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Survival of fetuses with severe oligohydramnios

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Summary

Objective: The aim of the present study was to identify predictive data on the short-term outcomes of fetuses with oligohydramnios. *Materials and Methods:* A retrospective study of all pregnancies diagnosed with oligohydramnios was performed. *Results:* A total of 17 fetuses (seven males, seven females, and three unknown) with oligohydramnios were treated from 2004 to 2011. Oligohydramnios was first diagnosed at a 21.6 ± 4.2 weeks gestation. Terminations of pregnancy before 22 weeks were identified in five cases, and intrauterine fetal deaths occurred in two cases. Ten neonates were born alive, five cases survived over 28 days, and five cases died within 48 hours. Prognostic factors for survival included birth weight (2,457 ± 480 grams in survivors *vs.* 1973 ± 124 grams in non-survivors; $p < 0.05$) and the mean amniotic fluid index (AFI) (2.32 ± 1.19 cm in survivors *vs.* 0.46 ± 0.68 cm in non-survivors; $p < 0.05$). *Conclusion:* All patients who survived had a mean AFI > 1.0 cm.

Key words: Amniotic fluid index; Kidney disease; Neonate; Oligohydramnios; Pulmonary hypoplasia.

Introduction

Severe oligohydramnios indicates significant global fetal renal dysfunction and is a risk factor for the development of pulmonary hypoplasia [1, 2]. Few data about early neonatal outcomes associated with severe oligohydramnios are available. This lack of data may be explained by the fact that termination of pregnancy (TOP) is still frequently practiced for fetuses with severe oligohydramnios [3].

Although recent progress in pulmonary management, as well as in treatment of infants with pulmonary hypoplasia and severe chronic kidney disease, has considerably improved the prognosis of infants with renal insufficiency [4-8], factors predictive of the prognosis of fetuses with severe oligohydramnios have yet to be elucidated. Amniotic fluid volume has long been considered the first prognostic factor of renal function from early gestation because fetal urine accounts for more than 80% of its production. Therefore, oligohydramnios is considered the primary indication to proceed with more invasive testing and the best predictor of poor prognosis [9]. To the best of the authors' knowledge, only a few studies have evaluated the role of amniotic fluid as a single predictor of short-term outcome after birth, and no conclusion has been reached.

The presence of antenatal oligohydramnios in infants does not always result in a poor prognosis [7, 10]. The aim of the present study was to identify predictive data on the short-term outcomes of fetuses with severe oligohydramnios.

Materials and Methods

A retrospective study of all pregnancies with oligohydramnios from January 2004 through December 2011 was performed. Outcomes included mortality and morbidity. The amniotic fluid index (AFI) was routinely measured at each gestational age. Dedicated and trained sonographers performed the sonographic examinations and calculated the AFI. Oligohydramnios was defined as a generalized reduction of amniotic fluid with an AFI of five cm or less during the course of gestation [9, 11]. In each case, the AFI was measured using the method described by Phelan *et al.* [11]. The AFI, gestational age, and fetal weight at the time of delivery were investigated. Cases with multiple anomaly syndrome, multiple-fetus pregnancy, and premature rupture of the membranes were excluded from the study.

Patients were divided into three groups. The survivors' group was defined as infant survival for more than 28 days. The non-survivors' group was defined as born alive but died within 28 days. The intrauterine fetal death (IUFD)/TOP group included fetuses that were terminated prior to 22 weeks' gestational age or IUFD. Clinical information, including sex, gestational age, birth weight, gestational weeks when oligohydramnios was first noted, respiratory outcome, presence of pneumothorax necessitating drainage of the cavity space, and the use of inhaled nitric oxide, was reviewed for each patient. Venous blood sampling, including pH, partial pressure of carbon dioxide (pCO_2) and base excess (BE), were investigated in neonates admitted to the neonatal intensive care unit (NICU). No cases had amnioinfusions during the prenatal period, and no patient required peritoneal dialysis in the neonatal period.

