Placental Abruption and Adverse Perinatal Outcomes

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ORIGINAL CONTRIBUTION

PLACENTAL ABRUPTION RESULTS from a cascade of pathophysiological processes ultimately leading to the separation of the placenta prior to delivery. Pregnancies complicated by abruption result in increased frequency of low birth weight, preterm delivery, stillbirth, and perinatal death. Attempts to understand this condition have focused on describing its etiology, with little attention directed toward evaluating its sequelae on outcomes of pregnancy. Even among studies that have reported associations between placental abruption and adverse perinatal outcomes, many have been based on unadjusted analysis without adequate control for the influences of potential confounding factors. Finally, the extent of placental detachment and its effect on adverse pregnancy outcomes and the dose-response gradients between the extent of placental separation and adverse pregnancy outcomes have not been examined.

The etiologies of low birth weight (<2500 g) are diverse and include early delivery (prematurity), fetal growth restriction, fetal intrinsic disorders (such as chromosomal disorders, genetic syndromes, or congenital infections), or a combination of these. Therefore, low birth weight, by itself, as an indication of fetal well-being is not helpful in trying to develop prevention strategies unless the various causal pathways that ultimately lead to this outcome are evaluated separately.

We designed this retrospective cohort study to address 2 objectives. First, to delineate the components of low birth weight, preterm delivery, and fetal growth restriction associated with abruption. The second objective was to evaluate the association between extent of placental separation and stillbirth and early delivery.

METHODS
This study was approved by the institutional review board, and was based on women who were delivered of a singleton birth at Mount Sinai Hospital, New York City, NY, between January 1986 and December 1996. Approximately two thirds of women who give birth at Mount Sinai Hospital are private patients, while the remaining third seek care through the clinic service. A
majority of private patients are from greater New York City, while most of the clinic patients come from neighboring Harlem and the South Bronx. Approximately 50% of the women who give birth at Mount Sinai Hospital are white (non-Hispanic), 25% are Hispanic, 20% are non-Hispanic black, and the remainder are Asian and other minorities. The Hispanic population is predominantly Puerto Rican. Detailed descriptions of the patient population have been published elsewhere.6

**Perinatal Database**

Data for this study were derived from a detailed, computerized perinatal database. The database includes extensive information on antepartum, intrapartum, and postpartum course in the hospital, assembled from computer-adapted medical record forms. The majority of these standardized forms are completed by the attending physician, and, to a lesser extent, by nurses. All forms are routinely reviewed for accuracy and completeness by a database coordinator. Routine review of the data is performed every month to address inconsistent information and missing data.

Information pertaining to gestational age includes date of last menstrual period and an obstetric estimate of the expected date of delivery, with an indication whether that estimate was based on menstrual date, sonography, or clinical estimate. In addition, a pediatric estimate based on the Ballard neonatal assessment was recorded.7 All these estimates were routinely compared for any significant discrepancies. Assignment of gestational age (in completed weeks) was based on the “best” obstetrical estimate. If gestational age based on menstrual dates differed by less than 2 weeks when compared with a sonographic estimate before the third trimester, then gestational age was assigned based on menstrual dates. If the patient was unsure of the date of her last menstrual period, or if the discrepancy was more than 2 weeks, then gestational age assignment was based on the sonographic assessment. The final assignment of gestational age was based on last menstrual period in 69% of births, ultrasound in 29%, and clinical estimate in 2% of births.

Placental abruption was defined as the partial or complete separation of the placenta prior to delivery of the fetus. This condition is based on a diagnosis by the attending or resident physician. In addition, the percentage of placental separation was also available for about 82% of women diagnosed as having abruption. This was based on gross clinical examination of the placenta by the attending obstetrician at the time of delivery.

The study population comprised 53,675 singleton births. We excluded 292 pregnancies with a diagnosis of placenta previa and a further 12 pregnancies with missing data on birth weight, leaving us with 53,371 births (occurring to 40,789 women) for analyses.

**Perinatal Outcomes**

Risk of stillbirth (occurring after 20 weeks) among pregnancies with and without placental abruption was evaluated, with further stratification based on the time of stillbirth (antepartum and intrapartum stillbirths). Abruption-related pregnancy outcomes were examined among singleton livebirths, including very low (<1500 g), moderately low (1500-2499 g), and all low birth weight (<2500 g) infants. These categories were compared with infants of normal birth weight (≥2500 g). Analyses relating to birth weight were further stratified based on gestational duration (preterm vs term delivery).

