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Bloody amniotic fluid during labor – Prevalence, and association with placental abruption, neonatal morbidity, and adverse pregnancy outcomes☆

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ABSTRACT

Objective: To study the association between bloody amniotic fluid (BAF) during labor and adverse pregnancy outcomes.

Study design: In the last 10 years we have implemented an institutional protocol that mandates obstetricians/midwives to report their subjective impression of the color of amniotic fluid (clear, meconium stained, bloody) during labor. The medical records, and neonatal charts of all singleton deliveries $\geq 37^{0/7}$ weeks between 2008–2018 were reviewed. The cohort was divided into two groups: clear AF (Clear group) and BAF (BAF group). Cases with meconium stained AF were excluded. The primary outcome was a composite of the following complications: umbilical Ph $\leq$ 7.1, seizures, hypoxic-ischemic encephalopathy, intra-ventricular hemorrhage, periventricular leukomalacia, hypoglycemia, hypothermia, mechanical ventilation, meconium aspiration syndrome, RDS, NEC, phototherapy, sepsis, or transfusion.

Results: Overall, 21,300 deliveries were reviewed, 20,983 (98.5%) in the Clear group and 317 (1.5%) in the BAF group. The rate of the primary outcome did not differ between the BAF (2.2%) and the Clear (2.1%) groups. The rate of placental abruption (both clinically and hystopathologically) did not differ between the groups (3.2% vs. 1.9% and 1.6% vs. 0.6%, respectively). BAF was associated with higher rates of labor induction (p = 0.002), assisted vaginal deliveries (p = 0.04), cesarean deliveries (p = 0.03), and lower birth weights (p = 0.03).

Conclusion: BAF observed in labor was not associated with composite adverse neonatal outcome, nor with placental abruption. BAF was associated with higher rates of labor induction, assisted vaginal deliveries, cesarean deliveries, and lower birth weights. These findings may assist obstetricians and neonatologists in the interpretation of BAF observed in labor.

Introduction

Placental abruption has traditionally been defined as the complete or partial separation of the placenta prior to delivery [1] with an estimated incidence of 0.4–1% of all pregnancies [2–5] and is a major cause of maternal morbidity and perinatal mortality [2,3,6,7]. Classic symptoms of placental abruption are vaginal bleeding, abdominal pain, uterine contractions, and uterine tenderness [8].

Amniotic fluid described as "bloody" upon membrane rupture is a finding that is familiar to every obstetrician and has traditionally been thought to be a risk factor of placental abruption. However, the association between bloody amniotic fluid (BAF) and placental abruption and other adverse pregnancy outcomes has not been studied before.

Starting October 2008 we have implemented an institutional protocol that mandates obstetricians and midwives to report their subjective impression of the color of amniotic fluid (clear, meconium stained, bloody) during every delivery (both vaginal and cesarean). Prior to October 2008, the color of amniotic fluid was described occasionally (not routinely), according to the medical team's judgment.

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Therefore, ten years after the implementation of the protocol, we aimed to study the correlation between BAF (subjectively described during delivery) and various adverse pregnancy outcomes including neonatal morbidities and the clinical and histopathological diagnosis of placental abruption in a very large cohort from a single university hospital.

Methods

Study population

The medical records, delivery charts, and neonatal charts of all singleton deliveries ≥ 37 gestational weeks between October 2008 (the time at which we began mandating the documentation of amniotic fluid characteristics in all delivery reports) and July 2018 from a single university hospital were reviewed. We excluded all deliveries < 37 weeks, multiple pregnancies, terminations of pregnancy, intra uterine fetal deaths (IUFDs), pregnancies with a known major fetal malformation, cases with meconium stained amniotic fluid (as these cases were widely studied and in order to purely study the effect of BAF), and cases with missing data. The study was approved by our institutional ethical review board (decision number 0232-16-WOMC dated 28/11/2017).

Exposure

Maternal demographics, neonatal outcomes, and pregnancy complications were compared between deliveries in which BAF was documented during delivery ("BAF group") and deliveries in which the amniotic fluid was described as clear ("Clear group").

Data collection

The following characteristics were collected from the medical chart of each patient: maternal age, gravidity, parity, pre-pregnancy weight and height (from which the body mass index (BMI) was calculated), gestational diabetes mellitus (GDM), pre-gestational diabetes mellitus, chronic hypertension, preeclampsia, smoking, gestational age at delivery, pre-pregnancy diagnosis of thrombophilia (defined as any thrombophilia, inherited or acquired, that necessitated thrombo-prophylaxis) [9,10], drug abuse, oligohydramnios, polyhydramnios, epidural, and trials of labor after a previous cesarean delivery (TOLAC).

