The placenta in meconium staining: lesions and early neonatal outcome

H. G. Kaspar[1,2], *M.D.*; A. Abu-Musa[2], *M.D.*; A. Hannoun[2], *M.D.*; M. Seoud[2], *M.D.*; M. Shammas[2], *M.D.*; I. Usta[2], *M.D.*; A. Khalil[2], *M.D.*

Departments of Obstetrics and Gynecology[2] & Pathology and Laboratory Medicine[1]
American University of Beirut, Medical Center Beirut (Lebanon)

Summary

Purpose: To evaluate the immediate neonatal outcome and the presence of various placental lesions in 96 pregnancies with meconium-stained amniotic fluid.

Materials and methods: The patients were divided into a group with acute (N = 41) and subacute and chronic (N = 55) meconium staining of the placenta. Apgar scores, arterial cord pH and admission to the neonatal intensive care unit (NICU) were determined in addition to the findings on gross and microscopic examination of the placentas.

Results: Of the 53 live births with subacute and chronic meconium staining, 13% had Apgar Scores ≤ 7 at 5 minutes compared to 7% with acute meconium staining. Similarly, a significantly lower umbilical artery pH was determined in the former group [(32%) versus (7%)], ($p<0.01$). When 9 different pathologic lesions of the placenta were evaluated microscopically, the frequency of villous vascular thrombosis (25.4%), infarcts (38%), acute chorioamnionitis (20%), villous edema (9.1%) and villitis (14.5%) was significantly higher in the group with longer meconium exposure compared to the other group (2.4%), (9.7%), (7.3%), (0%), and 1 (2.4%), respectively. In addition, when tested for 4 different lesions, cases with acute meconium were less likely to have one or more lesions. When one or more placental lesions were found, NICU admission rate was significantly higher in the patients with subacute and chronic meconium.

Conclusion: Subacute and chronic meconium discharge is associated with significant placental lesions and an increased risk of adverse pregnancy outcome in the immediate neonatal period.

Key words: Placenta; Meconium; Placental vascular thrombosis; Chronic villitis; Infarcts; Chorangiosis; Spiral artery; Villous edema.

Introduction

The remarkable inconsistencies in the literature about the significance of meconium detected during labor and delivery in relation to fetal hypoxia and acidosis obviate the need for further insight into the placentas with meconium discharge. Several investigators portrayed meconium discharge as a sign of intrapartum asphyxia and/or cerebral palsy [1-7]. Nevertheless others believe that meconium is poorly associated with fetal acidosis, hypoxia, and distress [8-10]. Meconium toxicity and the resulting vascular damage were recognized only over the past decade [11-12]. Similarly, a significant association between vascular lesions in the placenta, especially the increasingly recognized thrombotic lesions, and adverse pregnancy outcome has recently been described [13-17]. However, to our knowledge, an association of meconium staining with placental lesions in relation to pregnancy outcome has not been previously evaluated. This study is an attempt to suggest a relationship between meconium discharge, its duration, and the presence of significant placental lesions that may underlie an adverse pregnancy outcome.

Revised manuscript accepted for publication September 6, 1999

Materials and Methods

Study population. The study group included 96 placentas with meconium staining from patients who delivered at the American University of Beirut Medical Center during the period extending between September 15, 1995 and October 30, 1997. Data were collected prospectively including the patient's age, parity, prenatal care, labor and delivery characteristics, birth weight, Apgar scores, cord pH, presence and consistency of meconium in the amniotic fluid, and neonatal intensive care unit (NICU) admission. Umbilical artery pH was not obtained in two fetuses with intrauterine fetal demise.

Placental examination. The placentas were examined in the fresh state and differentiation between various types of meconium staining of the fetal surface was made using characteristics of the membranes, chorionic plate and umbilical cord [18]. Placentas with acute meconium staining are defined as those having a blue-green, glistening surface, covered with light-green, slimy meconium. On the other hand, when the membranes are slippery, edematous and with dark discoloration, the placentas are grouped under subacute meconium staining. Chronic meconium staining is defined by the presence of a dull and diffuse, muddy umbilical cord, partially or completely stained.