Assessment of gestational duration in relation to placental abruption included very preterm (<32 weeks), moderately preterm (32-36 weeks), and all preterm deliveries (<37 weeks), and were compared with term (≥37 weeks) deliveries. Primary clinical manifestations leading to preterm delivery were classified as (1) membrane rupture prior to onset of labor; (2) spontaneous preterm labor; and (3) medically indicated preterm delivery, defined as early delivery due to obstetric intervention. For analyses pertaining to clinical manifestations of preterm delivery, we excluded women whose pregnancies were treated with tocolytic agents and terminated after 37 weeks because such pregnancies may have resulted in preterm delivery had tocolysis not been performed. Finally, we examined the association between abruption and fetal growth restriction, the latter defined as infants whose birth weight fell below the 10th percentile for gestational age after adjustment for sex and race/ethnicity based on US national standards.8 Since norms used for defining growth restriction were available for pregnancies that ended between 25 and 42 weeks, women whose pregnancies terminated outside this range were excluded from this particular analysis. Growth-restricted neonates were further divided into preterm or term delivery.

**Covariates**

The database contains extensive information on sociodemographic, lifestyle risk factors, gynecologic history, and obstetric history, as well as medical complications and procedures related to the current pregnancy. Sociodemographic characteristics include maternal age, parity, marital status, self-reported information on race/ethnicity (non-Hispanic white, Hispanic, non-Hispanic black, and other), and type of insurance coverage or payment source (third party, Medicaid, self-pay, and other). Lifestyle factors included cigarette smoking and alcohol and drug (marijuana, methadone, heroin, and cocaine) use during pregnancy.

Details on obstetric history included prior abortion, prior premature birth, and family history of hypertensive disorders, bleeding disorders, and diabetes. Details on obstetric complications of pregnancy included preexisting or chronic hypertension, mild and severe preeclampsia, pregnancy-induced hypertension, gestational and insulin dependent diabetes, oligohydramnios and polyhydramnios, pyleonephritis, renal disease, and incompetent cervix.

**Statistical Analysis**

We calculated risks of adverse pregnancy outcomes, including stillbirth, low birth weight, preterm delivery, and fetal growth restriction in relation to
Relative risks were adjusted for patient status (clinic vs private), smoking, drug abuse, chronic hypertension, and preeclampsia. The effect of abruption on the outcome was evaluated by computing both the unadjusted and adjusted relative risks (aRRs). Adjusted odds ratios were derived from multivariable logistic regression analysis after controlling for potential confounding variables. The unadjusted and adjusted odds ratios were then transformed to aRRs based on the methods described by Zhang and Yu.5

An important assumption of regression models is that observations are independent of one another. However, analyses of multiple pregnancies to the same woman violates the independence assumption and failure to account for intracluster dependence will often result in biased variances of the effect measure (ie, odds ratios) from the multivariable regression models. In order to account for this dependence, we fit all regression models using generalized estimating equations procedure.10 Adjusted odds ratios and 95% confidence intervals (CIs) estimated from multivariable logistic regression models based on generalized estimating equations carry the same interpretation as those derived from a simple logistic regression model.

Risks of stillbirth and preterm delivery in relation to the degree of placental separation was generated by allowing smooth terms for the extent of placental separation. The smooth terms were based on the restricted cubic spline smoothing procedure.11 Cubic splines are nonparametric smoothing procedures that do not impose any restrictions on the shape of the distribution. Several regression models for stillbirth and preterm delivery were fit by allowing different smoothing criteria based on the number of knots; the most parsimonious model for these outcomes evaluated based on the likelihood-ratio test11 was retained. Knot locations for the model for stillbirth were assigned at 0%, 5%, and 70% placental separation, while the locations for the model for preterm delivery were assigned at 0%, 10%, 30%, and 50%

Patient status (clinic vs private) and race/ethnicity were included in all mod-
els for adjustment. Other potential confounding variables were considered for adjustment if their presence in the regression model changed the odds ratio for placental abruption by at least 10%. Parity was categorized as nulliparous, 1 through 3 pregnancies, and more than 3 pregnancies. Similarly, 3 indicator variables for women of black, Hispanic, and other race/ethnicity were constructed, and each was compared with white women.

