Abruptio placentae and perinatal death: A prospective study

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Abruptio placentae caused 3.96 perinatal deaths per 1,000 births in a large prospective study. Intrapartum but not prepartum maternal hypertension was observed in the fatal cases. Decidual necrosis at the placental margin and large placental infarcts were the most characteristic placental abnormalities. The decidual necrosis was correlated with maternal cigarette smoking and low pregnancy weight gains in the abruption placentae cases. The fetuses and neonates who died had a pattern of growth retardation characteristic of antenatal undernutrition, indicating that poor maternal nutrition during pregnancy may have contributed to the genesis of the abruptio placentae. (AM. J. OBSTET. GYNECOL. 128: 740, 1977.)

ABRUPTIO PLACENTAE is initiated by hemorrhage into the decidua basalis which then splits, leading to separation of the portion of the placenta adjacent to the split. The disorders with which it has been associated, trauma, uterine tumors, hydramnios, short umbilical cords, and congenital anomalies, will explain only a very small proportion of the premature separations.[1, 2] Maternal hypertension which damages uterine and decidual arteries could explain many more of the cases but its role is uncertain because not all investigators have found the frequency of hypertension to be significantly increased in pregnancies that end with abruptio placentae.[1, 2] The present study analyzed these and many other factors that might be involved in abruptio placentae by utilizing the data available in a large prospective study of pregnancy.

Patients and methods

The Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke provides a unique opportunity to study the pathogenesis of abruptio placentae prospectively. It followed the course of 53,518 pregnancies in 12 hospitals affiliated with United States medical schools between 1959 and 1966 and recorded events of gestation, labor, delivery, and the neonatal period.[4, 5]

The senior author of the present paper reviewed the clinical and postmortem material, including microscopic sections, from the 3,987 unsuccessful pregnancies and infant deaths. Four specially trained technicians reviewed microscopic sections from the 31,494 well-preserved placentas. Nonroutine abnormalities were checked by the senior author.

After the first trimester of pregnancy, enough information was available to give 86 per cent of the deaths a prime diagnosis intended to identify the disorder that initiated the course to death. One hundred and thirty-eight stillbirths and 74 postnatal deaths were placed in the abruptio placentae category when inspection showed an adherent retroplacental clot with depression or disruption of the underlying placental tissue or when there were otherwise classical clinical findings including external or occult bleeding, increased firmness of the uterus, and death between 20 weeks of gestation and the twenty eighth postnatal day with evidence of hypoxia including aspirated squames and petechiae on the surface of the visceral organs.[1, 3] The uterus was often tender.

Efforts were made to determine if maternal weight gains were optimal in the pregnancies that ended in fatal abruptio placentae. To do so, a bar graph was

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Supported by United States Public Health Service Contract NO1-NS-3-2311.

Received for publication January 5, 1977.

Revised February 28, 1977.

Accepted March 3, 1977.

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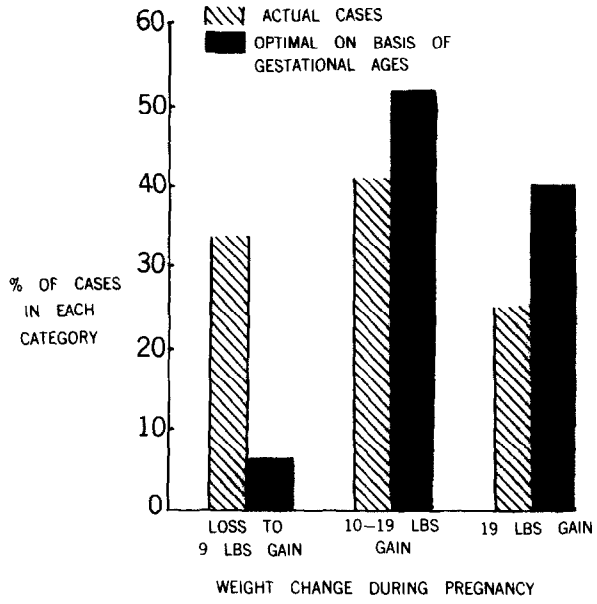

Fig. 1. The distribution of abruptio placentae cases in various maternal weight gain categories. The actual distribution in the present study is compared with a distribution based on optimal maternal gains for gestational ages for the same cases.