All placentas were processed in the pathology laboratory. At least one section of umbilical cord and membranes and four sections of placental parenchyma including the chorionic plate and maternal surface were obtained. A single investigator with expertise in placental pathology reviewed hematoxylin and eosin (H&E) slides in a blinded fashion. The lesions were assigned to nine major categories including infarcts, chorangiosis,

stem villous and fetal artery thrombosis, hemorrhagic endovasculitis, chronic villitis of unknown etiology (CVU), spiral artery thrombosis, retroplacental hematoma with indentation, diffuse villous edema, and acute chorioamnionitis.

The diagnosis of infarction, chorangiosis, hemorrhagic endovasculitis and villous edema was based on the criteria described below. Diagnosis of placental infarction was made when there were numerous, large (> 2 cm in greatest dimension), more centrally located infarcts, confirmed by microscopic examination. When the infarcts were few, small, and located at the margin, this diagnosis was not made. Chorangiosis was strictly defined as the presence of 10 or more vascular channels, in 10 or more villi, in at least 3 different placental areas. Hemorrhagic endovasculitis was defined when obliteration of the villous capillaries, thrombosis, and variable degrees of extravasation of erythrocytes into the villous stroma occurred [20]. Diffuse villous edema was defined by large vacuoles in the villous stroma in at least 1% of all terminal villi [17].

Statistical analysis. The chi square test was used to compare the two groups with acute versus subacute and chronic meconium staining with respect to Apgar scores, umbilical artery pH, individual placental lesions, and number of placental lesions. The level of significance was set at ≤.1.

Results

All 96 pregnancies were between 36 and 41 weeks of gestation. The characteristics of patients with meconium stained amniotic fluid are presented in table 1. The two groups with acute, and subacute and chronic meconium staining were not significantly different with respect to age, parity, labor and mode of delivery. Two patients with acute meconium discharge had gestational diabetes, and none had insulin-dependent diabetes. Two pregnancies were complicated by pre-eclampsia. None of the patients was known hypertensive. Two pregnancies ended with intrauterine fetal demise (IUFD).

The amniotic fluid in 48 patients was subjectively described as "thin", 35 of whom had placentas with characteristics of acute meconium staining. Of the 55 patients with subacute and chronic meconium staining of the placenta, the amniotic fluid in only 42 patients was labeled as moderate-to-thick. The absence of meconium laden macrophages at the chorionic surface and membranes, which was demonstrated in all placentas with acute meconium staining, indicates meconium exposure of less than 2 to 3 hours. Meconium-laden macrophages were detected in the remaining placentas indicating meconium exposure for a longer period of time [21].

The frequency of fetuses with Apgar scores ≤ 7 and umbilical artery pH ≤ 7.2 is depicted in table 2. Low Apgar scores at 1 min were not significantly different between the two groups, however, 7 (13%) fetuses had Apgar scores < 7 at 5 min in the subacute and chronic meconium staining group compared to only 1 (2%) in the acute meconium staining group (p<.05). Similarly, lower umbilical artery was significantly more frequent in the group with longer meconium exposure [17 (32%)] compared to the other group [3 (7%),] (p<.01).

The frequency of 9 placental lesions is listed in table 3. Five lesions were significantly more encountered in the

Table 1. — *Characteristics of 96 pregnancies with meconium stained amniotic fluid.*

	Acute meconium staining	Subacute and chronic meconium staining	Total
Age			
16-20	7	3	10
21-30	24	35	59
31+	10	17	27
Parity			
Parous	20	26	46
Nulliparous	21	29	50
Labor			
Spontaneous	14	21	35
Oxytocin used	26	30	56
Not in labor	1	4	5
Delivery			
Vaginal	32	44	76
C-Section	9	11	20

*No statistical significance between either group with respect to all parameters.

