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Article

The Impact of Bloody Amniotic Fluid on Delivery and Early Neonatal Outcomes

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Abstract: Information on the effect of bloody amniotic fluid during labor at term is scarce. This study assessed risk factors and obstetrical outcomes in labors complicated by bloody amniotic fluid. All nulliparas with singleton pregnancy, who underwent a trial of labor ≥ 37 weeks of gestation, in a single tertiary center, over six years were included. Obstetrical, delivery and neonatal outcomes were compared between deliveries with bloody amniotic fluid or clear amniotic fluid. Overall, 11,252 women were included. Among them, 364 (3.2%) had bloody amniotic fluid and 10,888 (96.7%) had clear amniotic fluid. Women with bloody amniotic fluid were characterized by shorter duration of the second stage of labor and higher rate of cesarean delivery due to non-reassuring fetal heart rate. The rates of cord pH < 7.1 and NICU admissions were also higher. In multivariate logistic regression analysis, cesarean delivery, cord blood pH < 7.1 and NICU admission were independently associated with increased odds ratio for bloody amniotic fluid. Bloody amniotic fluid at term is associated with adverse outcomes and must be considered during labor.

Keywords: bloody amniotic fluid; placental abruption; adverse maternal outcomes; adverse neonatal outcomes

1. Introduction

The color of the amniotic fluid during labor varies and may range from clear, meconium-stained, yellow to bloody, which can indicate different clinical situations, and accordingly may be associated with adverse outcomes. Bloody amniotic fluid (BAF) during labor can be a sign of placental abruption [1–5].

Placental abruption refers to the premature detachment of the placenta from its attachment in the uterus prior to the birth of a fetus. In addition to BAF, other clinical findings of placental abruption include abdominal pain, uterine tenderness, uterine contractions and non-reassuring fetal heart rate (NRFHR) [6,7]. The incidence of placental abruption during labor varies depending on the population studied and is estimated to occur in about 1% of all pregnancies [8–10]. Risk factors for placental abruption include advanced maternal age, hypertensive disorders including chronic hypertension, preeclampsia and gestational hypertension, smoking, previous placental abruptions, trauma and multiple gestations [11–13]. Its management depends on the severity of the abruption, maternal and fetal conditions and the gestational age [14–17].

BAF should be differentiated from blood-stained mucus during labor. The latter is a normal and expected sign of cervical dilatation and labor progression. It is usually clear or streaked with pink or red blood and is caused by breakage of maternal blood vessels in the cervix [18]. This mucus plug may be passed when the cervix begins to dilate. BAF, on the other hand, is usually colored by bright red blood [19,20]. Only a few studies investigated the association between BAF and pregnancy outcomes. Gluck et al. [4] examined the effect of BAF during labor among 317 deliveries. There were higher rates of labor induction, instrumental deliveries and cesarean deliveries comparing to deliveries with clear amniotic fluid. However, BAF was not associated with a difference in neonatal outcomes or in the composite adverse neonatal outcome. Neonatal morbidity is a commonly used

indicator of the quality of maternity care and neonatal wellbeing, particularly where data is restored objectively in a computerized system [5]. Using a composite outcome of neonates should include morbidity that is associated with long term sequela such as, respiratory morbidity, assisted ventilation, hypoglycemia, admission to the NICU, hyperbilirubinemia, cerebral hemorrhage, and convulsions.

Due to the lack of data regarding BAF during labor, the present study examined risk factors for BAF and its effects on maternal and neonatal outcomes including parameters that were not evaluated in previous work [4].

2. Materials and Methods

This retrospective study included all nulliparas singleton deliveries that underwent trial of labor at ≥ 37 weeks gestation, in a single tertiary center, from January 2014 to October 2020.

Exclusion criteria were deliveries with meconium amniotic fluid, multiple pregnancies, or intrauterine fetal demise.

The study cohort was divided to deliveries with BAF during labor (BAF group) and to deliveries with clear amniotic fluid (control group). BAF was determined by the obstetrician and was documented in the delivery report.