constructed to compare the distribution of the present abruptio placentae cases in various maternal weight gain categories with a distribution based on optimal weight gains for gestational ages of the same cases (Fig. 1). Optimal weight gain was considered to be 24 pounds at term. This and intermediate values for shorter gestations were derived from the published works of Niswander and Gordon[5] and Hytten and Leitch.[6]

Placental weights and body measurements from well-preserved cases were recorded from clinical charts and pathologists' records. We calculated these weights and measurements in percentages of mean values for infants of the same gestational age from the study who survived.[7]

Statistical methods

Details of over 1,000 demographic, hereditary, social, medical, and postmortem variables analyzed in the study have been previously published.[4, 5] The chi-square test in two-way contingency tables was used at a probability level of 0.1 to reduce the variables to a smaller group which might have biological significance for abruptio placentae. Cases in which observations were missing for a particular variable were excluded only in analyses involving that variable, so that the statistical analyses were based on the entire data set.

A log-linear model analysis of contingency tables was carried out on the smaller set of variables. The interrelationships of all possible pairs of these variables were determined on the frequency of perinatal death due to abruptio placentae. Tests for zero three-factor interaction were performed in the resulting three-way contingency tables. Variables which had a significant influence on the frequency of fatal cases of abruptio placentae without having significant interactions with other variables are found in Table I. Variables which had interactions of possible significance are found in Figs. 2 to 7.

Table I. The relationship of various maternal factors to perinatal deaths caused by abruptio placentae

Factor	*Perinatal mortality rate*	*P value*
Seizures by gravida		
Present	8.1	<0.023
Absent	3.7	
Lowest Hemoglobin (Gm. %)		
<8.0	15.3	
8-9.9	4.3	<0.001
>9.9	3.4	
Pregnancy weight gain (over 37 weeks' gestation) (pounds)		
0-9	1.6	
10-19	0.9	<0.1
>19	0.6	
Cigarettes per day		
None	3.3	
1-10	4.7	<0.06
11-20	5.2	
Over 20	5.2	
Intrapartum hypertension		
Present	6.7	<0.019
Absent	3.9	
Sex of infant		
Male	4.7	<0.018
Female	3.3	
No. of previous abortions		
0	3.3	
1	4.6	<0.023
2-3	7.5	
>3	4.4	
No. of prior perinatal deaths		
0	3.0	
1	9.4	
2-3	8.5	<0.001
>3	22.2	
No. of prior preterm deliveries		
0	2.9	
1	6.7	<0.001
2-3	8.5	
>3		

Results

The perinatal mortality rate due to abruptio placentae was 3.96/1,000 births in the study. This made the disorder the second most frequent cause of perinatal death in the Collaborative Perinatal Project. The disorder had peak frequencies between 20 and 29 weeks and after 38 weeks of gestation (Fig. 8).

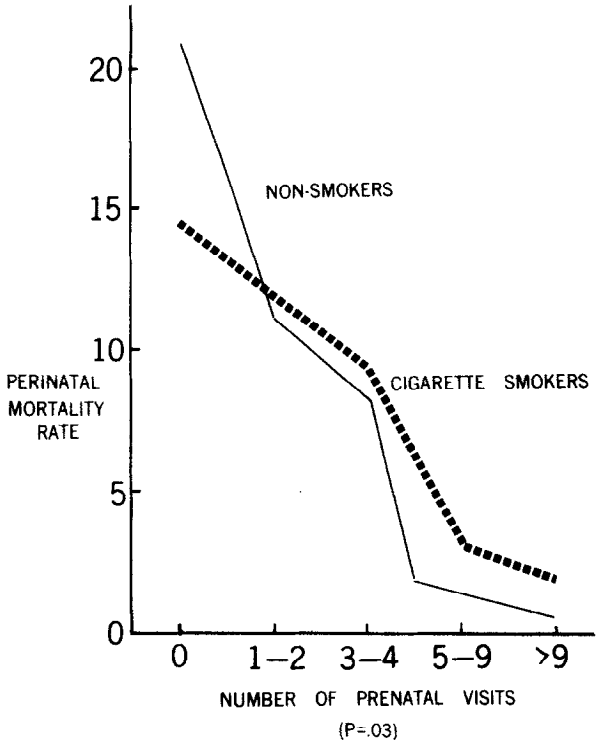

Fig. 2. Abruptio placentae was more common in cigarette smokers than in nonsmokers who made clinic visits for prenatal care.