Statistical analysis

The distributions of data were tested using the Shapiro-Wilk test. If the data were normally distributed, the *t*-test was used. If the data were not normally distributed, the Mann-Whitney U test was used. Data are reported as means ± standard deviation. Differences

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Table 1. — *Patients' characteristics.*

Patient	Year	Sex	GA, weeks (diagnosis)	GA, weeks (delivery)	BW, g	AFI (cm)	Apgar score (1 and 5 min.)	Mother's age	Delivery method	Diagnosis	Pneumot-horax	NO therapy	Survival or death (days)
1	2011	Male	16	32	1868	1.3	1/5	33	CS	DK	Yes	Yes	Death (1)
2	2011	Male	20	36	3104	1.2	3/7	34	CS	HK	-	Yes	Survival
3	2011	Female	19	36	2019	0	4/8	30	Vaginal	RA	Yes	Yes	Death (1)
4	2011	/	17	18	-	1.0	-	32	TOP	RA	-	-	-
5	2011	Male	22	38	2830	3.7	8/9	39	Vaginal	HK	-	-	Survival
6	2010	Female	21	34	2040	2.1	8/8	31	Vaginal	DK	-	Yes	Survival
7	2010	Female	22	24	-	1.4	-	36	IUFD	21trisomy	-	-	-
8	2010	Male	21	35	1900	0	2/4	31	Vaginal	ARPKD	-	Yes	Death (1)
9	2010	/	20	21	-	0	-	29	TOP	RA	-	-	-
10	2009	Male	16	20	238	3.6	-	31	TOP	ARPKD	-	-	-
11	2009	/	18	20	-	0	-	31	TOP	ARPKD	-	-	-
12	2009	Female	27	34	2084	1.2	5/7	21	CS	ARPKD	Yes	Yes	Survival
13	2006	Female	28	34	2170	0	1/3	28	Vaginal	DK	-	-	Death (0)
14	2005	Male	31	39	2228	3.4	5/7	29	CS	DORV	-	-	Survival
15	2005	Female	25	26	684	0	-	37	IUFD	unknown	-	-	-
16	2004	Male	24	37	1907	1.0	8/8	30	CS	PUV	Yes	Yes	Death (2)
17	2004	Female	20	20	422	1.0	-	31	TOP	ARPKD	-	-	-

GA: gestational age; BW: body weight; AFI: amniotic fluid index; NO: nitric oxide; CS: cesarean section; IUFD: intrauterine fetal death; TOP: termination of pregnancy; DK: dysplastic kidney disease; ARPKD: autosomal recessive polycystic kidney disease; HK: hypoplastic kidney; RA: renal aplasia; PUV: posterior urethral valves.

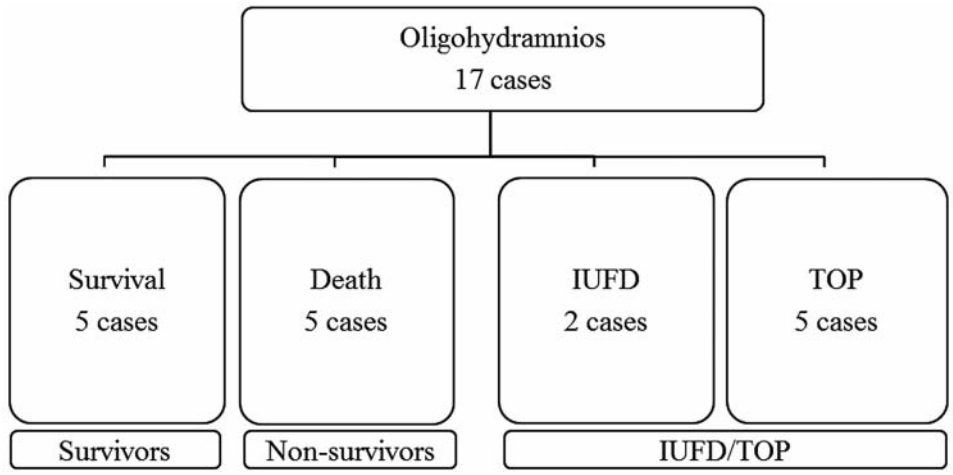

Figure 1. — Schematic presentation of 17 fetuses with oligohydramnios.

in patients' characteristics between survivors and non-survivors were evaluated by the chi-square test for categorical data. Probability values of less than 0.05 were considered significant. All data analyses were performed with a commercially-available statistical analysis software package (SPSS).