2.1. Data collection

Data were retrieved from the electronic medical records of the women and the neonates. Maternal baseline characteristics included maternal age, gestational age at delivery and BMI (kg/m^2). The risks factors that were assessed include diagnosis of diabetes mellitus (DM), pre-gestational DM (PGDM) or gestational DM (GDM), which was based on either a one-step or two-step approach. The one-step approach was consisted of an oral glucose tolerance test with a 75-gram glucose overload that measures plasma glucose concentration at fasting state, 1 hour, and 2 hours after glucose administration. A positive result was defined as 1 blood glucose value above the target value at each interval, (fasting - 92, 1 hour- 180, 2-hours 153 mg/dl). The twostep approach consisted of a screening, non-fasting oral 50-gram glucose load, with blood glucose measurement at 1 hour later. A positive result is defined as a blood glucose value of 140 mg/dl or higher. A positive screening test was followed by a diagnostic test that consisted of a 100-gram oral glucose load with glucose measurements at fasting and 1, 2, and 3 hours after glucose administration. A positive test was defined when higher blood glucose of the target values (95,180 155,140 mg/dl, respectively) was observed, smoking at least ≥ 10 cigarettes per day for more than a year, hypertensive disorders (chronic hypertension, gestational hypertension, or preeclampsia). Labor and delivery characteristics included labor induction, use of epidural, duration of the second stage, instrumental delivery, cesarean delivery (CD), CD due to NRFHR, nuchal cord and true knot.

Maternal and neonatal outcomes included retained placenta, maternal blood transfusion, neonatal birthweight as was recorded in the labor ward, , rate of small for gestational age ((SGA) defined as birthweight $< 10^{\text{th}}$ percentile according to local growth charts) [21], 5-minute Apgar score as was given by the senior pediatrician who attend the delivery, cord pH, phototherapy treatment as indicated by a pre-established nomograms, neonatal intensive care unit (NICU) admission indicated by anticipation of neonatal complications, neonatal hypoglycemia defined by a serum glucose level $< 40 \text{ mg}\%$, respiratory distress with mechanical ventilation indicated by oxygen requirements and blood gases results, cerebral hemorrhage diagnosed by an ultrasound and interpreted by a pediatric radiologist, and convulsions recorded either by an Electroencephalogram (EEG) or Cerebral Functional Monitoring (CFM).

According to departmental protocol, in all deliveries with BAF, a pediatrician performs an initial assessment of the neonate in the delivery room. Complications that indicated NICU admission included, respiratory distress defined either by tachypnea ≥ 60 breaths per minute or dyspnea defined as using accessory muscles during breathing, apnea episode defined as cessation of breath that leads to hypotonia, bradycardia, desaturation below 80% or unresponsiveness to tactile stimulus.

2.2. Statistical analysis

The statistical analyses were conducted utilizing SPSS-28 software (IBM Corp., Armonk, NY, USA). Nominal data were described as numbers and percentages. Continuous variables were described using means and standard deviations. Metric variables were analyzed with t-test. Chi-squared was used to analyze discrete variables. Data were considered statistically significant when the P-value was <0.05. Multivariable logistic regression model was applied for BAF and adjusted for maternal age, BMI, nulliparity, week of gestational age, epidural anesthesia, HTN/preeclampsia, and induction of labor.

3. Results

During the study period, 11,252 nulliparous with a singleton fetus delivered in our institution and met the inclusion criteria. Among them 364 (3.2%) women had BAF, and 10,888 (96.7%) women had clear amniotic fluid.

3.1. Demographic characteristics

Maternal characteristics of the study groups are presented in Table 1. The BAF group was characterized by older maternal age (29.4 ± 5.1 years vs. 28.3 ± 5.0 years, $p < 0.001$). There were no differences between groups in gestational age at delivery, maternal BMI > 30, DM, smoking, or hypertensive disorders.

Table 1. Baseline characteristics.

Characteristic	Amniotic fluid		P-value
	Bloody (n = 364)	Clear (n = 10,888)	
Maternal age (years \pm SD)	29.36 ± 5.05	28.32 ± 5.03	<0.001
Gestational age (weeks + days \pm SD)	$39+1 \pm 1$	$39+1 \pm 1$	0.905
BMI > 30 (kg/m ²) (n, %)	15 (4.1)	653 (6.0)	0.114
Diabetes (n, %)	33 (9.1)	1,162 (10.7)	0.328
Smoking (n, %)	16 (4.4)	517, 4.7	0.756
Hypertension / Preeclampsia (n, %)	20 (5.5)	448 (4.1)	0.193
Male fetus (n, %)	193 (53.0)	5,475 (50.3)	0.303

Data are presented as n (%) or mean \pm SD or median (range). BMI,- body mass index; Diabetes includes pre-gestational and gestational diabetes.