**RESULTS**
During the study period, of a total of 53,371 pregnancies (occurring to 40,789 women) resulted in a singleton birth, of which 530 (1%) were complicated by placental abruption. The incidence of abruption increased with increasing parity, although an association with maternal age was not apparent (TABLE 1). Black women, smokers, and drug abusers were all at increased risk for abruption.

Frequency of stillbirth (occurring after 20 weeks' gestation) among women with abruption was 5.3% compared with 0.5% among all other pregnancies, resulting in an 8.9-fold (95% CI, 6.0-13.0) aRR (TABLE 2). The association was stronger for intrapartum than antepartum stillbirths.

Among livebirths, birth weight and gestational age were examined as continuous variables as well as categorical outcomes. Infants born to mothers with placental abruption weighed, on average, 494 g less than infants born to women without this condition, after adjustment for potential confounding variables (TABLE 3). Similarly, pregnancies complicated by abruption ended approximately 2 weeks earlier than other pregnancies.

Risks of giving birth to a low-birth weight infant among women with and without placental abruption were 34.7% and 6.7%, respectively (TABLE 4), yielding an aRR of 3.9 (95% CI, 3.5-4.4). The association was much stronger for very preterm (gestational age <32 weeks) births than for moderately preterm (32-36 weeks) births. The association between abruption and clinical manifestations of preterm delivery revealed stronger aRRs among those with spontaneous preterm labor as the precipitating cause. Preterm deliveries after premature rupture of membranes and intervention for medical indications had smaller but substantially elevated relative risks.

Risks of growth-restricted babies among women with and without placental abruption were 14.3% and 8.1%, respectively (TABLE 5), conferring an aRR of 2.0 (95% CI, 1.5-2.4) in relation to placental abruption.

**Table 4.** Placental Abruption and Low Birth Weight Among Livebirths, Mount Sinai Hospital, New York, 1986-1996†

<table>
<thead>
<tr>
<th>Birth Weight, g</th>
<th>Abruption, No. (%) (n = 502)</th>
<th>Nonabruption, No. (%) (n = 52566)</th>
<th>Unadjusted RR (95% CI)</th>
<th>Adjusted RR (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All births</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>174 (34.7)</td>
<td>3524 (6.7)</td>
<td>5.2 (4.6-5.8)</td>
<td>4.6 (4.0-5.3)</td>
</tr>
<tr>
<td>&lt;1500</td>
<td>58 (11.6)</td>
<td>554 (1.1)</td>
<td>13.5 (10.4-17.1)</td>
<td>11.4 (8.6-15.0)</td>
</tr>
<tr>
<td>1500-2499</td>
<td>116 (23.1)</td>
<td>2970 (5.7)</td>
<td>4.6 (3.9-5.3)</td>
<td>4.1 (3.4-4.8)</td>
</tr>
<tr>
<td>≥2500</td>
<td>328 (65.3)</td>
<td>49042 (93.3)</td>
<td>5.8 (5.2-6.4)</td>
<td>5.3 (4.8-5.9)</td>
</tr>
<tr>
<td>Preterm births (&lt;37 wk)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>149 (74.9)</td>
<td>2329 (48.7)</td>
<td>1.8 (1.7-1.9)</td>
<td>1.8 (1.7-1.9)</td>
</tr>
<tr>
<td>&lt;1500</td>
<td>58 (29.2)</td>
<td>548 (11.5)</td>
<td>5.9 (5.3-6.4)</td>
<td>5.5 (4.8-6.4)</td>
</tr>
<tr>
<td>1500-2499</td>
<td>91 (45.7)</td>
<td>1781 (37.2)</td>
<td>2.2 (2.1-2.3)</td>
<td>2.1 (2.0-2.2)</td>
</tr>
<tr>
<td>≥2500</td>
<td>50 (25.1)</td>
<td>2453 (51.3)</td>
<td>3.0 (2.7-3.3)</td>
<td>2.9 (2.6-3.2)</td>
</tr>
<tr>
<td>Term births (≥37 wk)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>25 (8.3)</td>
<td>1195 (2.5)</td>
<td>3.0 (2.0-4.1)</td>
<td>2.6 (1.8-3.9)</td>
</tr>
<tr>
<td>&lt;1500</td>
<td>0 (0)</td>
<td>6 (0)</td>
<td>13.5 (8.5-20.9)</td>
<td>11.4 (7.3-17.1)</td>
</tr>
<tr>
<td>1500-2499</td>
<td>25 (8.3)</td>
<td>1189 (2.5)</td>
<td>3.0 (2.0-4.1)</td>
<td>2.7 (1.8-3.9)</td>
</tr>
<tr>
<td>≥2500</td>
<td>278 (91.7)</td>
<td>46589 (97.5)</td>
<td>5.8 (5.2-6.5)</td>
<td>5.5 (5.0-6.0)</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; CI, confidence interval; and ellipses, not applicable. Percentages may not sum to 100 due to rounding.
†RRs were adjusted for patient status (clinic vs private), parity, race/ethnicity, smoking, drug abuse, chronic hypertension, and preeclampsia.

