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The ultrasonographic assessment of the fetal thorax and fetal breathing movements in the prediction of pulmonary hypoplasia

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Summary

Comparison was made of fetal breathing movements (FBM) and thoracic measurements in the prenatal diagnosis of pulmonary hypoplasia. In 20 pregnancies with oligohydramnios due to premature and prolonged rupture of the membranes (PROM) the presence or absence of FBM was assessed, the internal thoracic and cardiac circumferences were measured and the internal thoracic and lung areas calculated. All 5 infants with absent FBM died from pulmonary hypoplasia in the neonatal period and all 15 with FBM present survived. The internal thoracic circumference of 3 of the fetuses that developed pulmonary hypoplasia and 1 of those that did not were below the 2.5th centile of a reference range constructed from 76 normal pregnancies. Similarly, the lung areas were below the 2.5th centile of our reference range in 3 fetuses who developed pulmonary hypoplasia and 2 of those that survived. The absence of FBM was found to be the most accurate predictor of pulmonary hypoplasia in pregnancies complicated by oligohydramnios due to PROM.

fetal breathing; fetal thoracic circumference; fetal lung area; oligohydramnios; pulmonary hypoplasia.

Introduction

Oligohydramnios due to premature and prolonged rupture of the membranes (PROM) is frequently associated with neonatal death due to pulmonary hypoplasia [15]. The absence of fetal breathing movements (FBM) and a reduced

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thoracic circumference have recently been suggested as useful markers in the prenatal prediction of pulmonary hypoplasia [2,12]. In this study the presence or absence of FBM, the internal thoracic circumference (ITC) and the lung area of fetuses from pregnancies with PROM were determined by real time ultrasonography and the results compared to those from normal pregnancies. The aim of the study was to establish a normal range of second and third trimester fetal thoracic measurements and to compare FBM and thoracic measurements in the prenatal diagnosis of pulmonary hypoplasia.

Patients and Methods

The presence or absence of FBM was noted and the internal thoracic and cardiac circumferences measured in 20 fetuses from pregnancies complicated by oligohydramnios due to PROM. No fetus was suffering from severe IUGR. All pregnancies had been referred to our unit from other centres at 21—33 weeks gestational age; membrane rupture had occurred from 1 to 9 weeks prior to referral. The diagnosis of rupture of the membranes and continuous drainage of amniotic fluid was made from the clinical history and confirmed by the use of nitrozin sticks. Oligohydramnios was confirmed at referral and defined as the absence of an amniotic fluid pool of greater than 1-cm in diameter measured in two planes. The results were then compared to those from 76 sequential normal pregnancies that were undergoing routine ultrasound examinations at 18—36 weeks gestation. Assessment of gestational age was made from the menstrual history and confirmed by measurement of the fetal femur length, rather than the biparietal diameter, because in the oligohydramnios group there was often dolichocephaly.

The study was strictly cross-sectional and all ultrasound examinations were made using a real time curvilinear 3.5 MHz transducer (Hitachi EUB 340). A transverse section of the fetal thorax was taken at the level of the four-chamber view of the heart, during fetal apnoea, and direct measurements were made of the internal and thoracic cardiac circumference (heart in diastole) on the screen with an electronic calliper. Using these measurements the internal thoracic and cardiac areas were calculated assuming both areas to be circular; lung area was defined as the difference between the two areas. Reproducibility studies were performed on 10 control patients and 10 with oligohydramnios selected at random. Polaroid copies were made of the ultrasound examinations and each was then presented to a single observer who was unaware of the clinical details of the patients, on six separate occasions. The intrasubject reproducibility of both ITC and lung area was expressed as the coefficient of variation and for both the control population and the patients with oligohydramnios was $\leqslant 6\%$. FBM were defined as absent if no regular thoracic movements lasting more than 60 s were seen during a period of 2 h. A gap of more than 6 s between breaths was defined as cessation of breathing [14]. This stringent definition of FBM was employed as it has been used extensively in the literature [9,18,19] and differentiates FBM from fetal gasps which are often seen in compromised fetuses [13].

From the pregnancies complicated by PROM the diagnosis of pulmonary hypoplasia was made in those infants who survived if: (a) high pressure ventilation (> 30 cmH_2O) was necessary both for resuscitation and during subsequent respiratory support; (b) artificial ventilation was required for longer than one month; (c) a chest radiograph at one week of age was reported by a radiologist unaware of the infant's clinical details demonstrating small volume lungs.

Postmortem examinations were performed in all cases of intrauterine or neonatal death. Pulmonary hypoplasia was diagnosed if the ratio of lung weight to body weight was less than 0.012 and the radial alveolar count less than or equal to 4.1 [1].

Statistical analysis

The relationship of the internal thoracic circumference and the lung area to gestational age in the normal pregnancies was established using a Spearman's rank correlation coefficient. To test whether the timing of onset or duration of oligohydramnios had any effect on the internal thoracic circumference of lung area, the observed values in the fetuses from the PROM pregnancies were subtracted from the expected mean for gestation (ΔITC or Δlung area) and a linear regression analysis performed. Differences in the data of infants who survived and those who developed pulmonary hypoplasia were assessed for statistical significance using a Wilcoxon rank sum test.