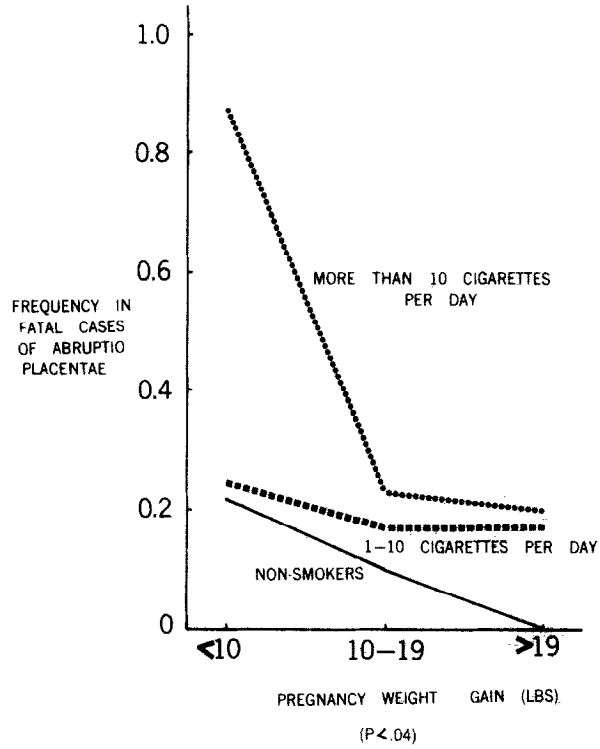

Fig. 4. The effect of smoking on necrosis of the decidua basalis at the margin of the placenta was greatest in the category of lowest maternal gestational weight gain in the abruptio placentae cases.

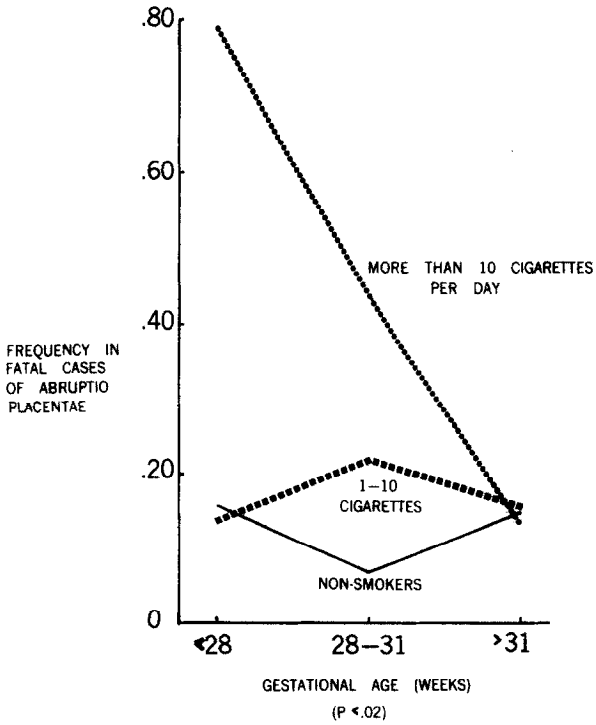

Fig. 3. The effect of smoking on necrosis of the decidua basalis at the margin of the placenta was greatest at the earlier gestational ages in abruptio placentae cases.