Table 2. — *Frequency of subacute and chronic meconium staining in relation to Apgar scores and umbilical artery pH.*

	Acute meconium staining (N=41)	Subacute and chronic meconium staining (N = 53)*	p
Apgar scores ≤ 7			
1 min.	7 (17%)	10 (19%)	> .2
5 min.	1 (2%)	7 (13%)	< .05
Umbilical artery pH ≤ 7.2	3 (7%)	17 (32%)	< .01

* Umbilibal artery pH was not obtained in 2 fetuses with intrauterine fetal demise.

Table 3. — *The frequency of subacute and chronic meconium staining of the placenta in relation to significant placental lesions.*

	Acute meconium staining (N=41)	Subacute and chronic meconium staining (N=55)	p
Vascular thrombosis	1 (2.4%)	14 (25.4%)	< .01
Hemorrhagic endovasculitis	0	2 (3.6%)	> .1
Chorangiosis	1 (2.4%)	2 (3.6%)	> .1
Infarct of the placenta*	4 (9.7%)	21 (38%)	< .01
Acute chorioamnionitis	3 (7.3%)	11 (20%)	< .01
Spiral artery thrombosis	0	2 (3.6%)	> .1
Diffuse villous edema	0	5 (9.1%)	< .05
Retroplacental hematoma	1 (2.4%)	3 (5.4%)	> .1
Chronic villitis of unknown etiology	1 (2.4%)	8 (14.5%)	< .05

* Central and multiple infarcts (gross) with microscopic confirmation.

Table 4. — *Relationship between the number of 4 selected placental lesions and extent of meconium staining.*

Number of lesions*	Acute meconium staining (N=41)	Subacute and chronic meconium staining (N = 55)	p
0	33 (80%)	18 (33%)	< .001
1	4 (10%)	28 (51%)	<. 01
2	1 (3%)	7 (13%)	<. 05
3	0	2 (3%)	> .2
4	0	0	

* Features analyzed include infarcts, villous vascular thrombosis, villous edema and chronic villitis of unknown etiology (CVU).

Table 5. — *Relationship between the number of all placental lesions in meconium stained placentas and the number of admissions to the neonatal intensive care unit (NICU).*

	Admissions to NICU
Acute meconium staining (N=41)	5 (12.2%)[e]
No placental lesions (N=31)	3 (9.6%)[ac]
One or more placental lesions (N=10)	2 (20%)[ad]
Subacute and chronic meconium staining (N=53)	18 (34%)[e]
No placental lesions (N=19)	2 (10.5%)[bc]
One or more placental lesions (N=34)	16 (47%)[bd]

a: p<.05; b: p<.01; c; p>0.2; d: p<.01; e: p<.01.

group with subacute and chronic meconium as compared to acute meconium staining: 14 (25.4%) versus 1 (2.4%) for vascular thrombotic lesions, 21 (38%) versus 1 (2.4%) for infarcts, 11 (20%) versus 3 (7.3%) for acute chorioamnionitis, 5 (9.1%) versus 0 (0%) for diffuse villous edema, and 8 (14.5%) versus 1 (2.4%) for chronic villitis of unknown etiology. The frequency of the remaining 4 lesions including chorangiosis, hemorrhagic endovasculitis, spiral artery thrombosis and retroplacental hematoma with indentation was not statistically significant between the two groups.

When analyzed for 4 selected vascular lesions that included infarcts, villous edema, fetal vascular thrombosis, and chronic villitis of unknown etiology (table 4), there were no lesions in 33 (80%) placentas with acute meconium, which was significantly higher than the placentas with subacute and chronic meconium staining (p<.001). The latter group was also more likely to have one [28 (51%) versus 4 (10%)] or two [7 (13%) versus 1 (3%)] lesions (p<0.01). There were only 2 placentas with 3 lesions and none with 4 lesions.