**Table 5.** Placental Abruption and Preterm Delivery Based on Antecedent Clinical Presentations Among Livebirths, Mount Sinai Hospital, New York, 1986-1996†

<table>
<thead>
<tr>
<th>Abruption, No. (%) (n = 502)</th>
<th>Nonabruption, No. (%) (n = 52566)</th>
<th>Unadjusted RR (95% CI)</th>
<th>Adjusted RR (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All preterm births</td>
<td>199 (39.6)</td>
<td>4782 (9.1)</td>
<td>4.4 (3.9-4.8)</td>
</tr>
<tr>
<td>Membrane rupture</td>
<td>44 (8.8)</td>
<td>2000 (3.8)</td>
<td>3.2 (2.4-4.1)</td>
</tr>
<tr>
<td>Preterm labor</td>
<td>112 (22.3)</td>
<td>1790 (3.4)</td>
<td>7.5 (6.3-8.7)</td>
</tr>
<tr>
<td>Medical indication</td>
<td>36 (7.2)</td>
<td>892 (1.7)</td>
<td>5.8 (4.2-7.9)</td>
</tr>
<tr>
<td>Very preterm births</td>
<td>72 (14.3)</td>
<td>685 (1.3)</td>
<td>13.6 (10.9-16.8)</td>
</tr>
<tr>
<td>Membrane rupture</td>
<td>21 (4.2)</td>
<td>265 (0.5)</td>
<td>11.8 (7.6-17.9)</td>
</tr>
<tr>
<td>Preterm labor</td>
<td>39 (7.9)</td>
<td>255 (0.5)</td>
<td>21.5 (15.6-29.2)</td>
</tr>
<tr>
<td>Medical indication</td>
<td>8 (1.6)</td>
<td>142 (0.3)</td>
<td>8.7 (4.3-17.4)</td>
</tr>
<tr>
<td>Moderately preterm births</td>
<td>127 (25.3)</td>
<td>4097 (7.8)</td>
<td>3.7 (3.2-4.3)</td>
</tr>
<tr>
<td>Membrane rupture</td>
<td>23 (4.7)</td>
<td>1735 (3.3)</td>
<td>2.0 (1.3-2.9)</td>
</tr>
<tr>
<td>Preterm labor</td>
<td>73 (14.8)</td>
<td>1535 (2.9)</td>
<td>6.2 (5.0-7.7)</td>
</tr>
<tr>
<td>Medical indication</td>
<td>28 (5.7)</td>
<td>750 (1.4)</td>
<td>5.5 (3.8-7.8)</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; CI, confidence interval. Percentages may not sum to 100 due to rounding.†RRs were adjusted for patient status (clinic vs private), parity, race/ethnicity, smoking, drug abuse, chronic hypertension, and preeclampsia.
Among women with abruption, the extent of placental separation was available in 82% (435/530) of pregnancies. Of these 435 pregnancies, 54% had less than 25% placental separation; 16% had 25% through 49%; 13% had 50% through 74%; and 17% had over 75%. Extent of placental separation had a profound effect on stillbirth (Figure), especially among those with severe placental separation (aRR for 75% placental separation, 31.5; 95% CI, 17.0-58.4). However, the risk of preterm delivery was increased substantially even in pregnancies with mild placental separation (aRR for 25% separation, 5.5; 95% CI, 4.2-7.3) (Figure).

**COMMENT**

Over the last decade, the incidence of prematurity has remained fairly stable in the United States at 10%. Despite recent advances in our understanding of the physiology of parturition, prevention of prematurity and low birth weight continue to pose clinical and public health concerns. Placental abruption has been associated with a 20% to 40% rate of preterm delivery. Our results extend information on the relationship of abruption and low birth weight and prematurity by demonstrating that much of the contribution of abruption to low birth weight is mediated through shortened gestations, and, to a lesser extent, through growth restriction. We observed aRRs on the order of 2 through 11 for low birth weight and 2 through 16 for preterm delivery in the presence of abruption.