3.2. Labor and delivery characteristics

Labor and delivery characteristics of the study groups are presented in Table 2. As compared to the clear amniotic fluid group the BAF group was characterized by shorter duration of the second stage of labor (114 ± 74 minutes vs. 103 ± 69 minutes, $p = 0.009$, respectively). No difference was found in the CD rate between the study groups (53 (14.6%) in the BAF vs. 1389 (12.7%) in the clear amniotic fluid group). However, it was found that the rate of CD due to NRFHR was higher with BAF (37 (10.2%) vs. 768, (7%), respectively, $p = 0.023$). There was no difference between groups in the rate of labor induction, using of epidural anesthesia, intrapartum fever, instrumental deliveries, nuchal cord or true knot in the umbilical cord.

Table 2. Labor and delivery characteristics.

Characteristic	Amniotic fluid		P-value
	Bloody (n = 364)	Clear (n = 10,888)	
Labor induction, n (%)	120 (32.9)	3,379 (31.0)	0.284
Epidural, n (%)	295 (81.0)	8,840 (81.2)	0.947
Second stage duration, min \pm SD	103 ± 69	114 ± 74	0.009
Intrapartum fever, n (%)	22 (6.0)	600 (5.5)	0.661

Instrumental delivery, n (%)	60 (16.5)	1,981 (18.2)	0.405
Cesarean delivery, n (%)	53 (14.6)	1389 (12.7)	0.311
Cesarean delivery due to NRFHR, n (%)	37 (10.2)	768 (7.0)	0.023
Nuchal cord, n (%)	75 (20.6)	2,597 (23.8)	0.225
True knot, n (%)	1 (0.2)	81 (0.7)	0.313

Data are presented as n (%) or mean \pm SD or median (range). CD, cesarean delivery; NRFHR, non-reassuring fetal heart rate.

3.3. Maternal and neonatal outcomes

Maternal and neonatal outcomes are presented in Table 3. There were higher rates of cord pH < 7.1 (4.4% vs. 1.5%, $p < 0.001$) and NICU admissions (2.2% vs. 0.9%, $p = 0.012$) among neonates in the BAF group as compared to the clear amniotic fluid group. Neonatal birthweights, as well as the rate of retained placenta, maternal blood transfusion, SGA, 5-minute Apgar score < 7, neonatal hypoglycemia, cerebral hemorrhage, neonatal convulsions, respiratory distress required mechanical ventilation and use of phototherapy, were all similar between the groups.

Table 3. Maternal and neonatal outcomes.

Outcome	Amniotic fluid		P-value
	Bloody (n = 364)	Clear (n = 10,888)	
Retained placenta, n (%)	20 (5.5)	468 (4.3)	0.27
Maternal blood transfusion, n (%)	7 (1.9)	181 (1.7)	0.702
Neonatal birthweight, g \pm SD	3186 \pm 411	3190 \pm 417	0.844
Small for gestational age, n (%)	43 (11.8)	1,210 (11.1)	0.676
5-minute Apgar < 7, n (%)	3 (0.8)	46 (0.4)	0.252
pH < 7.1, n (%)	16 (4.4)	166 (1.5)	<0.001
Phototherapy, n (%)	17 (4.7)	575 (5.3)	0.504
NICU admission, n (%)	8 (2.2)	98 (0.9)	0.012
Neonatal hypoglycemia, n (%)	2 (5.5)	67 (6.1)	0.826
Respiratory distress with mechanical ventilation, n (%)	2 (0.55)	48 (0.44)	0.805
Cerebral hemorrhage, n (%)	0	2 (0.01)	0.791
Convulsions, n (%)	0	4 (0.03)	0.708

Data are presented as n (%) or mean \pm SD or median (range). SGA, small for gestational age; NICU, neonatal intensive care unit.

3.4. Multivariable logistic regression

To characterize independently variables that are associated with BAF, we used multivariate analysis adjusted for maternal age, week of gestational age, BMI, diabetes, hypertension/preeclampsia, induction of labor and epidural anesthesia. It was found that BAF was independently associated with CD due to NRFHR, blood cord pH < 7.1 and NICU admission (Table 4).

Table 4. Multivariate analysis model for adverse outcomes associated with bloody amniotic fluid.

Variable	OR	95% Confidence interval		P-value
		Lower	Upper	
Cesarean delivery due to NRFHR	1.643	1.046	2.582	0.031
pH < 7.1	2.502	1.19	5.262	0.016
NICU admission	3.176	1.335	7.555	0.009

Multivariable logistic regression model was applied for bloody amniotic fluid and adjusted for maternal age, week of gestational age, BMI, diabetes, hypertension /preeclampsia, induction of labor and epidural anesthesia.

