Ultrasound Obstet. Gynecol. 7 (1996) 108–113

Outcome of singleton pregnancies with severe oligohydramnios in the second and third trimesters

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Key words: OLIGOHYDRAMNIOS, SECOND AND THIRD TRIMESTERS, SINGLETONS, OUTCOME

ABSTRACT

We evaluated the significance of severe oligohydramnios, or anhydramnios, in the second and third trimesters, by determining the range of etiologies as well as the differences in fetal and neonatal outcome. All prenatal ultrasound results on pregnancies found to have severe oligohydramnios over a 7.5-year period at 13–42 weeks' gestation were retrospectively collected. Follow-up results were obtained from review of medical records, autopsies and pathology reports. A total of 250 singleton pregnancies met the criteria of having severe oligohydramnios. A bimodal distribution in gestational age at diagnosis was seen, with more cases diagnosed at 13–21 weeks and at 34–42 weeks. Fetal abnormalities were present in 50.7% of those diagnosed with severe oligohydramnios in the second trimester and in 22.1% of those in the third trimester. There were 10.2% and 85.3% survivors when severe oligohydramnios was diagnosed in the second and third trimesters, respectively. The rate of aneuploidy was at least 4.4% for the entire singleton population. A bimodal distribution of pregnancies presenting with severe oligohydramnios represents two different naturally occurring populations in terms of both etiology and prognosis.

INTRODUCTION

Assessment of the presence or absence of oligohydramnios has been part of the prenatal sonographic evaluation for the past 15 years. Manning and colleagues[1] in 1981 initially showed the association of oligohydramnios with intrauterine growth restriction. Since that time, much work has focused on determining the association of oligohydramnios with various adverse obstetric outcomes.

Severe oligohydramnios represents the most extreme end of the spectrum of those pregnancies complicated by diminished amniotic fluid volume. The etiologies for the presence of severe oligohydramnios include fetal malformations (most often involving the genitourinary tract), premature rupture of membranes and placental insufficiency[2,3].

In this study, we sought to evaluate the significance of severe oligohydramnios in the second and third trimesters, by determining the range of etiologies as well as the differences in fetal and neonatal outcomes.

METHODS

The patient population attending our ultrasound facility is predominantly ambulatory and represents a mix of low- and high-risk patients, with treatments including a combination of routine scans and referrals for second opinion. We retrospectively collected all prenatal ultrasound results during a 7.5-year period, from February 1987 to July 1994, on singleton pregnancies found to have severe oligohydramnios on prenatal sonography. Pregnancies with intrauterine fetal demise at the time of diagnosis were excluded. All multiple pregnancies were excluded. The final study population included all singleton fetuses scanned between 13 and 42 weeks' gestation whose sonograms showed severe oligohydramnios and a live gestation, and for whom postnatal follow-up information was available.

Our criteria for the diagnosis of severe oligohydramnios, or anhydramnios, was based on the subjective evaluation of absence of amniotic fluid noted sonographically. Ultrasound examinations were performed using an Acuson 128XP-10 with a variable focus transducer of 3.5–5 MHz. Vaginal scans were performed as necessary for optimal imaging in the second trimester in patients without a

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Received 9-8-95
Revised 12-10-95
Accepted 12-11-95

history of ruptured membranes. Standard fetal biometry and detailed morphological assessment were performed at the time of the scan.

Follow-up information was obtained by review of the mothers' and infants' medical records as well as autopsies and placental pathology reports. This information included mode and gestational age at the time of delivery as well as infant weight, Apgar score and any malformations identified.

For the evaluation of the results, the patients were divided into groups by gestational age and the etiology for the oligohydramnios, including intrauterine growth restriction, premature rupture of membranes, placental abruption, anomalies and idiopathic oligohydramnios (presumed to be uteroplacental insufficiency, but without documented growth restriction). Intrauterine growth restriction was defined as a birth weight of less than the 10th centile for gestational age. The diagnosis of premature rupture of membranes was made by standard clinical assessment. Abruptio placentae was an obstetric diagnosis made clinically. The classification of anomalies was based on examination of newborns and pathological confirmation.

Statistical analysis was performed using the χ^2 or Fisher exact test, as appropriate. Differences were considered to be statistically significant when $p < 0.05$.