Gestational age was calculated based on the woman's first ultrasound examination in the pregnancy and last menstrual period [11]. A woman was considered to have diabetes mellitus if she had a diagnosis of type 1/type 2 in the medical record or gestational diabetes mellitus based on the National Diabetes Group criteria [12]. Chronic hypertension and preeclampsia were diagnosed according to the current American College of Obstetricians and Gynecologists criteria [13] which were fully adapted by our institution for hypertensive disorders diagnosis and management.

Oligohydramnios was defined as amniotic fluid index ≤ 5 cm and polyhydramnios as amniotic fluid index ≥ 24 cm [14].

Immediately after birth, all neonates were examined by pediatricians. Birth weight percentiles for gestational age were assigned using the updated local growth charts [15]. Small for gestational age (SGA) was defined as actual birth-weight ≤ 10th percentile for gestational age. The following data were collected from the neonatal records: cord blood pH, sepsis (positive blood or cerebrospinal fluid culture), need for blood transfusion, need for phototherapy, respiratory distress syndrome, meconium aspiration syndrome, need for mechanical ventilation or support, necrotizing enterocolitis, intraventricular hemorrhage (all grades), hypoxic ischemic encephalopathy, seizures, hypoglycemia (blood glucose <40 mg/dL), hypothermia, and death.

The following data regarding pregnancy outcome were collected from the chart of each patient: induction of labor, placental abruption, mode of delivery (vaginal, assisted vaginal, or cesarean including the indication for cesarean delivery), intrapartum fever, chorioamnionitis, revision of the uterine cavity, manual removal of the placenta, postpartum hemorrhage (that necessitated medical and/or surgical treatment), and postpartum blood transfusion.

Intrapartum fever was defined as elevated temperature 38.0 °C or greater during labor with no other signs of chorioamnionitis. Clinical chorioamnionitis was diagnosed in the presence of maternal fever (temperature 38.0 °C or greater) with no evidence of an extra uterine cause accompanied by at least two of the following: fetal tachycardia, maternal tachycardia, leukocytosis, uterine tenderness, or new onset of foul-smelling vaginal discharge [16].

The clinical diagnosis of placental abruption was made on clinical grounds in women experiencing a new onset of vaginal bleeding and frequent painful contractions or blood clot attached to the placenta at the time of delivery. On some occasions, the diagnosis was based on ultrasonographic evidence of retro placental hematoma.

The histopathological diagnosis of placental abruption was made by a single well-trained pathologist. As part of our departmental protocol, in every case of pregnancy complications placentas are sent for histopathological evaluation, along with background data of the case and clinical suspicion (the pathologist is not blinded to the presumed diagnosis). Placental pathology examinations were performed using our standard protocol according to the "Amsterdam" criteria [17], as previously reported by us [18,19]. Each placenta was fixed in formalin, and at least 5 samples were embedded in paraffin blocks for microscopic assessment. Placental hemorrhages (marginal, and retro-placental hematoma) were assessed as part of the maternal vascular malperfusion assessment.

Primary outcome

The primary outcome was a composite variable of neonatal morbidity, defined as any of the following: Umbilical Ph ≤ 7.1, seizures, hypoxic-ischemic encephalopathy, intra-ventricular hemorrhage, periventricular leukomalacia, hypoglycemia, hypothermia, mechanical ventilation, meconium aspiration syndrome, respiratory distress syndrome, necrotizing enterocolitis, phototherapy, sepsis, or transfusion.

Secondary outcome

Secondary outcomes were placental abruption, mode of delivery, and maternal morbidity, including: intrapartum fever, chorioamnionitis, revision of the uterine cavity, manual removal of the placenta, post-partum hemorrhage, and maternal bold transfusion.

Data analysis

Data analysis was performed utilizing SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA). Data were presented as follows: continuous variables are presented either as mean ± SD or as median and range, as appropriate. Categorical variables are presented as n (%). Continuous parameters were compared by the Student *t*-test and categorical variables by the chi [2] with Yates' correction test or the Fisher exact test, as appropriate. A statistically significant p value of $p < 0.05$ was defined.

Multivariate regression analysis models were used to identify the independent association of BAF and various adverse outcomes.