Ethical Permission

Ethical permission was granted for this study by the King's College Hospital Ethics Committee.

Results

In the normal pregnancies there was a significant linear correlation between the ITC and lung area and gestational age (ITC = 0.64 × gestational age (weeks) − 0.122, $r = 0.95$, $P < 0.001$; lung area = 1.031 gestational age (weeks) − 14.52, $r = 0.89$, $P < 0.001$.

Of the 20 babies from pregnancies complicated by PROM, 15 survived and five died within 24 h of birth from respiratory failure and at necropsy they all had evidence of pulmonary hypoplasia. Although of the 15 survivors, 8 infants had respiratory distress syndrome, they did not require high pressure or long-term ventilation and their chest radiographs at one week of age were not reported as showing pulmonary hypoplasia. In the five fetuses who subsequently died of pulmonary hypoplasia irregular breathing movements were occasionally witnessed. However, none of these episodes were sustained for a 60 s period [4]. In three of these fetuses the ITC and lung areas were below the 2.5th centiles of the reference range. In all 15 infants who survived FBM were present. The ITC and lung areas were within the 95% confidence limits in 14 and 13 of these cases, respectively.

There was no significant correlation ($r < 0.2$) between ΔITC and Δlung area and either the gestation at PROM or the interval between PROM and the

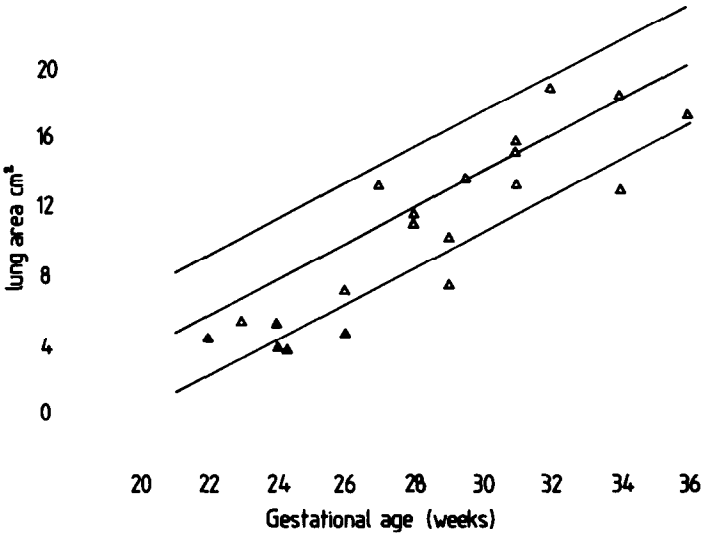

Fig. 1. The internal thoracic circumference from 20 pregnancies with PROM plotted on the mean and 95% confidence limits of the normal range for gestation. △, fetuses with breathing movements; ▲, fetuses without breathing movements.

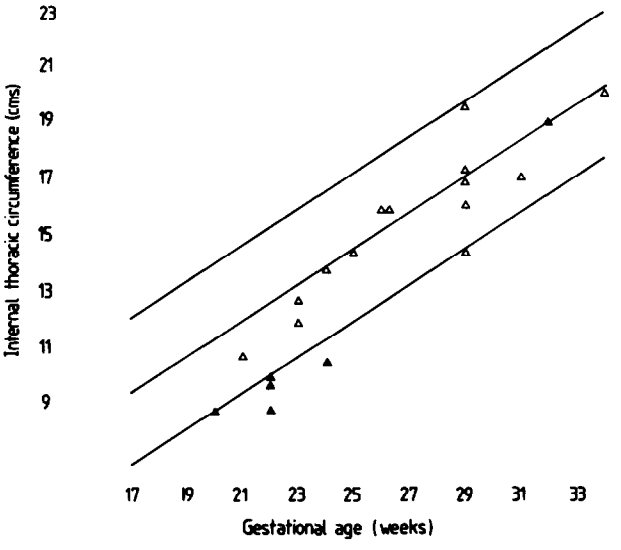

Fig. 2. The "lung area" in fetuses from 20 pregnancies with PROM plotted on the mean and 95% confidence limits of the normal range for gestation. △, fetuses with breathing movements; ▲, fetuses without breathing movements.

TABLE I

Ultrasonographic findings of patients with and without pulmonary hypoplasia.

Outcome	No. of patients	Gestation (range in weeks)		FBM absent	ITC < 2.5%	Lung area < 2.5%
		At onset of PROM	At delivery			
Pulmonary hypoplasia (all died)	5	15—24	24—27	5	3	3
Survived, no pulmonary hypoplasia	15	18—32	24—40	0	1	2

ultrasound examination. The ΔITC and Δlung area, however, were significantly smaller in the five fetuses who developed pulmonary hypoplasia than the 15 who did not, $P < 0.05$. There was no significant difference in the duration of oligohydramnios (onset of PROM to delivery) between the babies that died (median 9 weeks, range 1—11 weeks) and those that survived (median 6 weeks, range 1—14 weeks), but the onset of PROM was at a significantly earlier gestation in those that developed pulmonary hypoplasia (see Table I), $P < 0.05$). In six of the survivors, however, the onset of PROM was also at or below 24 weeks gestation.