RESULTS

A total of 250 pregnancies met the criteria of having severe oligohydramnios diagnosed sonographically between 13 and 42 weeks, with postnatal follow-up information available.

Figure 1 shows the gestational age distribution at diagnosis of severe oligohydramnios in the singleton pregnancies. A bimodal distribution is seen with peaks at 13–21 weeks and 34–42 weeks. These fetuses were evaluated by trimesters.

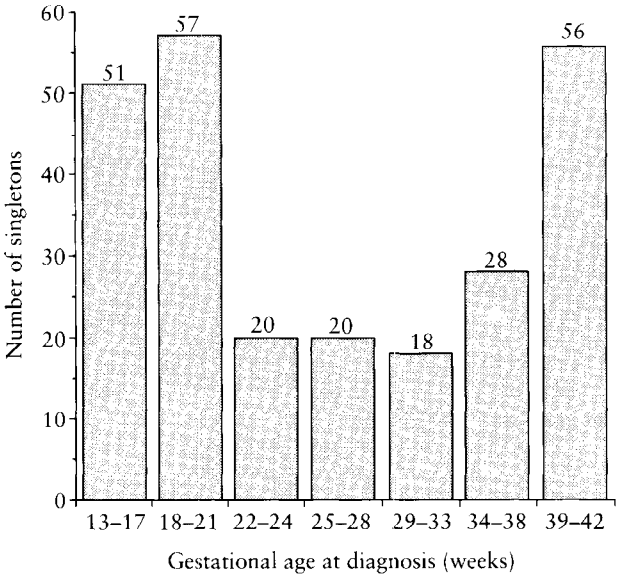

Figure 1 Gestational age distribution of singleton pregnancies with severe oligohydramnios from 13 to 42 weeks' gestation

Second-trimester diagnosis

There were 128 fetuses first noted to have severe oligohydramnios between 13 and 24 weeks (considered the second trimester). The postnatal diagnoses are shown in Figure 2. Of these second-trimester fetuses, 65 (50.7%) had fetal anomalies and only one survived – this fetus had bilateral mild–moderate hydronephrosis. Although most of the patients carrying these fetuses elected termination of pregnancy, the vast majority of the malformations in this category were considered to be lethal urinary tract anomalies. The distribution of the abnormalities in the fetuses of all trimesters is shown in Table 1. All but two fetuses with

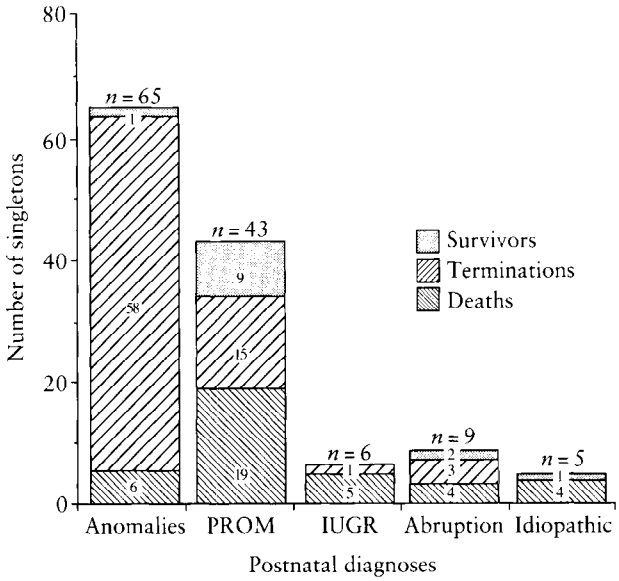

Figure 2 Number of second-trimester singletons classified according to postnatal diagnoses, divided into those who are survivors, those that underwent termination of pregnancy, and those that ended in spontaneous death. PROM, premature rupture of membranes; IUGR, intrauterine growth restriction

Table 1 Anomalies of singleton fetuses with oligohydramnios

	Gestational age (weeks)		
	13–24	*25–40+*	*Total*
Number of anomalies/total fetuses	65/128 (50.7%)	27/122 (22.1%)	92/250 (37%)
Potter's syndrome*	46	8	54
Infantile polycystic kidneys		5	5
Minor renal anomaly		1	1
Multiple anomalies	6		6
Posterior urethral valves	2	3	5
Skeletal anomaly	1		1
Central nervous system anomaly	1	2	3
Marfan's syndrome		1	1
Gastrointestinal anomaly		2	2
Body stalk defect	1		1
Hydrops/cystic hygroma	2		2
Aneuploidy	6	5	11

*Renal agenesis and other lethal renal abnormalities associated with oligohydramnios as characterized by Potter[4,5]

severe malformations were correctly identified sonographically as being anomalous. One was scanned at 14 weeks and, at termination at 16 weeks, was found to have omphalocele. The other was scanned at 22 weeks and was found at delivery to have a unilateral cleft lip and palate. The lack of amniotic fluid acoustic window presumably limited the sonographic structural survey.