4. Discussion

The current study assessed risk factors and perinatal outcomes of deliveries complicated with BAF at term. We found that BAF was associated with older maternal age and shorter duration of the second stage of labor. Additionally, CD due to NRFHR, cord pH ≤ 7.1 and NICU admissions were independently associated with BAF during labor.

Although vaginal bleeding and contractions are the classical clinical features of placental abruption, the few studies that examined the association between BAF at term and adverse outcomes reported inconclusive results. Based on previous studies, it has been found that parity and advanced maternal age were found as risk factors for placental abruption [20,22,23]. These studies included nulliparous and parous women with different gestational ages. In the current study, only nulliparas were included, and it was found that advanced maternal age is a risk factor for BAF.

In contrast to earlier studies [24–26], the current research failed to find any correlation between smoking and high blood pressure to BAF. Inconclusive results were found in studies that included only placental abruption at term [4,20]. However, it cannot be ruled out that the results in those studies might differ with a larger sample size.

According to the results of the present study, the duration of the second stage of labor was significantly shorter in cases of BAF compared to those with clear amniotic fluid. A possible mechanism for this phenomenon is related to the activity of thrombin. Thrombin has been shown to induce myometrial contractions [27,28]. In cases of placental abruption early in pregnancy, this may cause preterm labor [29,30]. Similarly, placental abruption at term during labor might shorten the second stage of labor, due to thrombin-induced uterine contractions. As few studies have addressed this point, further research is needed to assess the duration of the second stage of labor in the presence of BAF.

The results of the current research support those of previous studies which reported that BAF increases the likelihood of CD in cases where NRFHR is diagnosed [10,20]. Neonatal birth weight was not different between deliveries complicated with BAF at term to those who had clear amniotic fluid. In addition, the incidence of small for gestational age infants was similar between the study groups, indicating that BAF is an event that usually is not associated with long term changes in fetal blood supply and hence the birth weight is similar. Although rate of cord pH < 7.1 was higher in deliveries complicated with BAF at term, this did not result in higher neonatal complications such as respiratory distress syndrome or hypoglycemia as was described by other studies [4,10]. Neonatal hypoglycemia was not different between BAF deliveries and normal amniotic fluid deliveries, and the incidence was around 5% of deliveries. Asymptomatic early neonatal hypoglycemia can be diagnosed after birth but the long term neurodevelopmental outcome varied with other morbidities [22]. Hypoglycemia is the most common metabolic disturbance occurring in the neonatal period. Screening at-risk infants and the management of low blood glucose levels in the first hours to days of life is a frequent issue in the care of the newborn infant. Yet, a clear definition of neonatal hypoglycemia is lacking. Current screening guidelines and management algorithms are based on limited evidence, relying more on expert opinion to guide recommendations. In cases of BAF our local policy is to test neonatal glucose levels at 2 hours of age when hypoglycemia is most anticipated [3]. The results of this study do not support measuring glucose levels after BAF deliveries. The higher NICU admission in our study as compared to previous study [4] might be a result of a local policy of admitting deliveries complicated with BAF for observation even without neonatal complications or increased morbidity. Another explanation may be related to the relatively large sample size in the current study. pH < 7.1 was significantly higher in deliveries complicated with BAF at term, however of note is the 5-minute Apgar score which was not different between BAF and clear amniotic fluid deliveries (table 30). The Apgar score as a proven useful tool for rapid assessment of the neonate, however it is often poorly correlated with other indicators of intrapartum neonatal well-being. Apgar at 5 minutes is a measure that is commonly used to identify infants with poor birth outcomes, however it was found to be is a poor descriptor of neonatal morbidity [26]. Combination of Apgar score and umbilical cord pH measurement in high-risk pregnant mother could better detect jeopardized baby. Therefore, our study results indicating a cord pH ≤ 7.1 to be independently

associated with BAF during labor but not 5- minutes Apgar score, should be evaluated in further studies.

Limitations of this study stem from its retrospective design. In addition, placental pathology was not available. Another limitation could be that the indication for NICU admission was not prospectively design and although these indication stated in the method section were clear, it might be that some clinicians were not following them very strictly.

Despite its limitations, the study had several strengths, including the relatively large cohort and the same management protocol in a single medical center. Furthermore, the detailed neonatal complications evaluated in this study are well documented by a computerized data recording.