Results

A total of 30,215 deliveries occurred at our institution during the study period. After excluding cases of preterm deliveries, multiple pregnancies, intrauterine fetal demise (IUFD), terminations of pregnancy, known malformations, meconium stained amniotic fluid, and cases with missing data – 21,300 deliveries were analyzed: 20,983 (98.5%) in the "Clear group" and 317 (1.5%) in the "BAF group" (Fig. 1).

Maternal demographics of the two groups are presented and compared in Table 1. Patients in the BAF group were more likely to be nulliparous than patients in the Clear group (40.7% vs. 32.6%, respectively, $p < 0.001$). The two groups did not differ in terms of any other background demographics (including age, gestational age at delivery, BMI, diabetes, chronic hypertension, preeclampsia, smoking, thrombophilia, drug abuse, oligohydramnios, polyhydramnios, epidural use, and TOLAC).

Neonatal outcomes are presented in Table 2. The rate of the primary outcome (composite adverse neonatal outcome) did not differ between the BAF group and the Clear group (2.2% vs. 2.1%, $p = 0.5$). There was a statistically significant difference in terms of birth weight between the groups (3218 ± 456 g in the BAF group vs. 3276 ± 478 g in the Clear group, $p = 0.03$) and a higher rate of meconium aspiration syndrome in the BAF group compared to the Clear group (0.9% vs. 0.07%, $p < 0.001$). This association remained significant after controlling for GA at delivery, smoking, TOLAC, and mode of delivery (aOR = 7.8, 95% CI 3.3–24.0). All other neonatal outcomes did not differ between the groups.

Table 3 presents pregnancy outcomes of the study groups. Compared to the Clear group, there were higher rates of both assisted vaginal deliveries (6.9% vs. 4.5%, $p = 0.04$) and cesarean deliveries (21.5% vs. 16.6%, $p = 0.03$) in the BAF group. There was also a higher rate of inductions of labor in the BAF group (28.4% vs. 20.6%, $p < 0.01$) compared to the Clear group. Other pregnancy outcomes including both clinical and histopathological placental abruption, chorioamnionitis, and maternal blood transfusions did not differ between the groups. The sensitivity and positive predictive value for BAF and clinical placental abruption were very low (2.5% and 3.1% respectively) while the specificity and negative predictive value were, as expected, very high (98.5% and 98.1% respectively).

Discussion

The aim of this paper was to study the correlation between BAF (subjectively described during delivery) and various adverse pregnancy outcomes including neonatal morbidities and the clinical and histopathological diagnosis of placental abruption. Our main findings were: 1) BAF was subjectively described in about 1.5% of the term singleton deliveries studied. 2) BAF was not associated with our primary outcome of composite adverse neonatal outcome. 3) BAF was associated with a higher rate of both assisted vaginal and cesarean deliveries. 4) BAF was not associated with placental abruption (both clinically and by histopathological diagnosis).

BAF has been studied in the past mostly in the context of amniocentesis for genetic and other indications [20–22]. Data regarding the finding of BAF during labor are very sparse. Tikkanen et al. [8], described the clinical presentation of placental abruption in a study of 198 cases from Finland. Their study demonstrated BAF in 93 (47%) of the cases. Xu et al. [23], in a study of placental abruption from China described BAF as one of the factors that differs between cases of postnatally confirmed diagnosis vs. postnatally ruled out diagnosis of placental abruption. None of the previous studies aimed to use clear amniotic fluid during labor as controls, nor aimed to study the association of BAF with histopathological diagnosis of placental abruption. Importantly, none of the previous studies aimed to correlate BAF with adverse neonatal outcomes.

In the current study we did not demonstrate any association between BAF observed in labor and placental abruption diagnosed both on clinical and histopathological basis. We have demonstrated very low sensitivity and positive predictive value (2.5% and 3.1% respectively) for BAF and clinical placental abruption, though the specificity and negative predictive value were, as expected, very high (98.5% and 98.1% respectively). We hypothesize that the amniotic fluid is probably commonly stained during labor with blood from sources other than the placenta (probably from the cervix and from lacerations in the vagina and perineum) or is an indication for labor induction (in cases of ruptured membranes with the presence of BAF) which made the association with placental abruption (a rare event by itself) very weak. The association we have found between BAF and induction of labor (which involves mechanical or pharmacological cervical ripening) support this assumption.