Forty-three (33.6%) patients in the second trimester had premature rupture of membranes and nine of these fetuses survived (21%). Detailed information on the survivors is shown in Table 2. There were 19 fetuses with premature rupture of membranes who succumbed to fetal or neonatal death and 15 patients who elected termination of pregnancy subsequent to the diagnosis of premature rupture of membranes and severe oligohydramnios.

Half of the surviving fetuses with premature rupture of membranes had this complication after an amniocentesis. There were 15 patients who developed severe oligohydramnios after amniocentesis. Five (33.3%) subsequently re-accumulated fluid to a normal volume and all delivered liveborn infants. The other ten pregnancies continued to have severe oligohydramnios without re-accumulation of amniotic fluid and none of these pregnancies resulted in liveborns. There were 28 patients with premature rupture of membranes who did not have amniocentesis. Four (14.3%) of these fetuses survived, although none was found to have re-accumulation of fluid. There was no difference in the proportion of survivors between those who did and those who did not have amniocentesis (p, not significant). Two patients in the amniocentesis group, despite return of normal fluid, had limb position abnormalities on newborn examination.

Among the nine fetuses with abruption, only two survived (Table 2). There were six fetuses who were diagnosed as having intrauterine growth restriction in the second trimester, and there were no survivors. There were five fetuses with idiopathic oligohydramnios, one of which survived (also shown in Table 2). In summary, there were only 13 (10.2%) survivors of the total 128 second-trimester singleton pregnancies with severe oligohydramnios (Table 2).

Third-trimester diagnosis

There were 122 fetuses of 25–42 weeks (considered the third trimester) in our study; the breakdown of postnatal diagnoses for these fetuses is shown in Figure 3. Overall, there were 104 (85.3%) survivors of those diagnosed with severe oligohydramnios in the third trimester compared to 13/128 (10.2%) of those diagnosed in the second trimester ($p < 0.0001$). Unlike the second-trimester fetuses, the majority of pregnancies in the third trimester category had

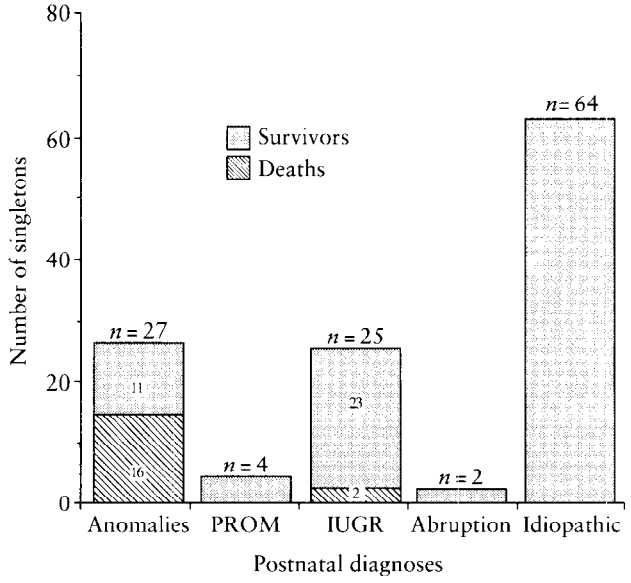

Figure 3 Number of third-trimester singletons classified according to postnatal diagnoses, divided into those who are survivors and those that ended in perinatal death. PROM, premature rupture of membranes; IUGR, intrauterine growth restriction