Table 5 analyzes NICU admission of neonates in the two groups in relation to the presence or absence of placental lesions. Eighteen (34%) neonates with acute and chronic meconium staining were admitted to NICU compared to 5 (12.2%) neonates in the other group (p<0.01). In the subgroups with no placental lesions, the admission rate was not statistically significant (9.6 and 10.5% for the acute, and the subacute and chronic meconium staining respectively, p<.2). However, significantly more admissions [16 (14.7%)] were seen in the placentas with one or more lesions in the subacute and chronic group than those with acute meconium [2 (20%)], (p<.01). Similarly, the rate of admission was significantly higher when one or more lesions were encountered than when no lesions were encountered in each group: 16 (47%) versus 2 (10.5%), p<.01 for the subacute and chronic meconium, and 2 (20%) versus 3 (9.6%), p<.01 for the acute meconium group.

Discussion

Several reports support a traditional concept that meconium reflects fetal acidosis and hypoxia [1-7]. Our study concurs with these investigators as demonstrated by the finding of lower Apgar scores at 5 min, low umbilical artery pH and higher NICU admission rate in the group of subacute and chronic meconium staining as compared with that of acute meconium discharge. In contrast, other investigators did not find a correlation between meconium staining of the amniotic fluid and fetal hypoxia and acidosis [8-10, 22-24]. Meconium release is even portrayed as a normal response to vagal stimulation through umbilical cord occlusion, and consequently triggers gastrointestinal peristalsis [25]. Pathologic examination of the placenta was not available in all these reports.

In this study, vascular thrombotic events were frequent pathologic findings encountered in placentas with longer exposure to meconium. These may reflect a coexisting coagulopathy in the fetus or may be caused by inflammatory mediators released during a fetoplacental inflammatory response. A coexisting coagulopathy is usually supported by the presence of chorionic vascular thrombosis, while villous vascular thrombosis may be a consequence of circulating inflammatory mediators [13-17]. Our study did not differentiate between these two lesions, nor did it address the issue of inflammatory mediators. The significance of vascular thrombosis in the placenta in relation to adverse pregnancy outcome has been increasingly recognized [14-17, 26]. Whether these vascular lesions trigger meconium discharge or they are caused by it remains to be elucidated.

Non-marginal infarction of the placenta is portrayed among the features reflecting low uteroplacental blood flow [21]. This was the most frequent finding in placentas with longer exposure to meconium in our study. Other associated features of uteroplacental blood flow including diffuse villous edema and chronic villitis of unknown etiology were also significantly higher in this group compared to that with acute exposure. These associated lesions were not seen in all placentas with infarct. Although this study, in the authors' view, is the first to find a significantly increased frequency of lesions that reflect placental hypoperfusion in the group with longer exposure to meconium, a cause-effect relationship also remains open for further investigation.

In conclusion, this paper demonstrates an increased prevalence of significant placental lesions and an adverse immediate neonatal outcome with longer exposure to meconium.

References

[1] Gregory G. A., Gooding C. A., Phibbs R. H., Tolley W. H.: "Meconium aspiration in infants – a prospective study". *J. Pediatr.*, 1985, *85*, 848.

[2] Michell J., Schulman H., Fleischer A. *et al.*: "Meconium aspiration and fetal acidosis". *Obstet. Gynecol.*, 1985, *65*, 352.

[3] Starks G. C.: "Correlation of meconium-stained amniotic fluid during labor, early intrapartum fetal pH and Apgar scores as predictors of perinatal outcome". *Obstet. Gynecol.*, 1980, *65*, 352.

[4] Miller F. C., Sacks D. A.: "Significance of meconium during labor". *Am. J. Obstet. Gynecol.*, 1975, *122*, 573.

[5] Altshuler G., Herman A.: "A medicolegal imperative: placental pathology and epidemiology". In: Stevenson D. K., Sunshine P., eds. "Fetal and neonatal brain injury: mechanisms, management, and the risks of practice". Philadelphia, B. C. Decker, 1989, 250.