In the current study we have also found no association between BAF and the primary outcome of composite adverse neonatal outcome (which was defined a priori), despite a clinically-insignificant lower birthweight in the BAF group. This is explained by the lack of association with placental abruption. We did find higher rates of meconium aspiration in the BAF group. Although

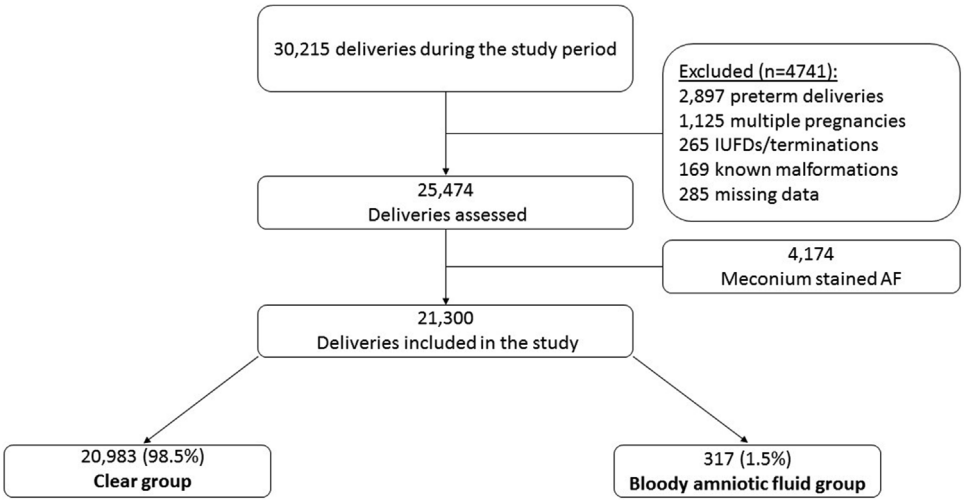

Fig. 1. xxx.

Table 1
Maternal demographics.

	Clear group (n = 20,983)	Bloody amniotic fluid group (n = 317)	*p* value
Maternal age (years)	29.8 ± 5.7	29.7 ± 5.4	0.8
Maternal age > 35 years (%)	3155 (15.2)	48 (15.1)	0.5
GA at delivery (weeks)	39.4 ± 1.3	39.5 ± 1.2	0.7
Gravidity	2.7 ± 1.6	2.6 ± 1.6	0.1
Parity	1.2 ± 1.2	1.1 ± 1.2	**0.02**
Nulliparity (%)	6770 (32.6)	129 (40.7)	<**0.01**
BMI (kg/m^2)	23.6 ± 3.6	23.5 ± 3.9	1.0
GDM/PGDM (%)	1516 (7.3)	20 (6.3)	0.3
Chronic hypertension (%)	163 (0.8)	4 (1.3)	0.2
Preeclampsia (%)	1365 (6.6)	22 (6.9)	0.4
Smoking (%)	2660 (12.9)	35 (11)	0.6
Thrombophilia (%)	420 (2.0)	11 (3.5)	0.1
Drug abuse (%)	133 (0.6)	4 (1.3)	0.2
Oligohydramnios (%)	66 (3.2)	10 (3.2)	1.0
Polyhydramnios (%)	54 (2.6)	2 (0.6)	0.2
Epidural (%)	14347 (69.2)	213 (67.2)	0.6
TOLAC (%)	819 (3.9)	12 (3.8)	1.0

Continuous variables are presented as mean ± SD and categorical variables as n (%). p-values in bold are statistically significant.
BMI – body mass index, GDM – gestational diabetes mellitus, PGDM - pregestational diabetes mellitus, TOLAC – trial of labor after a previous cesarean.

Table 2
Neonatal outcomes in the study groups.

	Clear group (n = 20,983)	Bloody amniotic fluid group (n = 317)	*p* value
Composite (primary outcome) (%)	438 (2.1)	7 (2.2)	0.5
Birthweight (gr)	3276 ± 478	3218 ± 456	**0.03**
SGA (%)	1845 (8.8)	30 (9.5)	0.75
Umbilical Ph ≤ 7.1 (%)	77 (0.4)	1 (0.3)	0.7
Seizures (%)	9 (0.04)	0 (0)	1.0
Hypoxic-ischemic encephalopathy (%)	4 (0.02)	0 (0)	1.0
Intra ventricular hemorrhage (%)	3 (0.01)	0 (0)	1.0
Periventricular leukomalacia (%)	0 (0)	0 (0)	1.0
Hypoglycemia (%)	130 (0.6)	2 (0.6)	1.0
Hypothermia (%)	3 (0.01)	0 (0)	1.0
Mechanical ventilation (%)	55 (0.3)	3 (0.9)	0.05
Meconium aspiration syndrome (%)	15 (0.07)	3 (0.9)	<**0.01** *
Respiratory distress syndrome (%)	6 (0.03)	0 (0)	1.0
Necrotizing enterocolitis (%)	2 (0.01)	0 (0)	1.0
Phototherapy (%)	172 (0.8)	1 (0.3)	0.5
Sepsis (%)	6 (0.03)	1 (0.3)	0.2
Transfusion (%)	19 (0.1)	1 (0.3)	0.3