Table 2 Survivors with second-trimester severe oligohydramnios

Gestational age at diagnosis (weeks)	*Ultrasound findings*	*Diagnosis*	*Gestational age at delivery* (weeks)	*Neonatal findings*
13	normal survey	PROM, S/P amniocentesis	38	3570 g
14	normal survey	PROM, S/P amniocentesis	38	3140 g, RDS, positional abnormalities
14.5	normal survey	PROM, S/P amniocentesis	34	2150 g
16	normal survey	PROM, S/P amniocentesis	40	3060 g
19.5	normal survey	PROM, S/P amniocentesis	37	2300 g, positional abnormalities
22	normal survey	PROM	29	1040 g, left CL & P, BIH, UT
22.5	normal survey	PROM	34	2160 g, positional abnormalities
23	normal survey	PROM	26.5	
23	abnormal lower extremities	PROM	33	1530 g, RDS, skeletal abnormalities
15.5	mild hydronephrosis	anomaly	40	4380 g, hydronephrosis
19	normal survey	abruptio placentae	26	
21.5	large fundal abruption	abruptio placentae	33.5	
21.5	normal survey	idiopathic	36.5	2550 g

PROM, premature rupture of membranes; RDS, respiratory distress syndrome; CL & P, cleft lip and palate; BIH, bilateral inguinal hernias; UT, undescended testes; S/P, single puncture

idiopathic oligohydramnios tending to occur toward the late third trimester. Sixty-four of the 122 (52.5%) fetuses with idiopathic oligohydramnios were normally grown and did not have evidence of malformations at birth. These occurred primarily in term or post-term pregnancies.

Twenty-seven of the 122 third-trimester fetuses (22.1%) had malformations; 11 (40.1%) survived. There was a significant improvement in the survival of those with malformations in the third trimester compared to those diagnosed in the second trimester, 11/27 vs. 1/65 ($p < 0.0001$). Table 1 shows that the majority of malformations in the third-trimester group were genitourinary tract abnormalities.

The four third-trimester fetuses with premature rupture of membranes all survived. There was a significant improvement in the survival for those with rupture in the third trimester compared to those with rupture in the second trimester, 4/4 vs. 9/43, $p < 0.01$. Twenty-three (92%) of 25 fetuses diagnosed as having intrauterine growth restriction survived. Two patients had placental abruptions and delivered liveborns.

Most of the fetuses with idiopathic severe oligohydramnios in the third trimester were over 39 weeks and the vast majority were delivered within 24 h of their sonogram. There was a significant difference in Cesarean section rate in the idiopathic oligohydramnios of > 33 weeks; those women who delivered less than 1 day after their ultrasound examination (16/46; 34.7%) had a lower Cesarean section rate compared to those whose deliveries were delayed for more than 1 day (9/13; 69.2%; $p < 0.03$).

Table 3 is a summary of the delivery data on the 122 fetuses with third-trimester severe oligohydramnios. There was a high incidence of neonatal or intrauterine death among fetuses with anomalies, resulting in a perinatal mortality rate of 593 per 1000. In summary, the third-trimester fetuses with severe oligohydramnios appeared to have a perinatal mortality rate of 148 per 1000 and Cesarean section rate of 46%, with 5-min Apgar scores of less than 7 in 21% of cases.

Chromosomal abnormalities were found in six of the second-trimester fetuses and five of the third-trimester group (p, not significant comparing the proportions in the second- and third-trimester groups). Four fetuses had Turner's syndrome (45,X), two had Down's syndrome (47,+21), two had triploidy and one each had trisomy 18, ring 13 and 47,XXX. The rate of chromosomal abnormalities for the entire singleton population of our study was at least 4.4%. Not all fetuses had karyotyping, so the exact denominator is not known. All fetuses with documented aneupoloidy had abnormal sonographic features in addition to the severe oligohydramnios.

DISCUSSION

Assessment of amniotic fluid volume is an integral part of antepartum fetal evaluation. Much debate has centered around the best method of evaluating oligohydramnios sonographically and the definition of clinically significant oligohydramnios. Manning and colleagues[1] suggested the absence of a pocket of amniotic fluid of ≥ 1 cm in any dimension as the definition for oligohydramnios. Comparison of subjective and semi-quantitative estimates of amniotic fluid volume have shown that subjective assessment of amniotic fluid volume by experienced sonologists proved to have high inter- and intraobserver agreement and correlated well with the single largest amniotic fluid pocket measurement[6–8]. Our study used a subjective assessment of complete amniotic fluid absence as our criterion for severe oligohydramnios and represents the most extreme end of the spectrum of pregnancies complicated by decreased amniotic fluid.