These results are in general agreement with what has been reported previously, but neither the etiologies of low birth weight (prematurity vs fetal growth restriction) nor the antecedent clinical presentations for preterm delivery in relation to abruption has been explored previously. Our results indicate that women with abruption were at substantially increased risk for preterm labor when compared with those with premature rupture of membranes or medical indication for preterm delivery. Similar results were reported in another study based on a national database. An association between peripheral placental separation and idiopathic preterm labor was demonstrated by Harris and colleagues, who observed that the incidence of fibrin deposition (both perivillous and marginal), decidual necrosis, and marginal and placental floor hemorrhage were greater among placentas of preterm compared with term pregnancies. The extravasation of blood at the placental margin may lead to decidual necrosis, which, in turn, could initiate the production of prostaglandin, thereby leading to preterm labor.

The second important finding of our study relates to the association between extent of placental separation and stillbirth and preterm delivery. Most notably, the risk of stillbirth increased dramatically for women with over 50% separation of the placenta, implying that these abruptions were probably the more severe and acute events. However, the risk for preterm delivery was increased substantially even among women with milder abruptions. Hurd and colleagues examined, through a descriptive study, the extent of placental separation in their series of 54 cases of abruption but did not present data on the association between degree of placental separation and outcome of pregnancy.

The findings on placental abruption noted here have clinical and public health implications. Established risk factors for placental abruption, such as cigarette smoking, drug use, chronic hypertension, pregnancy-induced hypertension, and preeclampsia, are potentially preventable. Some randomized trials and observational studies have shown that low dosages of aspirin (60 and 80 mg/d) and calcium supplementation (2 g/d) may prevent pregnancy-induced hypertension and preeclampsia. Similarly, prenatal patient counseling and education on the harmful effects of smoking and drug abuse during pregnancy can help to reduce the incidence of placental abruption and other adverse outcomes of pregnancy, including preterm delivery and growth restriction. Preterm birth prevention programs might, therefore, benefit if patients suspected to be at risk for developing abruption are identified. A high level of clinical suspicion for placental abruption in women presenting with preterm labor or premature rupture of membranes is clearly warranted. Clinicians should suspect abruption in patients presenting with spontaneous preterm labor or unexplained vaginal bleeding during the latter half of pregnancy. Other common symptoms such as uterine tenderness, excessive uterine contractions, and fetal distress are highly suggestive of placental abruption.

In our analysis pertaining to antecedent clinical presentations for preterm delivery (Table 5), we excluded term pregnancies in which the woman had undergone tocolysis. Although the efficacy of tocolytic agents in prolonging pregnancy is debatable, our exclusion makes the study group more homogeneous. We replicated the entire analysis presented in Table 5 with tocolyzed term pregnancies and the results (not presented) were essentially unchanged.

The extent of placental separation was largely based on an assessment by the attending obstetrician. This subjective assessment may have resulted in some misclassification, especially for the
milder forms of this condition. Women with severe hemorrhage due to placental abruption are more likely to be classified as having over 50% placental separation, whereas women with abruption without external bleeding (concealed hemorrhage) are more likely to be classified as having marginal separation of the placenta. The presence of severe hemorrhage may serve as a reliable marker for the severity of placental abruption.

With regard to residual confounding, drug use, especially crack or cocaine, is strongly associated with an increased risk for placental abruption, as well as low birth weight and preterm delivery, and self-report is limited in its effectiveness as a marker of drug use. Cigarette smoking during pregnancy is associated with a 2-fold risk for placental abruption. The low prevalence of cocaine, is strongly associated with an increased risk for placental abruption, as well as low birth weight and preterm delivery, and self-report is limited in its effectiveness as a marker of drug use. Cigarette smoking during pregnancy is associated with a 2-fold risk for placental abruption.

The results indicate that neonates born to mothers with abruption have poor rates of survival at birth and are delivered early compared with infants born to women without abruption. Much of the risk in low birth weight due to abruption is the consequence of shortened gestation, and, to a lesser extent, fetal growth restriction. Furthermore, the risk of stillbirth is dramatically increased for severe placental separation, but preterm delivery appears more common even among women with lesser degrees of placental separation.

**References**