5. Conclusions

BAF at term seems to be a marker for placental abruption and a bad prognosis. It was found to be a significant risk factor for adverse outcomes including higher rates of CS due to NRFHR, fetal cord pH ≤ 7.1 and NICU admissions. Given that these outcomes were found to be independently associated with BAF, a finding of BAF must be given substantial weight in the labor management decision-making process. Future research is needed regarding managing labor in case of BAF.

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References

1. Mitchell, S.; Chandrachan, E. Meconium-stained amniotic fluid. *Obstetrics, Gynaecology & Reproductive Medicine* **2018**, *28*, 120–124, doi:10.1016/j.ogrm.2018.02.004.
2. Addisu, D.; Asres, A.; Gedefaw, G.; Asmer, S. Prevalence of meconium stained amniotic fluid and its associated factors among women who gave birth at term in Felege Hiwot comprehensive specialized *BMC pregnancy and childbirth* **2018**.
3. Bandyopadhyay, T.; Bhatia, B. D.; Khanna, H. D. A study of oxidative stress in neonates delivered through meconium-stained amniotic fluid. *Eur. J. Pediatr.* **2017**, *176*, 317–325, doi:10.1007/s00431-016-2845-0.
4. Gluck, O.; Kovo, M.; Tairy, D.; Barda, G.; Bar, J.; Weiner, E. Bloody amniotic fluid during labor - Prevalence, and association with placental abruption, neonatal morbidity, and adverse pregnancy outcomes. *Eur. J. Obstet. Gynecol. Reprod. Biol.* **2019**, *234*, 103–107, doi:10.1016/j.ejogrb.2019.01.011.
5. Tikkanen, M. Placental abruption: epidemiology, risk factors and consequences. *Acta Obstet. Gynecol. Scand.* **2011**, *90*, 140–149, doi:10.1111/j.1600-0412.2010.01030.x.
6. Mei, Y.; Lina, Y. Clinical significance of primary symptoms in women with placental abruption. *J. Matern. Fetal Neonatal Med.* **2017**, *31*, 1–4, doi:10.1080/14767058.2017.1344830.
7. Oyelese, Y.; Ananth, C. V. Placental abruption. *Obstet. Gynecol.* **2006**, *108*, 1005–1016, doi:10.1097/01.AOG.0000239439.04364.9a.
8. Mæland, K. S.; Morken, N. H.; Schytt, E. Placental abruption in immigrant women in Norway: A population-based study. *Acta Obstetrica et ...* **2021**.
9. Lueth, A.; Blue, N.; Silver, R. M.; Allshouse, A.; Hoffman, M.; Grobman, W. A.; Simhan, H. N.; Reddy, U.; Haas, D. M. Prospective evaluation of placental abruption in nulliparous women. *J. Matern. Fetal Neonatal Med.* **2021**, 1–8, doi:10.1080/14767058.2021.1989405.
10. Pariente, G.; Wiznitzer, A.; Sergienko, R.; Mazor, M.; Holcberg, G.; Sheiner, E. Placental abruption: critical analysis of risk factors and perinatal outcomes. *J. Matern. Fetal Neonatal Med.* **2011**, *24*, 698–702, doi:10.3109/14767058.2010.511346.