There are several studies that have also evaluated the global effect of decreased amniotic fluid volume in pregnancy[2,9–11]. Bastide and associates[9] described 113 patients with severe oligohydramnios resulting in a perinatal mortality of 132/1000 and an incidence of major anomalies of 13.3%. Their study also demonstrated a bimodal distribution in gestational age of fetuses with severe oligohydramnios similar to that of our population. Shenker and co-workers[10] described 80 pregnancies complicated by severe oligohydramnios with a 49% survival rate overall. The survival rates were 84, 61 and 0% in fetuses with intrauterine growth restriction, premature rupture of membranes and renal anomalies, respectively. The survival rate in our study was very different in fetuses diagnosed with severe oligohydramnios in the second vs. the third trimester. The differences in etiologies and survival among all studies cited above as well as our study may be attributed to the differences in gestational age distribution of each population. Studies with a larger proportion of second- vs. third-trimester fetuses will have a higher perinatal mortality rate and/or more stringent criteria for the diagnosis of oligohydramnios.

Oligohydramnios can be subjectively divided into mild, moderate, severe and anhydramnios at 13–28 weeks, as shown by Moore and colleagues[12]. The most severe degrees

Table 3 Third-trimester oligohydramnios group delivery data

	Anomaly	*Idiopathic*	*IUGR*	*PROM*	*Abruption*	*Total*
Total patients	27	64	25	4	2	122
5-min Apgar score of < 7	18/27 (66.7%)	1/64 (1.6%)	4/25 (16%)	1/4 (25%)	2/2 (100%)	26/122 (21.3%)
Cesarean section rate	11/27 (40.7%)	26/64 (40.6%)	15/25 (60%)	2/4 (50%)	2/2 (100%)	56/122 (45.9%)
IUFD/neonatal death	16	0	2	0	0	18
PMR (per 1000)	593	0	80	0	0	148

IUGR, intrauterine growth restriction; PROM, premature rupture of membranes; IUFD, intrauterine fetal demise; PMR, perinatal mortality rate

of oligohydramnios correlated with worsening perinatal mortality and increased risk of pulmonary hypoplasia. In those with anhydramnios, none survived; pregnancies with severe oligohydramnios had a perinatal mortality eight times that of the group with moderate oligohydramnios[12]. Their conclusion was that complete anhydramnios was uniformly fatal in the second trimester, but that mild/moderate oligohydramnios may lead to intact fetal survival. Severe oligohydramnios in the second trimester and early third trimester was predictive of poor fetal outcome. Chamberlain and co-workers[6] showed similar results, suggesting that pregnancies with increasing severity of oligohydramnios had a higher incidence of intrauterine growth restriction, major congenital anomalies and perinatal mortality, when compared to those with normal amniotic fluid volume.

Intrauterine growth restriction is one of the most common complications associated with severe oligohydramnios[13,14]. Philipson and associates[13] reported that 40% of infants from pregnancies complicated by oligohydramnios were small for gestational age as compared with 8% without oligohydramnios. Golan and co-workers[14] reported a 24% incidence of intrauterine growth restriction from among 145 pregnancies complicated by second- or third-trimester oligohydramnios. In our study, the incidence of intrauterine growth restriction was 20.5% in the third trimester, although it was much lower in the second trimester, due to the large number of anomalous fetuses. Premature rupture of membranes represented one-third of second-trimester cases of oligohydramnios, whereas only 3% of those in the third trimester had premature rupture of membranes. This discrepancy was most probably due to our patient population, which was ambulatory and would not include third-trimester hospitalized patients with premature rupture of membranes. Hadi and associates[15] reported only a 6.7% survival of second-trimester fetuses with premature rupture of membranes vs. 89% survival in those fetuses with premature rupture of membranes in the third trimester. Moretti and Sibai[16] reported a perinatal survival rate of 13% in patients with premature rupture of membranes at less than 23 weeks' gestation and 50% in fetuses between 24 and 26 weeks. Our study showed a slightly better mid-trimester survival rate (21%) but not as high as that of Major and Kitzmiller[17], who described a 63% survival in 70 patients with premature rupture of membranes before 26 weeks.