Results

Seventeen neonates (seven males, seven females, and three unknown) fulfilled the criteria and were included in the study. TOP before 22 weeks of gestation was performed in five cases, and IUFD occurred in two cases. Oligohydramnios was first diagnosed at 21.6 ± 4.2 weeks' gestation (range, 16–31). Details of the patients and their clinical course are shown in Table 1.

Causes of oligohydramnios were determined in 16 patients, and included autosomal recessive polycystic kidney disease (n=5), renal agenesis (n=3), hypoplastic kidney (n=2), bilateral dysplastic kidney (n=3), and posterior urethral valve (n=1). One patient was diagnosed with double outlet right ventricle, and another patient with trisomy 21, although the pathogenesis of oligohydramnios was not clearly demonstrated. No diagnosis was made in one patient.

Figure 1 presents the survivors, non-survivors, and IUFD/TOP patients with oligohydramnios. In ten live-born neonates, five cases survived over 28 days, while five cases died within 48 hours due to pulmonary and renal complications. All ten live-born neonates were admitted to the NICU and underwent ventilation therapy. All five deaths occurring

Table 2. — *Comparison between survivors and non-survivors.*

	Survivors (n=5)	Non-survivors (n=5)	*p-value*
Male/female	3/2	3/2	NS
Mother's age, years	30.8 ± 6.6	30.4 ± 1.8	NS
GA (at first diagnosis), weeks	24.2 ± 4.7	21.6 ± 4.6	NS
GA (at delivery), weeks	36.2 ± 2.9	34.8 ± 1.9	NS
Birth weight, grams	2457 ± 480	1973 ± 124	$P < 0.05$
C-section/vaginal delivery	3/2	2/3	NS
Apgar score (1 min.)	5	2	NS
Apgar score (5 min.)	7	5	NS
pH	7.18 ± 0.05	7.05 ± 0.11	NS
pCO_2, mmHg	63.6 ± 6.4	87.7 ± 22.1	NS
BE, mEq/L	-6.56 ± 3.22	-9.88 ± 2.07	NS
Hb, g/dL	14.2 ± 2.2	16.8 ± 1.3	NS
Creatinine, mg/dL	0.72 ± 0.18	0.70 ± 0.08	NS
Pneumothorax	1	3	NS
NO therapy	3	4	NS

GA: gestational age; pCO_2: partial pressure of carbon dioxide; BE: base excess; Hb: hemoglobin; NO: nitric oxide; NS: not significant.

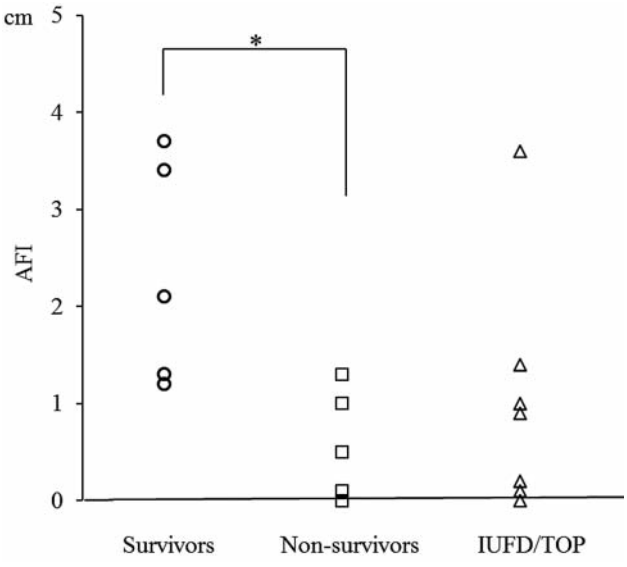

Figure 2. — Amniotic fluid index of survivors, non-survivors, and the intrauterine fetal death-termination groups. *$p < 0.05$.

in the neonatal period were due to respiratory failure within the first 48 hours of life; no cases were treated with dialysis.