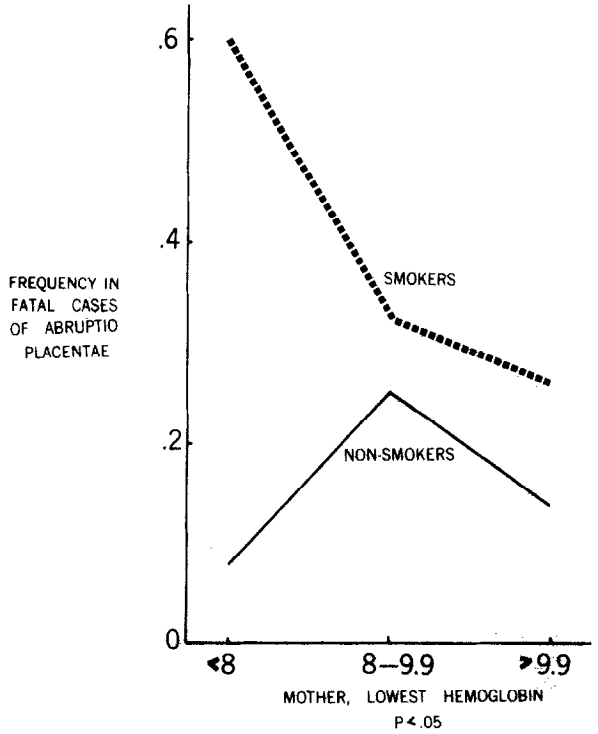

Fig. 5. The effect of smoking on necrosis of the decidua basalis at the margin of the placenta was augmented by maternal anemia in abruptio placentae cases.

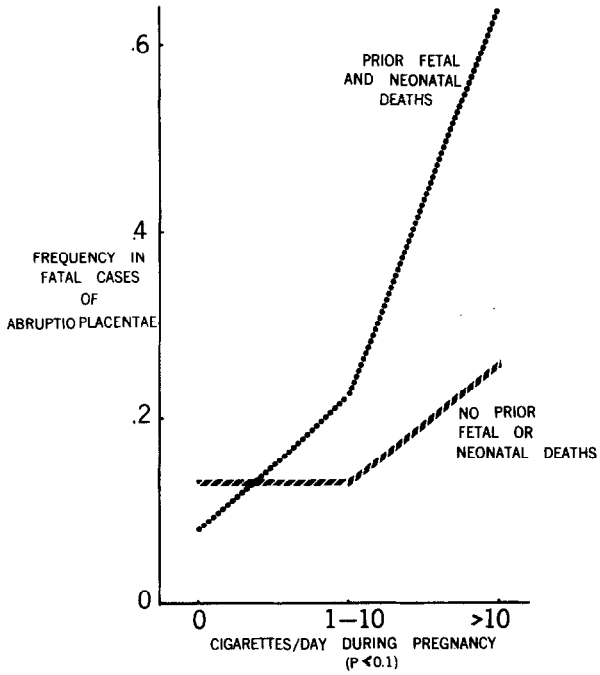

Fig. 6. Decidual necrosis at the margin of the placenta was more frequent in cases in which the mother had experienced previous fetal and neonatal losses. This effect was potentiated by heavy smoking during pregnancy.

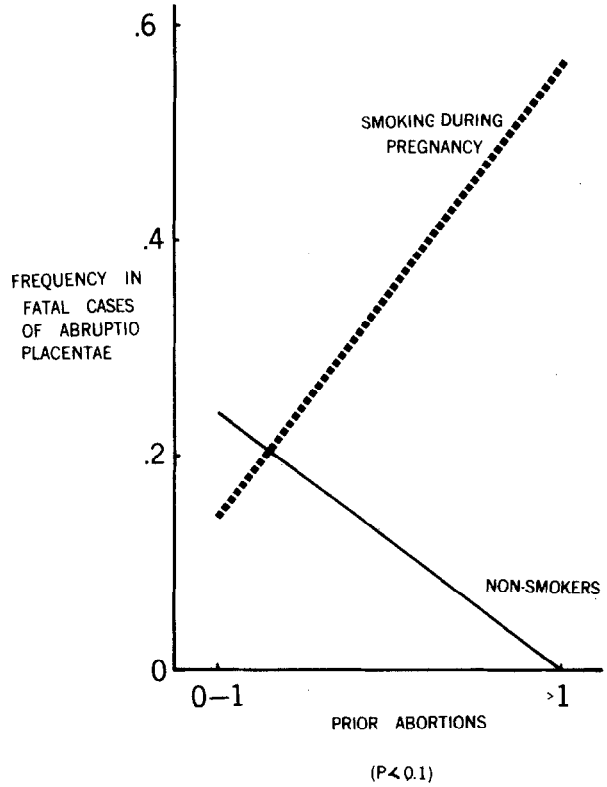

Fig. 7. Large placental infarcts were most common in cigarette smoking mothers who had experienced prior spontaneous abortions.

