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PLACENTAL VILLOUS EDEMA: A POSSIBLE CAUSE OF ANTENATAL HYPOXIA

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This study was undertaken to determine the relationship between the placental villous edema and the characteristic sequelae of antenatal hypoxia, i.e. the need for resuscitation at birth and low pH values in umbilical arterial blood. Placental villous edema was recognized by finding of open spaces within the cytoplasm of intervillous cells and in the interstitium of the villi.

The percentage of edematous villi was significantly higher in the group of newborns requiring resuscitation. The severity of the edema had a positive correlation with the need for resuscitation at birth and with the arterial blood pH values in the umbilical cord. Placenta praevia and maternal toxicosis were associated with high percentage of edematous villi. It is suggested that edema fluid interposed a barrier to gas exchange between mother and fetus. The capillaries were blocked by compression leading to reduction in blood flow through the villi. These abnormalities, if widespread, may reduce gas exchange.

It is suggested that hypoxia could partly be prevented by preventing the development of placental villous edema.

INTRODUCTION

There is a controversy in the literature about the clinical significance of placental villous edema. According to Aladjem et al. /1/ the villous edema as a sole finding is common in infants who have normal neonatal course. On the other hand, Naeye et al /5/ suggested that most of mortality and morbidity associated with chorioamnionitis and a number of other antenatal disorders are related to placental villous edema. The

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placenta is functioning as the fetus, respiratory and excretory system and any interference with its functional capacity is a source of great danger. The edematous villi may form a barrier to gas exchange between mother and fetus resulting in asphyxiation, which may cause widespread pathophysiologic alterations. The purpose of this study was to determine the relationship between the placental villous edema and the antenatal hypoxia.

PATIENTS AND METHODS

Fourty-eight term and 54 preterm neonates (gestational age less than 37 weeks) were analysed. Eight fetuses died in utero, and 40 full term deliveries were added as controls.

To determine the percent of edematous villi, 40 randomly selected microscopic fields were counted in each of three tissue sections taken from the center, midzone, and periphery of the placenta /5/. Placental villous edema was recognized by the finding of open spaces in the interstitium of the villi and within the cytoplasm of intravillous cells (see Figure 1).

The severity of edema was evaluated by determining the percent of edematous villi.

Neonatal resuscitation was defined as a need for bag and mask ventilation, intubation or assisted ventilation.

For determination of pH, blood was withdrawn from umbilical arteries immediately after birth.

The 99 % confidence interval was used to point the differences between the compared groups. Linear regression analysis was performed to determine the statistical significance of decreasing pH values.

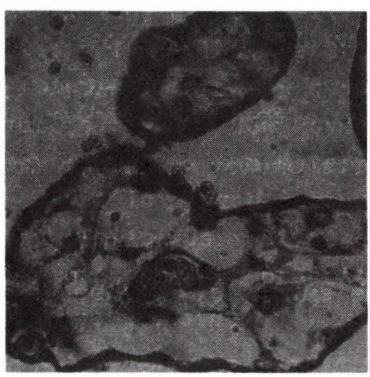

Fig 1. There are large open spaces within the villus. Edema has accumulated between capillary and trophoblastic covering of the villus.

RESULTS

The rate of edematous villi was significantly higher in the group of reanimated newborns (Table I). Villous edema was identified as the sole pathological finding. In this group abruptio placentae, compression of umbilical cord, placenta praevia, extended placental infarcts, and other well-known causes of intrauterine hypoxia were excluded. The comparison was made with newborns of similar birthweight and gestational age.

TABLE I
The rate of edematous villi

	Resuscitated newborns		Controls
Number of newborns	10		10
Mean birthweight (g)	2223		2196
Mean gestational age (wk)	35.2		35.5
Number of counted villi	4083		4773
Number of edematous villi	912		387
Percent of edematous villi	22.3%	$p < 0.001$	8.1%

There was a strong, positive correlation between the higher rate of edematous villi and the characteristic sequelae of antenatal hypoxia, i.e., the need for resuscitation at birth, or low pH values in umbilical arterial blood (Table II, Fig 2). No liveborn infant was found at higher edema rates, i.e. above 60 %.

