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Polyhydramnios is an independent risk factor for perinatal mortality and intrapartum morbidity in preterm delivery

Moshe Mazor[a,*], Fabio Ghezzi[a], Eli Maymon[a], Ilana Shoham-Vardi[b], Hillel Vardi[b], Rely Hershkowitz[a], Joseph R. Leiberman[a]

[a]*Department of Obstetrics and Gynecology, Soroka Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, P.O. Box 151, Beer-Sheva 84101, Israel*

[b]*Epidemiologic Unit, Soroka Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva 84101, Israel*

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Abstract

Objective: To investigate the clinical significance of polyhydramnios as a predictor of perinatal death and intrapartum morbidity in patients with preterm delivery. *Study design:* The study population consisted of 4211 patients with singleton gestation, intact membranes and preterm delivery (< 37 weeks). Two groups were identified and compared according to the sonographic assessment of the amniotic fluid volume: increased and normal amniotic fluid. Analyses were conducted for the entire cohort as well as for the cohort excluding from each group all cases with congenital malformations. Logistic regression was used to assess the unique contribution of polyhydramnios to mortality and morbidity in the presence of other known risk factors. *Results:* The prevalence of polyhydramnios among women who delivered preterm was 5% (210/4211) including and 3.7% (142/3818) excluding the cases of congenital malformations, respectively. Polyhydramnios was associated with a higher rate of diabetes, large for gestational age neonates, fetal malpresentation at delivery, previous perinatal death and with a lower Apgar score at 1 and 5 min. Polyhydramnios was an independent predictor of perinatal mortality and intrapartum morbidity. When adjusted for well recognized risk factors for perinatal mortality and intrapartum morbidity (e.g. diabetes, severe pregnancy induced hypertension, multiparity, congenital malformation, previous perinatal death, low gestational age at delivery), the presence of polyhydramnios significantly increased the rate of perinatal mortality (odds ratio (OR) 5.8; 95% confidence interval (CI) 3.68–9.11) and of intrapartum morbidity (OR 2.8; 95% CI 1.94–4.03). *Conclusion:* In the setting of preterm delivery, polyhydramnios is an independent risk factor for perinatal mortality and intrapartum complications even in the absence of congenital malformation and other conditions traditionally associated with increased perinatal mortality and morbidity.

Keywords: Polyhydramnios; Preterm delivery; Perinatal mortality; Intrapartum morbidity; Congenital malformation

1. Introduction

Preterm birth is the leading cause of perinatal morbidity and mortality worldwide [1]. A large body of evidence indicates that there is an association between the presence of intrauterine infection and premature delivery [2]. However, infection represents only a fraction of insults that may compromise the feto-maternal environment and lead to preterm labor and delivery [3]. Recently, Arias et al. suggested that vascular lesions of the placental bed and chronic villitis may play a role in the pathogenesis of utero-placental ischemia and consequently in the onset of preterm labor [4].

Another group of subjects with a potentially different mechanism for preterm birth consists of women with polyhydramnios. In this condition uterine overdistension may activate a uterine pressure sensitive system capable of initiating uterine contractility and labor [5,6]. This mechanism is invoked to explain the excess rate of premature delivery observed in multiple gesta-

* Corresponding author. Tel.: +972 7 400697; fax: +972 7 238529.

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tion [7,8]. To the best of our knowledge, the role of polyhydramnios as an etiologic risk factor for adverse perinatal outcome in the setting of preterm parturition has not been extensively investigated.

The purpose of this study was (1) to determine the prevalence of polyhydramnios in patients with preterm delivery and singleton gestation; (2) to describe the clinical and perinatal characteristics of these patients according to the amniotic fluid volume and the presence or absence of congenital malformations; (3) to explore the clinical significance of polyhydramnios in the context of perinatal death and intrapartum morbidity.