Maternal weight gain and fetal growth. Maternal weight gain was markedly suboptimal in a large proportion of the pregnancies that ended with perinatal death due to abruptio placentae (Fig. 1). There was an associated retardation of placental and fetal growth. Mean placental weights were 14 per cent lighter, mean body weights were 8 per cent lighter, mean body lengths were 3 per cent shorter, and mean head circumferences were the same as those in the surviving control infants of the same gestational age.

Gestational factors. In no case was there a history of external trauma to explain fatal abruptio placentae, but some of the 2.2-fold increase in deaths associated with epilepsy may have been due to trauma (Table 1). There was nearly a fivefold increase of fatal cases of abruptio placentae in mothers who had a hemoglobin level of 7.9 Gm. per cent or less recorded during pregnancy (Table 1). Some of these low hemoglobin values were the consequence of acute bleeding associated with the placental separation. The anemia in 11 of the gravid women was corrected by the administration of oral iron. There were no cases of megaloblastic anemia in the patients with abruptio placentae.

There was a 1.7-fold increase of abruptio placentae in gravid women with intrapartum diastolic blood pressures over 90 mm. Hg and systolic pressures over 140 mm. Hg. This hypertension was an intrapartum or very late gestational event because no significant increase in the frequency of hypertension was recorded in the fatal cases of abruptio placentae during prenatal visits before delivery. There was also no increase of placental infarcts in the patients with abruptio placentae and intrapartum hypertension, another indication that the hypertension was short duration.

The trimester in which a mother registered for prenatal care had no influence on the frequency of deaths from abruptio placentae, but gravid women who made many visits for prenatal medical care had the lowest perinatal mortality rates from the disorder (Fig. 9). This may have been due to better nutrition since those who made more visits had greater weight gains. At term, gravid women who had gained 9 pounds had made an average of 6.2 prenatal clinic visits; those who gained 10 to 19 pounds, 7.1 visits; and those who gained over 19 pounds, 7.2 visits. At each gestational age, gravid women with high weight gains had lower perinatal mortality rates due to abruptio placentae than did women with lower weight gains (Table I).

The number of perinatal deaths due to abruptio placentae was higher in cigarette smokers than in nonsmokers (Table I). This difference was enhanced if mothers who had no prenatal visits were excluded from the analysis (Fig. 2). Hydramnios, race, educational level, diabetes mellitus, and economic status had

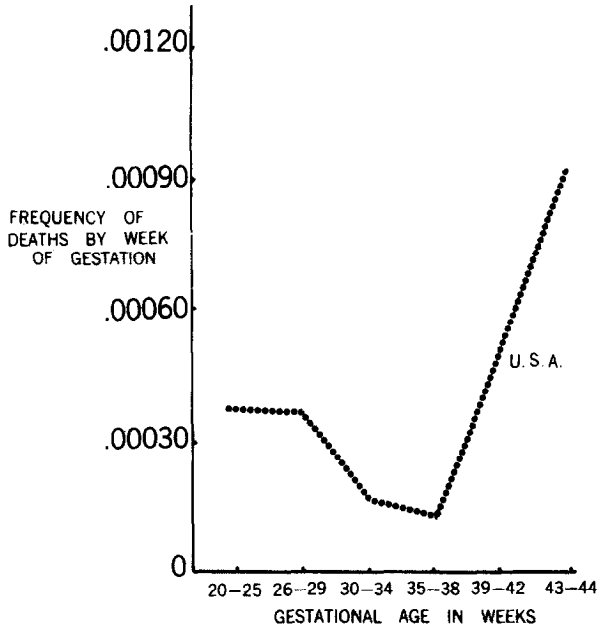

Fig. 8. Distribution of abruptio placentae cases by gestational ages.