Discussion

In normal pregnancies we demonstrated a linear growth of ITC and lung area with gestational age. These correlations are in agreement with previous studies that reported a linear growth of the external thoracic circumference with gestation [5,7,16]. In this study, however, the internal rather than the external thoracic diameter was selected as in the presence of oligohydramnios the landmarks of the latter measurements may be obscured. There has been considerable discussion over the last 10 years as to the selection of either the abdominal or thoracic circumference for both monitoring fetal growth and the diagnosis of different types of growth retardation, either symmetrical or asymmetrical [3]. In this study the reference range of ITC and lung area were established, not as indices for monitoring fetal growth, but to enable the diagnosis and monitoring of fetuses at risk of pulmonary hypoplasia.

All patients with PROM were referred from other centres and therefore preselected, so that no epidemiological statement can be made as to the incidence of pulmonary hypoplasia in the presence of oligohydramnios. The survival of the 15 babies in this series, however, with onset of oligohydramnios as early as 18 weeks gestation and in some cases of 15 weeks duration provides direct evidence that pulmonary hypoplasia and neonatal death is not an invariable consequence of prolonged PROM.

The present findings confirm our results from an earlier study which demonstrated an association between the presence of FBM and continuing lung growth [2]. Recently, breathing activity was reported, however, in four fetuses from pregnancies complicated by PROM who subsequently died of pulmonary hypoplasia [8]. This discrepancy may be explained by the use of different definitions of the presence of fetal breathing activity. Moessinger et al. [8] defined "breathing movements" by the presence of three breaths in a period of 6 s. We considered fetuses to be breathing if there were regular movements, at least 1 per 6 s, lasting for at least 1 min. Such a definition stressing the importance of sustained respiratory effort has been used extensively in the literature [9,12,14].

The necessity for persistent FBM for antenatal lung growth has been demonstrated by extensive animal research. For example, resection of the upper cervical cord in fetal rabbits results in cessation of FBM and the development of pulmonary hypoplasia [18]. Thus, it seems probable that the absence of FBM in

our series resulted in the development of pulmonary hypoplasia. We would suggest that these fetuses did not already have an existing pulmonary abnormality, because postnatally babies with pulmonary hypoplasia are capable of respiratory movements [6]. The results also suggest that "sustained" breathing activity rather than the short epochs described by Moessinger et al. [8] is important for continuing antenatal lung growth in the presence of oligohydramnios due to PROM.

It is unclear as to why some fetuses in pregnancies complicated by oligohydramnios due to PROM develop pulmonary hypoplasia and some do not. These results suggest that the earlier the onset of PROM the more likely pulmonary hypoplasia is to occur, but this study also demonstrates that amongst survivors there were some with similar early onset PROM to those that died. The duration of oligohydramnios due to PROM was not found to be significantly different in those that died to those that survived, furthermore, no correlation was found between the duration of oligohydramnios and ITC or lung area.

It may be that to prevent pulmonary hypoplasia a critical volume of amniotic fluid is necessary, which is undetectable by current methods for measuring amniotic fluid volume. Adequate intrathoracic space is necessary for normal lung growth; oligohydramnios may limit the intrathoracic space available for lung growth by physical compression of the uterus on the thorax and abdomen [11]. Thoracic compression and oligohydramnios produced by experimental urinary tract obstruction results in pulmonary hypoplasia. This abnormal lung growth is less marked if the thoracic compression is relieved by allowing the abdominal viscera to herniate into the amniotic cavity [11].

In severe oligohydramnios, those fetuses with a small chest may have a greater degree of thoracic compression which may also act by more effectively inhibiting FBM and thus leading to pulmonary hypoplasia. Certainly in this study those infants which developed pulmonary hypoplasia tended to have the smallest ITC and lung area, which may indicate a greater degree of fetal compression, but also could be interpreted as reduced antenatal lung growth. Alternatively, in the presence of severe oligohydramnios local uterine contractures, noted in sheep and monkeys, may be more severe [10]. Such uterine contractures may inhibit FBM and result in pulmonary hypoplasia, not only by a compressive effect but also by elevating prostaglandin levels, which are known to abolish FBM during labour [4].

Our results contrast with those of Nimrod et al. [12] who suggested that ultrasound measurement of the fetal thorax allows accurate prediction of pulmonary hypoplasia. In the present study, fetuses with pulmonary hypoplasia were assessed in the second trimester, when abnormalities of lung growth may not be so marked and this could explain our relative inability to detect such fetuses. Accurate detection of fetal abnormalities in the second, rather than the third, trimester of pregnancy is of the greatest importance, as intervention is possible.

The results of this study demonstrate that although thoracic and lung measurements tended to be lower in those babies who developed pulmonary hypopla-

sia, the only accurate method of predicting pulmonary hypoplasia in the second trimester of pregnancy was the absence of FBM.

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