2. Materials and methods

The study population consisted of consecutive patients who delivered preterm neonates at the Soroka Medical Center between January 1, 1985 and December 31, 1993 with singleton gestation and intact membranes. Patients with unreliable menstrual history, inadequate clinical assessment of gestational age, lack of prenatal care (defined as less than three visits at any prenatal care facility), presence of oligohydramnios or gestational age at delivery < 23 weeks were not included in the study. A delivery was considered preterm if it occurred before 37 weeks of gestation. According to the amount of amniotic fluid two groups of patients were identified: increased and normal fluid volume. Amniotic fluid volume was ultrasonographically estimated and all examinations were obtained with a real time scanner equipped with a 3.5/5 MHz transducer of appropriate focal length. A subjective evaluation by experienced sonographers and/or sonologists or a single vertical measurement of an amniotic fluid pocket or the maximum vertical depth in each section of the amniotic cavity after dividing the uterus in four quadrants. The sum of the four measurements in each quadrant represented the amniotic fluid index (AFI) [9]. Polyhydramnios was defined as an AFI greater than 25 cm or a single pocket greater than 8 cm or as a subjective estimation of increased amniotic fluid volume. The gestational age was determined by a reliable recollection of last menstrual period (with a history of regular cycles, a rise in basal body temperature, a positive urine βHCG test before 6 weeks' gestation, a pelvic examination findings in the first trimester consistent with the stated length of amenorrhea, fetal heart rate determined by continuous wave Doppler ultrasonography before 14 weeks of gestations) confirmed by an ultrasonographic examination within 20 weeks' gestation or by first trimester sonographic measurement of crown-rump length. The results of the sonographic examinations were available to the clinicians managing the patients.

Moderate and severe pregnancy induced hypertension (PIH) were defined as a systolic blood pressure of ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg and systolic blood pressure ≥ 160 mmHg or a diastolic blood pressure ≥ 110 mmHg, respectively in two occasion at least 6 h apart after 20 weeks' gestation [11].

Patients were defined as having diabetes if gestational diabetes (class A) or insulin dependent diabetes (class B-R), as defined by White [12] were observed.

The newborns were considered large for gestational age or small for gestational age when the birthweight was above the 90th or below the 10th percentile, respectively, according to the gestational age at delivery [13]. Perinatal death was defined as the occurrence of a stillbirth or a neonatal death within 28 days of life. Intrapartum morbidity was considered as the presence of at least one of the following conditions: Apgar score at 1 min ≤ 3, Apgar score at 5 min ≤ 7, prolapse of cord, fetal distress, abruptio placenta, cesarean section and postpartum hemorrhage. Clinical chorioamnionitis was diagnosed in the presence of a body temperature elevation to 37.8°C and two or more of the following criteria: uterine tenderness, malodorous vaginal discharge, fetal tachycardia and maternal leukocytosis (white blood cell count $> 15\,000$ cell/mm^3) [14].

2.1. Statistical analysis

All statistical analysis was performed with SPSS package. Either Mann-Whitney U-test or Student t-test was used for comparisons of continuous variables whereas comparisons of proportions were performed with chi square test or Fisher's exact test as required. All univariate analyses were done according to the presence or absence of fetal congenital malformations. Logistic regression was used to investigate the multivariate regression relationships of polyhydramnios between both perinatal mortality and intrapartum morbidity and different response variables. The explanatory variables were maternal age, gestational age at delivery, parity, presence of severe PIH, diabetes, a history of previous perinatal death, congenital malformation, birtweight, induction of labor and of fetal malpresentation during labor.

3. Results

During the study period, a total of 76 513 patients delivered at our institution and 5156 (6.7%) deliveries were preterm (< 37 weeks). The total number of patients with polyhydramnios was 1546 (2.0%). When women with lack of prenatal care during the pregnancy and those with oligohydramnios were excluded, 4211 patients with singleton pregnancy, intact membranes and a preterm delivery (between 23 and 37 weeks)

Table 1
Maternal characteristics according to the amniotic fluid volume and presence or absence of congenital malformation