11. Bellos, I.; Pergialiotis, V.; Papapanagiotou, A. Comparative efficacy and safety of oral antihypertensive agents in pregnant women with chronic hypertension: a network metaanalysis. *American Journal of ...* **2020**.
12. Shobeiri, F.; Masoumi, S. Z.; Jenabi, E. The association between maternal smoking and placenta abruption: a meta-analysis. *J. Matern. Fetal Neonatal Med.* **2017**, *30*, 1963–1967, doi:10.1080/14767058.2016.1235694.
13. Eubanks, A. A.; Walz, S.; Thiel, L. M. Maternal risk factors and neonatal outcomes in placental abruption among patients with Equal Access to health care. *J. Matern. Fetal Neonatal Med.* **2019**, 1–171, doi:10.1080/14767058.2019.1657088.
14. Ananth, C. V.; Lavery, J. A.; Vintzileos, A. M.; Skupski, D. W.; Varner, M.; Saade, G.; Biggio, J.; Williams, M. A.; Wapner, R. J.; Wright, J. D. Severe placental abruption: clinical definition and associations with maternal complications. *Am. J. Obstet. Gynecol.* **2016**, *214*, 272.e1–9, doi:10.1016/j.ajog.2015.09.069.
15. Ananth, C. V.; Vintzileos, A. M. Maternal-fetal conditions necessitating a medical intervention resulting in preterm birth. *Am. J. Obstet. Gynecol.* **2006**, *195*, 1557–1563, doi:10.1016/j.ajog.2006.05.021.
16. American College of Obstetricians and Gynecologists' Committee on Obstetric Practice, Society for Maternal-Fetal Medicine Medically Indicated Late-Preterm and Early-Term Deliveries: ACOG Committee Opinion, Number 831. *Obstet. Gynecol.* **2021**, *138*, e35–e39, doi:10.1097/AOG.0000000000004447.
17. Liabsuetrakul, T.; Meher, S.; WHO Intrapartum Care Algorithms Working Group Intrapartum care algorithms for liquor abnormalities: oligohydramnios, meconium, blood and purulent discharge. *BJOG* **2022**, doi:10.1111/1471-0528.16728.
18. Kouides, P. A. An update on the management of bleeding disorders during pregnancy. *Curr Opin Hematol* **2015**, doi:10.1097/MOH.0000000000000167.
19. Becher, N.; Adams Waldorf, K.; Hein, M.; Uldbjerg, N. The cervical mucus plug: structured review of the literature. *Acta Obstet. Gynecol. Scand.* **2009**, *88*, 502–513, doi:10.1080/00016340902852898.
20. Sheiner, E.; Shoham-Vardi, I.; Hallak, M.; Hadar, A.; Gortzak-Uzan, L.; Katz, M.; Mazor, M. Placental abruption in term pregnancies: clinical significance and obstetric risk factors. *J. Matern. Fetal Neonatal Med.* **2003**, *13*, 45–49, doi:10.1080/jmf.13.1.45.49.
21. Dollberg, S.; Haklai, Z.; Mimouni, F. B.; Gorfein, I.; Gordon, E.-S. Birth weight standards in the live-born population in Israel. *Isr Med Assoc J* **2005**, *7*, 311–314.
22. Sheiner, E.; Shoham-Vardi, I.; Hadar, A.; Hallak, M.; Hackmon, R.; Mazor, M. Incidence, obstetric risk factors and pregnancy outcome of preterm placental abruption: a retrospective analysis. *J. Matern. Fetal Neonatal Med.* **2002**, *11*, 34–39, doi:10.1080/jmf.11.1.34.39.
23. Brandt, J. S.; Ananth, C. V. Placental abruption at near-term and term gestations: pathophysiology, epidemiology, diagnosis, and management. *Am. J. Obstet. Gynecol.* **2023**.
24. Brandt, J. S.; Ananth, C. V. Placental abruption at near-term and term gestations: pathophysiology, epidemiology, diagnosis, and management. *Am. J. Obstet. Gynecol.* **2023**.
25. Anderson, E.; Raja, E. A.; Shetty, A.; Gissler, M.; Gatt, M.; Bhattacharya, S.; Bhattacharya, S. Changing risk factors for placental abruption: A case crossover study using routinely collected data from Finland, Malta and Aberdeen. *PLoS One* **2020**, *15*, e0233641, doi:10.1371/journal.pone.0233641.
26. Goldbart, A.; Pariente, G.; Sheiner, E.; Wainstock, T. Identifying risk factors for placental abruption in subsequent pregnancy without a history of placental abruption. *Int. J. Gynaecol. Obstet.* **2022**, doi:10.1002/ijgo.14446.
27. Buhimschi, C. S.; Schatz, F.; Krikun, G.; Buhimschi, I. A.; Lockwood, C. J. Novel insights into molecular mechanisms of abruption-induced preterm birth. *Expert Rev Mol Med* **2010**, *12*, e35, doi:10.1017/S1462399410001675.
28. Lockwood, C. J.; Kayisli, U. A.; Stocco, C.; Murk, W.; Vatandaslar, E.; Buchwalder, L. F.; Schatz, F. Abruption-induced preterm delivery is associated with thrombin-mediated functional progesterone withdrawal in decidual cells. *Am. J. Pathol.* **2012**, *181*, 2138–2148, doi:10.1016/j.ajpath.2012.08.036.
29. Rosen, T.; Kuczynski, E.; O'Neill, L. M. Plasma levels of thrombin-antithrombin complexes predict preterm premature rupture of the fetal membranes. *Journal of Maternal ...* **2001**.
30. Bączkowska, M.; Zgliczyńska, M.; Faryna, J.; Przytuła, E.; Nowakowski, B.; Ciebia, M. Molecular Changes on Maternal-Fetal Interface in Placental Abruption-A Systematic Review. *Int. J. Mol. Sci.* **2021**, *22*, doi:10.3390/ijms22126612.

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