All parameters are reports as n (%).
Values in bold represent statistical significance.
SGA – small for gestational age.
* This association remained after controlling for background confounders (aOR = 7.8, 95% CI 3.3–24.0).

Table 3
Selected pregnancy outcomes in the study groups.

	Clear group (n = 20,983)	Bloody amniotic fluid group (n = 317)	*p* value
Induction of labor (%)	4268 (20.6)	89 (28.4)	<**0.01**
Placental abruption (clinical) (%)	389 (1.9)	10 (3.2)	0.137
Placental abruption (histopathological) (%)	128 (0.6)	5 (1.6)	0.07
Cesarean delivery (%)	3441 (16.6)	68 (21.5)	**0.03**
Cesarean delivery due to NRFHRM (%)	929 (4.5)	12 (3.8)	0.7
Assisted vaginal delivery (%)	941 (4.5)	22 (6.9)	**0.04**
Intrapartum fever (%)	274 (1.3)	1 (0.3)	0.1
Chorioamnionitis (%)	90 (0.4)	1 (0.3)	1.0
Revision of the uterine cavity (%)	832 (4.0)	12 (3.8)	1.0
Manual removal of the placenta (%)	466 (2.2)	5 (1.6)	0.6
Post-partum hemorrhage (%)	1413 (6.8)	13 (4.1)	4.1
Maternal blood transfusion (%)	290 (1.4)	6 (1.9)	0.5

Parameters are reports as n (%) or mean ± SD.
Values in bold represent statistical significance.

cases of meconium stained amniotic fluid were excluded from the study, the possibility of new appearance of meconium stained amniotic fluid during labor, which was masked by the bloody color of amnion still exists. Yet, since the numbers are very small (3 cases in the BAF group) the clinical relevance of this association is probably not very important.

As expected, BAF was associated with a higher rate of assisted vaginal deliveries and cesarean deliveries compared to the Clear group. This is probably a manifestation of the common assumption that BAF is a sign of placental abruption which was not demonstrated in the current study. This is with accordance to the findings of similar rates of CD due to NRFHRM between the groups despite higher rate of CD in the BAF group. When recapitulating the findings of the recurrent study, we speculate that some of these interventions during labor probably represent an iatrogenic unnecessary burden.

The rates of post-partum hemorrhage and/ or maternal blood transfusion were similar between the groups, suggesting that although may indicate a non-placental source of bleeding, BAF is probably not associated with major bleeding.

Several strengths should be noted in the current study. First, according to our knowledge, this is the first attempt to study the association between BAF and adverse pregnancy outcomes. Second, the large cohort of over 30,000 deliveries from a single center over a 10 year period. Lastly, our ability to study separately the association of BAF with clinical and histopathological placental abruption.

Our study is not without limitations. First we are aware that the diagnosis of BAF was a subjective impression of the obstetrician or midwife during labor which was not defined or standardized prior to the study. Second, placental abruption itself is a clinical diagnosis which is somewhat arbitrary and also not well defined. Third, we have only collected short term neonatal outcomes. Lastly the use of a composite outcome may be viewed as a limitation of this study. However, we believe the use of a composite was necessary because the individual components of the composite are rare complications. We have described and validated the same composite neonatal outcomes in our previous publications with other pregnancy complications [19,24].

In conclusion, BAF observed in labor was not associated with composite adverse neonatal outcome, nor with placental abruption. BAF was associated with higher rates of labor induction, assisted vaginal deliveries, and cesarean deliveries, and slightly lower birth weights. These findings may suggest that though commonly considered as an "alert sign", BAF is not associated with poorer maternal or neonatal outcome. It may assist obstetricians and neonatologists in the interpretation of BAF observed in labor, and even prevent unnecessary interventions.

Conflict of interest

All authors report no conflict of interest.

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None.

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