8% sensitivity, 63.0% specificity, 60.0% PPV and 94.4% NPV. No correlation was found between the CCA and the AoP (p=0.48) nor the HPD (p=0.98).

Discussion

Principal findings

The results from this study conducted on a selected cohort of women with protracted active phase of labor demonstrate that the degree of flexion of the fetal head as measured at transabdominal ultrasound is related to the mode of delivery in OP as well as in non-OP fetuses, being head deflexion associated with an increased risk of cesarean delivery due to labor dystocia. Furthermore, fetal head station as measured at transperineal ultrasound by means of the HPD is independently associated with the likelihood of vaginal delivery in non-OP fetuses. Finally, in non-OP fetuses the degree of fetal head flexion correlates with the transperineal sonographic indicators of fetal head station.

Results in the context of what is known

The relationship of fetal head to spine – also referred to as “fetal attitude” – in the first-stage of labor has traditionally been considered to impact on fetal head descent and ultimately on labor outcome. Deflexed cephalic presentations are acknowledged to represent major determinants of obstructed labor (7,8,36). According to the mechanics of the human labor the descent of the presenting part through the birth canal is associated with a progressive flexion of the fetal head on the chest (5). On this basis, previous data from an unselected population of non-OP fetuses suggested that cephalic malpresentations in terms of deflexed fetal head are associated with a higher clinical station and an increased likelihood of obstetric intervention secondary to intrapartum dystocia (36). Consistently, a recent research conducted on 200 women found an increased incidence of cesarean delivery in fetuses showing sonographic features of head deflexion (43). In this study the degree of fetal head flexion was measured by means of the OSA in non-OP fetuses, while in OP fetuses a qualitative assessment of the fetal attitude was performed. However, this research did not include cases of labor dystocia, and the participating women were recruited at full cervical dilatation and not during the first-stage of labor (43).

Some studies previously evaluated the risk of obstetric intervention secondary to labor dystocia in relation to the position and the station of the fetal head at diagnosis of protracted active phase of labor (33-35,44-47). Under these circumstances, an increased likelihood of cesarean delivery due to labor dystocia was reported in fetuses with OP position and a high fetal station at transperineal ultrasound as demonstrated by a long HPD and a narrow AoP. Our study has confirmed a similar relationship between the sonographic indicators of fetal head station and the mode of delivery in fetuses in non-OP position but not in those in OP position, among whom labor induction proved to be independently associated with the likelihood of cesarean delivery.

Clinical implications

According to the recommendations of the International Society on Ultrasound in Obstetrics and Gynecology, intrapartum ultrasound is indicated in conditions of first-stage dystocia (31). Based on the findings from this study, the evaluation of the degree of flexion of the fetal head might be incorporated in the sonographic evaluation of cases of protracted active phase of labor. However, it is uncertain whether in such conditions the use of ultrasound can lead to an individualized management in terms of increased augmentation in the case of favorable conditions in terms of good head flexion and, conversely, anticipated caesarean delivery in the case of malpresentation with or without malposition of the presenting part.

Research implications

Based on our results, we believe that also subtle degrees of deflexion of the fetal head may preclude its descent through the birth canal by impairing the most favorable (suboccipito-bregmatic) diameter of the fetal head to negotiate the pelvic inlet, thus leading to dystocia requiring cesarean delivery (5,6).

Furthermore, this present study suggests that our ability in understanding the underlying cause of protracted active phase of labor may be improved thanks to the use of ultrasound. The finding of

outlier cases requiring cesarean delivery due to labor dystocia and characterized by a high head station (as witnessed by the narrow AoP and the long HPD) and no evidence of malposition and malpresentation (i.e. non-OP position and wide OSA) may be interpreted in terms of cephalo-pelvic disproportion. This hypothesis is supported by the fact that such cases were characterized by a lower maternal height and by a higher birthweight-to-maternal height ratio in comparison to "non-outliers". We do envisage that in these conditions any attempt to perform an instrumental vaginal delivery should be balanced against the risks of "true" obstructed labor. However, more research is required in order to clarify whether the head circumference (48,49), the maternal height (50-53) or other sonographic indices may be considered in the individualized management of the laboring woman diagnosed with protracted active phase of labor in cases characterized by non-OP position, wide OSA, narrow AoP and long HPD.

With regards to the degree of flexion of the fetal head in OP fetuses, ours is the first study describing a quantitative parameter – i.e. the CCA – for the assessment of the degree of flexion of the fetal head, which we show to be associated with a fair sensitivity and NPV in the prediction of CS due to labor dystocia. The low specificity and positive predictive value of the CCA suggest that the degree of flexion of the fetal head may vary across labor and may not represent the only determinant of labor arrest in OP fetuses.

While we first describe the CCA as a sonographic indicator of flexion in OP fetuses, no correlation could be demonstrated between the CCA and the AoP nor the HPD. This is likely to be dependent on the different – and thus far unexplored – mechanics of the fetal head descent in OP compared to the non-OP fetuses.

Strengths and limitations

This is the first study evaluating the sonographic indices of fetal head flexion which can be measured on transabdominal ultrasound in women with protracted active phase of labor. Another strength is

that this study was prospectively conducted at three Units with dedicated expertise in intrapartum ultrasound, which has allowed the collection of several ultrasound parameters within a selected population of women at risk of cesarean delivery due to protracted active phase of labor.

With regards to the limitations, we acknowledge that our cohort was not powered for adverse maternal and perinatal outcomes. Therefore, more research is warranted in order to understand whether the deflexion of the fetal head in conditions of protracted active phase of labor impacts on maternal and fetal outcomes other than on the mode of delivery. Another limitation is represented by the fact that the measurement of the CCA may be challenging, and its intra- and inter-observer reproducibility was not preliminary tested. However, it is important to note that all the research scans were performed by a small number of investigators with expertise on ultrasound in labor, therefore we believe that in such context a variability in the CCA measurements is highly unlikely. Therefore, it is uncertain whether the use of such sonographic parameter can be easily implemented outside the context of Units with expertise on ultrasound in labor such as those participating to this present study. We acknowledge that additional malpresentations such as asynclitism, which are known to impact the labor course (54-60), were not evaluated in this study. Such limitation needs to be taken into account in a clinical context where different types of malpresentation may coexist and contribute in determining a protracted active phase of labor.

Finally, the “non-consecutive” enrolment may be accounted as a potential source of bias, even though we believe that the wide number of the enrolled patients together with the strict inclusion criteria allow to overcome such potential limitation.

Conclusions

In conclusion, this work shows that within a selected cohort of women with protracted active phase of labor, the evaluation of the sonographic indices of fetal head flexion is associated with the incidence of labor dystocia leading to cesarean delivery in OP as well as in non-OP fetuses, while the head station is related to the mode of delivery in non-OP but not in OP fetuses. This research supports the sonographic assessment of the degree of flexion of the presenting part in conditions of protracted active phase of labor, and suggest that intrapartum ultrasound may contribute in the categorization of the etiology of the dystocia and support the individualized management of conditions of protracted active phase of labor.

Conflict of interest statement

The Authors state no financial disclosures nor conflict of interest related to the content of this research.

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