Table 2 shows the associations between prenatal and postnatal variables and survival until discharge. Sex, mother's age, gestational age, and delivery method (cesarean section or vaginal delivery) were not significantly different between the survivors and non-survivors groups. No differences were found between survivors and non-survivors regarding the Apgar score (one minute), Apgar score (five minutes), pH, pCO_2, BE, hemoglobin, serum creatinine, pneumothorax, or inhaled nitric oxide therapy. No difference was observed in chest X-ray findings between survivors and non-survivors.

Prognostic factors for survival included birth weight (2,457 ± 480 grams for survivors *vs.* 1,973 ± 124 grams for non-survivors; $p < 0.05$). The data indicated that non-survivors were born with lower birth weight. Figure 2 shows the comparison of AFI data among the survivors, non-survivors, and IUFD/TOP groups. The AFI value was significantly different between the survivors and non-survivors groups (mean AFI 2.32 ± 1.19 cm in the survivors *vs.* 0.46 ± 0.68 cm in the non-survivors; $p < 0.05$), while no significant differences were seen between the IUFD/TOP group and either the survivors or non-survivors groups. All patients who survived beyond the neonatal period had a mean AFI > 1.0 cm.

Discussion

In this study, five out of ten live-born patients (50%) with severe oligohydramnios survived beyond the neonatal period. The present study indicates that a substantial percentage of fetuses with severe oligohydramnios could survive.

The AFI values were significantly greater ($p < 0.05$) in survivors than in non-survivors (Figure 2). Furthermore, all patients who survived beyond the neonatal period had a mean AFI > 1.0 cm. Therefore, an AFI value of 1.0 cm might be used as a cutoff value to discriminate survivors from non-survivors.

The earlier detection of a severe reduction in amniotic fluid, the more likely critical pulmonary hypoplasia is, and the early detection of oligohydramnios has long been regarded as an indicator of poor outcome [12, 13]. In recent studies, Klaassen *et al.* found that non-survivors had a significantly earlier diagnosis of oligohydramnios than survivors. A diagnosis of oligohydramnios prior to 30 weeks was associated with a higher overall mortality than that after 30 weeks gestation [7]. However, it is not clear if earlier diagnosis is correlated with poor outcome in the population diagnosed prior to 30 weeks. In the present study, gestational age at first diagnosis was 21.6 ± 4.6 weeks in non-survivors and 24.2 ± 4.7 weeks in survivors; although non-survivors were diagnosed earlier than survivors, the difference was not significant. In fact, some patients with a very early diagnosis (patients 2, 5, and 6 diagnosed at less than 22 weeks) survived. Therefore, if it is identified at an early gestational age, gestational age at first identification of oligohydramnios may not be correlated with poor outcome. This might indicate that amniotic fluid volume reflects kidney dysfunction with greater accuracy than early diagnosis of oligohydramnios in patients with severe oligohydramnios.

Prenatal assessment of lung volume might give useful information; however, some studies claimed that it did not contribute to prognostic information in oligohydramnios [14]. In the present study, the retrospective analysis of post-

natal chest radiographs for lung hypoplasia did not show a significant correlation with short-term outcome. The best oxygenation index of the first day was used as a surrogate marker for predicting outcomes of congenital diaphragmatic hernia patients [15]. Recently, Mehler *et al.* suggested that the best oxygenation index of the first day may be a reliable predictor of respiratory prognosis in children born with oligohydramnios [16]. These data could not be examined in the present study because all patients' oxygenation data were not available. The present data showed that pH, pCO_2, and BE data tended to be worse in non-survivors than in survivors; however, these differences were not significant.

The present study has some limitations. This was a retrospective analysis and the selected patient group was a small sample size. Additionally, as the predictive ability of the AFI to identity oligohydramnios was reported to be between 11% and 27% [17], the use of AFI to differentiate values is to be interpreted with caution. Nevertheless, AFI remains the most important factor when obstetricians evaluate the amniotic fluid of oligohydramnios patients. Therefore, despite its limitations, AFI remains a useful, inexpensive, and repeatable method of evaluating amniotic fluid that can be easily calculated in any ultrasonographic assessment.

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