TABLE II

Clinical symptoms and severity of villous edema

Rate of edematous villi	≤ 20 %	21-40 %	41 -60 %	61-80 %
Number of liveborns	74	15	5	0
Number of newborns with				
- good respiration	62	4	0	-
- resuscitation	9	6	4	-
- grunting	3	5	1	-
Mean pH values	7.28	7.21	7.17	-
Number of stillborns	7	0	0	1

The difference in pH values is significant ($p < 0.05$).

In the graph shown in Fig. 2, the width of the bar shows the 99 % confidence interval for the difference observed in the clinical symptoms. The larger the sample size the shorter the length of the bar. If the bar fails to cross the 0 line, the observed difference is likely less than 1 % to occur by chance.

Placenta praevia was generally associated with high percentage of edematous villi. In 3 of our 4 newborns with resuscitation the mean rate of edematous villi was 42 %. By contrast, the fourth newborn with placenta praevia had normal respiration and the rate was 10 %.

Similar observation was made in the cases of maternal toxicosis. In 2 of our 3 newborns with resuscitation the mean rate of edematous villi was 38 %. On the other hand, in one case of maternal eclampsia the infant was born in good condition, with excellent respiration, and the rate of edematous villi was 5 %.

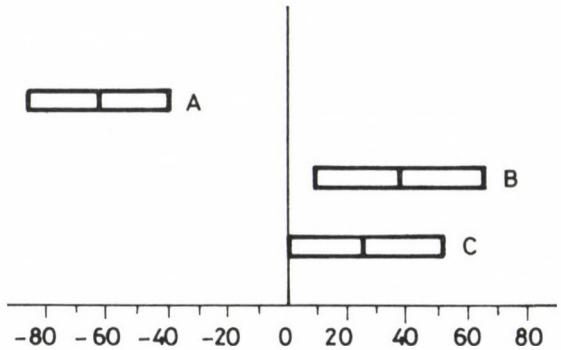

Fig 2. The 99 % confidence interval for percentage point differences for clinical symptoms between newborns with lower ($\leqslant$20 %) and higher (21-60 %) degree of placental villous edema (see Table II).
A: newborns with good respiration,
B: newborns needing resuscitation,
C: newborns with grunting.
Only liveborns are included. Negative numbers indicate fewer cases in the group of newborns with higher percentage of edema.

DISCUSSION

Findings in this study support the possibility that antenatal hypoxia is related to placental villous edema. In the group of newborns which were resuscitated (Table I) the placental villous edema was the sole pathological finding. No other disorders of pregnancy and delivery were identified.

There was a strong, positive correlation between the higher percentage of placental villous edema and the morbidity of newborns (Table II, Fig 2). No fetus survived the most severe degree of edema (above 60 %). The pH values decreased significantly as the edema progressively increased.

In the cases of placenta praevia and maternal toxicosis the conditions of the newborns were better related to the severity of villous edema than to the maternal illness. In the most severe form of maternal toxicosis, the newborn was in good general condition and showed a low-degree villous edema. By contrast, the newborns with high percentage of edema required

resuscitation and the maternal illness was mild.

On the basis of histological findings we can explain why the newborns are sick following the development of placental villous edema. The edema fluid, accumulating between intravillous capillary and the throphoblastic covering of the villus, forms a barrier to gas exchange between mother and fetus. In addition, the intravillous capillaries are compressed by edema fluid, leading to reduced circulation in the villi. These abnormalities, if widespread, may reduce gas exchange.

The pathophysiology of the villous edema is unknown. It clearly originates in the fetus /5/. Chorioamnionitis and a number of other antenatal disorders are related to placental villous edema /5/. Catecholamines might play some role in the development of villous edema. Lagercrantz and Bistoletti have shown that catecholamines are released by stressed human fetus /4/. Catecholamines can cause pulmonary edema in humans /3,6,7/. Before birth the pulmonary and systemic circulations are directly connected through the foramen ovale and ductus arteriosus and any increase in left ventricular filling pressure may increase hydrostatic pressure in the placental villous capillaries /5/. Prostaglandins were also considered as a cause of villous edema /2/.

Our findings are similar to that reported by Naeye et al /5/. The results in this study raise the possibility that some cases of antenatal hypoxia could be prevented by eliminating or reversing the development of placental villous edema.

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