The outcome for second-trimester pregnancies with severe oligohydramnios is reportedly dismal. The association with such pregnancies of an elevated maternal serum α-fetoprotein level is virtually always associated with abortion or perinatal death[18–22]. These fetuses have a high incidence of malformations, although, even in the absence of structural abnormalities, the perinatal mortality is high[18–22]. Several studies show that second-trimester fetuses with both severe oligohydramnios and fetal malformations do not survive[18–23]. Our study is consistent with these observations, with only one of 65 (1.5%) anomalous fetuses with severe oligohydramnios in the second trimester surviving. The outcome was better (41%) in third-trimester anomalous fetuses with severe oligohydramnios. This difference in survival rate may be due in part to the fact that most fetuses with Potter's syndrome were diagnosed at less than 24 weeks' gestation and that a number of the malformations diagnosed after 30 weeks were not renal in origin.

Our study shows that the population of fetuses with severe oligohydramnios presenting in the third trimester represents a different group from those with second-trimester oligohydramnios. The outcome was considerably better for the patients diagnosed with oligohydramnios after 24 weeks. Twenty-two per cent of those with third-trimester severe oligohydramnios had congenital anomalies, compared to 50% in the second-trimester group. An overwhelming majority (98%) of all other patients diagnosed with third-trimester severe oligohydramnios delivered liveborn infants. The majority of these patients had idiopathic oligohydramnios, most of which were at term. As no diagnosis was found adequately to explain the severe oligohydramnios, these patients are presumed to have had relative uteroplacental insufficiency not severe enough to produce a clinically recognizable growth disturbance. While most of these patients were delivered very soon after the diagnosis of severe oligohydramnios was made, over 10% were delivered more than 2 weeks after the sonogram. This was more common with earlier gestations, and almost one-half of those diagnosed with severe oligohydramnios at 34–38 weeks' gestation were delivered > 7 days after the sonogram. In our series, there were no mortalities in those with idiopathic severe oligohydramnios in the third trimester, although our overall gross perinatal mortality rate was 148/1000, similar to that noted by Bastide and colleagues[9]. We can speculate that most of the perinatal deaths may be attributed to other etiological factors rather than idiopathic ones in pregnancies complicated by severe oligohydramnios.

Our rate of aneuploidy in those with severe oligohydramnios was at least 4.4%. This was evenly distributed throughout the second and third trimesters. Since not all fetuses had karyotyping, the incidence of aneuploidy may be higher. All of these patients had anomalies noted on ultrasound scanning in addition to the severe oligohydramnios. Consideration should be given to karyotyping fetuses with congenital malformations and severe oligohydramnios in both the second and third trimesters.

Several limitations in our study should be mentioned. First, the patients scanned in our ultrasound laboratory represented a mix of low and high perinatal risk, some of whom were referred for questions on ultrasound screening. In addition, the vast majority of our patients were ambulatory. These two factors had an impact on our study population most probably resulting in a higher number of patients with anomalies and a decreased number of patients with premature rupture of membranes compared to a hospital-based practice. Second, the lack of a control group makes it impossible to reach clinically useful recommendations regarding timing for delivery, for example in third-trimester patients with severe oligohydramnios of idiopathic etiology. More study in this area would be

needed to provide guidelines, which are beyond the scope of this report.

Our study demonstrates a cross-section of second- and third-trimester pregnancies complicated by severe oligohydramnios in terms of etiology and outcome. On the basis of our data, there appears to be a bimodal distribution in the pregnancies presenting with severe oligohydramnios, with two naturally different populations of patients in terms of both etiology and prognosis associated with the oligohydramnios. The second-trimester pregnancies complicated by oligohydramnios of this magnitude had a 50% incidence of lethal malformations and an overall 90% mortality for the entire population at 13–24 weeks. The overall survival of the fetuses in the third-trimester group was 85%, with all but two of the deaths attributed to lethal renal anomalies. Even fetuses with growth restriction, premature rupture of membranes and abruption had a far better outcome when diagnosed in the third rather than the second trimester. It is likely that, although the data were gathered continuously throughout both trimesters, the bimodal distribution and different outcome for our cases in the second vs. the third trimester were due to the very different patient populations represented; most of the patients with lethal fetal malformations in the second trimester dropped out of the ongoing pregnancy pool, thus resulting in a very different population of patients with third-trimester severe oligohydramnios, many of whom probably had a late onset of amniotic fluid deficiency.

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