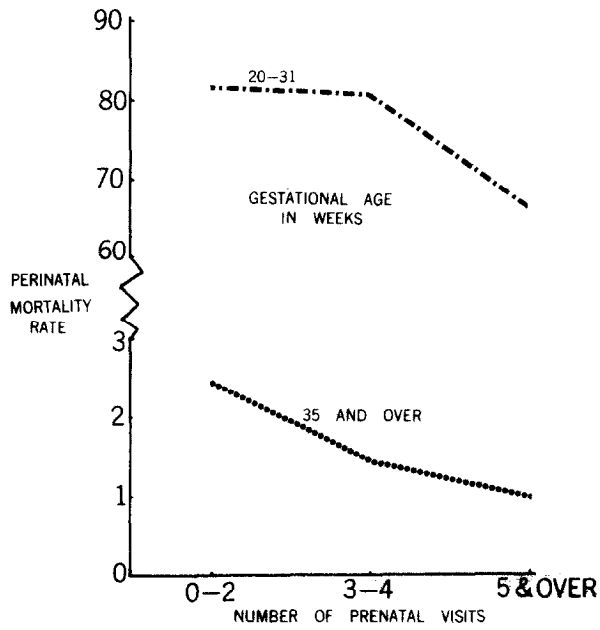

Fig. 9. At each gestational age, there was a lower frequency of fatal cases of abruptio placentae in gravid women who made a large number of clinic visits than in those who made fewer visits.

no significant influence on perinatal deaths due to abruptio placentae, but male babies were more likely to die than female babies (Table I). This excess of male deaths was found with about equal frequency in fetuses and neonates. There was no significant increase of fatal cases of abruptio placentae with increasing maternal age or parity, but there were large increases when a mother reported prior unsuccessful pregnancies and preterm deliveries (Table I). Mothers with uterine leiomyomas had twice the frequency of fatal cases of abruptio placentae as did those without leiomyomas. Of the mothers with perinatal deaths due to abruptio placentae, 21 per cent developed at least mild evidence of hemorrhagic shock following the abruptio placentae but none died. The use of oxytocin either to induce or to augment labor had no effect on the frequency of fatal cases of abruptio placentae.

Placental abnormalities. Fatal abruptio placentae cases had an increased frequency of thrombosed arteries and necrosis of the decidua basalis, particularly at the margins of the placenta (Table II). Large recent infarcts and stromal fibrosis in the terminal villi were the most striking abnormalities in the parenchyma of the placentas. The various lesions had a similar frequency whether the infants were macerated, were fresh stillborn, or died in the neonatal period. None of the fatal cases of abruptio placentae had an umbilical cord less than 20 cm. long so none of the cords were considered to be abnormally short.

In fatal cases of abruptio placentae, decidual necrosis at the placental margin had about twice the frequency when the gravid patient's weight gain was under 10 pounds as when weight gains were over 19 pounds. The decidual necrosis was most common in the heaviest smokers. This association was greatest at the lower gestational ages and in pregnancies in which the gravid patient had a low weight gain, was anemic, or had a history of prior unsuccessful pregnancies (Figs. 3 to 6). The association in cases of abruptio placentae of large placental infarcts with smoking was entirely in those who had a history of prior spontaneous abortions (Fig. 7).

Normal pregnancies also had a positive correlation between smoking and decidual necrosis at the margin of the placenta. The smokers had a 8.6 per cent frequency and the nonsmokers had a 7.4 per cent frequency of decidual necrosis at term when the gravid women were normotensive and had a weight gain over 20 pounds ($P < 0.03$). The frequencies of large infarcts in the two groups were 5.0 and 3.9 per cent ($P < 0.001$). The normal pregnancies also had a positive correlation between low pregnancy weight gain and decidual necrosis but not between low weight gain and placental infarcts. Normotensive, nonsmoking gravid patients who had gained less than 10 pounds at term had a 9.6 per cent frequency of decidual necrosis at the placental margin while those who had gained over 20 pounds had a frequency of 7.3 per cent

Table II. The frequency of placental abnormalities in perinatal deaths due to abruptio placentae compared with the frequency of such abnormalities in infants who survived