[6] Altshuler G., Arizawa M., Molnar-Nadasdy G.: "Meconium induced umbilical cord vascular necrosis and ulceration: a potential link between the placenta and bad pregnancy outcome". *Obstet. Gynecol.*, 1992, *79*, 1992.
[7] Spinillo A., Fazzi E., Capuzzo E., Stronati M., Piazzi G., Ferrari A.: "Meconium-stained amniotic fluid and risk for cerebral palsy in preterm infants". *Obstet. Gynecol.*, 1997, *90*, 519.
[8] Yeomans E. R., Gilstrap III L. C., Leveno K. J., Burris J. S.: "Meconium in amniotic fluid and fetal acid-base status". *Obstet. Gynecol.*, 1989, *48*, 175.
[9] Fenton A., Steer C.: "Fetal distress". *Am. J. Obstet. Gynecol.*, 1962, *83*, 354.
[10] Ramin S. M., Gilstrap III L. C., Leveno K. J., Dax J. S., Little B. B.: "Acid-base significance of meconium discovered prior to labor". *Am. J. Perinatol.*, 1993, *10* (2), 143.
[11] Altshuler G., Hyde S.: "Meconium-induced vasoconstriction: a potential cause of cerebral and other fetal hypoperfusion and of poor pregnancy outcome". *J. Child. Neurol.*, 1989, *4*, 137.
[12] Sepuldeva W. H., Gonzalez C., Cruz M. A., Rudolph M. I.: "Vasoconstrictive effect of bile acid on isolated human placental chorionic veins". *Eur. J. Obstet. Gynecol. Biol.*, 1991, *42*, 211.
[13] Rayne S. C., Kraus F. T.: "Placental thrombi and other vascular lesions: classification, morphology, and clinical correlations". *Path. Res. Pract.*, 1993, *189*, 2.
[14] Kraus F. T.: "Placental thrombi and related problems". *Semin. Diagn. Pathol.*, 1993, *10*, 275.
[15] Kraus F. T.: "Placenta: thrombosis of fetal stem vessel with fetal thrombotic vasculopathy and chronic villitis". *Pediatr. Pathol. Lab. Med.*, 1996, *16*, 143.
[16] Kraus F. T.: "Cerebral palsy and thrombi in placental vessels of the fetus: insights from litigation". *Hum. Pathol.*, 1997, *28*, 246.
[17] Redline R. W., Wilson-Costello D., Borawski E., Fanaroff A. A., Hack M. H.: "Placental lesions associated with neurologic impairment and cerebral palsy in very low-birthweight infants". *Arch. Pathol. Lab. Med.*, 1998, *122*, 1091.
[18] Bernirschke K., Kaufman P.: "Anatomy and pathology of the placental membranes". In: "Pathology of the Human Placenta". 3rd ed., New York, Springer Verlag, 1995, 268.
[19] Altshuler G.: "The placenta". In: "Surgical pathology of the Female Reproductive System and Peritoneum". Sternberg S., Mills S. E., eds. New York, Raven Press, 1991, 31.
[20] Sander C. H.: "Hemorrhagic endovasculitis and hemorrhagic villitis of the placenta". *Arch. Pathol. Lab. Med.*, 1980, *104*, 371.
[21] Altshuler A.: "Role of the placenta in perinatal pathology (revisited)". *Pediatr. Pathol. Lab. Med.*, 1996, *16*, 207.
[22] Fenton A., Steer C.: "Fetal distress". *Am. J. Obstet. Gynecol.*, 1962, *83*, 354.
[23] Leslie D. W.: "Antepartum meconium staining of the liquor amnii". *Br. J. Med. J.*, 1959, *2*, 612.
[24] Abramovici H., Brandes J. M., Fuchs K., Timor-Tritsch I.: "Meconium during delivery: a sign of compensated fetal distress". *Am. J. Obstet. Gynecol.*, 1974, *118*, 1974.
[25] Hon E. H., Bradfield A. H., Hess O. W.: "The electronic evaluation of the fetal heart rate. V. The vagal factor in fetal bradycardia". *Am. J. Obstet. Gynecol.*, 1961, *82*, 291.
[26] Redline R. W., Pappin A.: "Fetal thrombotic vasculopathy: the clinical significance of extensive avascular villi". *Hum. Pathol.*, 1995, *26*, 80.

Address reprint requests to:
HANNA KASPAR, M. D.
Departments of Obstetrics and Gynecology
American University of Beirut, Medical Center
P. O. Box 113-6044
Beirut (Lebanon)