Placental abnormality	*Control cases with surviving infants (%)*	*Cases with infant death due to abruptio placentae (%)*	*P value*
Decidua			
Fibrinoid in arterial walls	1.9	5.7	<0.005
Thrombosis in arteries	0.9	4.7	<0.001
Basalis at margin of placenta			
Necrosis	8.3	22.6	<0.001
Infiltration of neutrophils	15.9	25.9	<0.008
Infiltration of lymphocytes	36.9	36.3	>0.1
Basalis in central areas of placenta			
Necrosis	2.3	9.4	<0.001
Infiltration of neutrophils	8.0	19.3	<0.001
Infiltration of lymphocytes	36.6	33.5	>0.1
Capsularis			
Necrosis	12.9	18.9	<0.06
Infiltration of neutrophils	27.0	38.2	<0.1
Infiltrations of lymphocytes	52.2	51.9	>0.1
Villi			
Stromal fibrosis terminal villi	10.7	32.1	<0.001
Gross infarcts, 3 cm. diameter	3.2	12.7	<0.001
Gross infarcts, 3 cm. diameter	18.0	16.5	>0.1
Microscopic infarcts	15.2	31.1	<0.001

($P < 0.01$). Large infarcts had frequencies of 5.1 and 4.5 per cent in the two groups ($P > 0.1$).

Comment

Findings in the present study indicate that several traditional explanations for abruptio placentae play a minor role in the disorder while some seldom considered factors may make a major contribution to its genesis. Short umbilical cord, hydramnios, and abdominal trauma will explain only a few cases of the disorder whereas primary placental abnormalities appear to have a major role. The two placental lesions most strongly associated with abruptio placentae were necrosis of the decidua basalis at the margin of the placenta and large placental infarcts. Some of the infarcts were old but most were recent. In most cases the infarcts probably served as a nidus for initiating the separation, but other infarcts were probably secondary to the separation, the infarcted area having lost contact with the well-oxygenated maternal blood. The infarcts were most common just before term, an indication that most were probably the cause rather than the consequence of the abruptio placentae.

Decidual necrosis may well be the more common lesion leading to abruptio placentae, particularly at the earlier gestational ages. When it develops at the periphery of the placenta, it is in a position to initiate a premature separation of the organ. In some instances the decidual necrosis may be secondary to the abruptio placentae, but we believe in many cases it is primary because it was so strongly associated with smoking and low maternal weight gain in both the abruptio placentae and non–abruptio placentae cases. The frequency of the necrosis increased with the number of cigarettes smoked each day, an association augmented by maternal anemia. This raises the possibility of a hypoxemic or ischemic origin of the necrosis. The administration of nicotine to pregnant rhesus monkeys appears to cause vasoconstriction in the uterine circulation.[8] Such vasoconstriction could be responsible for the decidual necrosis, particularly at the margin of the placenta where a relative stasis of blood flow may exist.[9]

The relationship between smoking and decidual necrosis was much greater around midgestation than late in pregnancy, raising the possibility that smoking may contribute to the excessive losses experienced earlier in gestation by women who smoke.[10] Heavy smoking also augmented both the frequency of decidual necrosis at the placental margin and large placental infarcts in cases of abruptio placentae in which mothers had a history of previous unsuccessful pregnancies. Thus, smoking may play a role in the repeat abortions and fetal losses experienced by some women through these mechanisms of placental damage.

There was no increase in large placental infarcts in fatal abruptio placentae cases in which the mothers were hypertensive at the time of delivery. This suggests that the hypertension was of short duration because such infarcts are common in women who are chronically hypertensive during pregnancy.[11] In fact, there

was no increase in the frequency of prelabor maternal hypertension recorded in the fatal cases of abruptio placentae in the present study. Therefore, the increased hypertension recorded during labor in fatal cases of abruptio placentae likely reflected the consequences of rather than caused the abruptio placentae.

There was an inverse relationship between the number of maternal visits for prenatal medical care and mortality rates from abruptio placentae. Nutritional advice given during the clinic visits may have had some role in the prophylaxis. Gestational weight gains were suboptimal in a high proportion of the pregnancies that ended with fatal abruptio placentae. The infants who died were undergrown for their gestational age and had values for head circumference and body length that were either normal or less retarded than values for placental and body weights. This growth pattern has long been recognized as characteristic of fetal undernutrition, and its presence in these infants supports the view that the mothers were undernourished during gestation.[12] Although gravid women who smoke may eat less than nonsmokers, it would appear from data in the present study that undernutrition and smoking have independent actions in the genesis of abruptio placentae. If their roles are confirmed, there is hope through programs of public education for markedly reducing the frequency of perinatal deaths due to this disorder.

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