Variables	Excluding congenital malformations			Including congenital malformations		
	Normal amniotic fluid ($n = 3818$)	Increased amniotic fluid ($n = 142$)	Significance	Normal amniotic fluid ($n = 4001$)	Increased amniotic fluid ($n = 210$)	Significance
Maternal age (year, mean ± S.D.)	27.7 ± 6.6	29.8 ± 5.9	NS	27.8 ± 6.7	29.1 ± 6.3	NS
Gravidity (median, range)	2 (1–22)	4 (1–15)	NS	2 (1–22)	4 (1–15)	NS
Parity (median, range)	3 (1–20)	3 (1–14)	NS	3 (1–18)	3 (1–14)	NS
Bedouin subjects (n)	1291 (33.8%)	52 (36.6%)	NS	1377 (34.4%)	90 (42.9%)	$P < 0.02$
Chronic hypertension (n)	133 (3.5%)	8 (5.6%)	NS	144 (36.0%)	9 (4.3%)	NS
Diabetes class A (n)	179 (4.7%)	25 (17.6%)	$P < 0.00001$	193 (4.8%)	27 (12.9%)	$P < 0.00001$
Diabetes classes B to R (n)	70 (1.8%)	15 (10.6%)	$P < 0.00001$	78 (19.5%)	17 (8.1%)	$P < 0.00001$
Severe PIH (n)	251 (6.6%)	4 (2.8%)	NS	264 (6.6%)	4 (1.9%)	$P < 0.01$
Moderate PIH (n)	183 (4.8%)	10 (7.0%)	NS	190 (47.5%)	13 (6.2%)	NS
Previous perinatal death (n)	372 (9.7%)	21 (14.8%)	$P < 0.05$	409 (10.2%)	27 (12.9%)	NS

NS, not significant; S.D., standard deviation of the mean.

remained as the study population. Among these women, 4001 had normal amniotic fluid while 210 (5%) had polyhydramnios. The prevalence of polyhydramnios was significantly higher in patients who delivered a preterm neonate than in those who delivered at term (5% (210/4211) vs. 1.9% (1335/71357), $P < 0.001$).

In the study population the rate of congenital anomalies was significantly higher in women with polyhydramnios than in those with normal amniotic fluid volume (32.4% (68/210) vs. 4.6% (183/4001); $P < 0.0001$). Due to this difference between the two groups, the findings are reported for the entire cohort as well as for the cohort excluding the cases with congenital malformations. However, no significant difference was found in the proportion of congenital malformations attributed to abnormal karyotype between patients with polyhydramnios and normal amniotic fluid (3% (2/68) vs. 8.7% (16/183); $P = 0.19$).

Maternal characteristics according to the amniotic fluid volume and the presence of fetal malformations are presented in Table 1. Patients with polyhydramnios had an higher incidence of diabetes than those with normal amniotic fluid. There was a higher prevalence of previous perinatal death in patients with polyhydramnios than in those with a normal amniotic fluid volume only when cases without congenital malformations were considered. A comparison of the clinical and perinatal characteristics of patients with polyhydramnios and those with a normal amount of amniotic fluid is shown in Table 2. Apgar score at 5 min ≤ 3, abruptio placenta and the occurrence of intrapartum fetal death were significantly higher in patients with polyhydramnios only when the cases of congenital malformations were included in the analysis.

Univariate analysis indicated a significant association of gestational age, presence of congenital malformations, grand multiparity, birthweight, induction of labor, fetal malpresentation during labor and the presence of polyhydramnios with the occurrence of perinatal mortality (OR: gestational age = 0.64 (CI 0.62–0.66), $P < 0.00001$; presence of congenital malformations = 9.39 (CI 7.31–20.7), $P < 0.00001$; grand multiparity = 1.79 (CI 1.46–2.2), $P < 0.0001$; birtweight (100 g increments) = 0.77 (CI 0.76–0.79), $P < 0.0001$; induction of labor = 6.92 (CI 5.53–8.66), $P < 0.0001$; fetal malpresentation during labor = 2.27 (CI 1.81–2.85), $P < 0.00001$; polyhydramnios = 5.7 (CI 4.35–7.55), $P < 0.00001$). The presence of severe PIH, nulliparity, a history of previous perinatal death and maternal age greater than 35 years were not found to be significant predictors of perinatal death. On the other hand, the presence of diabetes had a significant protective effect on the occurrence of perinatal death (OR = 0.53 (CI 0.36–0.79), $P < 0.01$). When all these covariates were entered into a logistic regression model, the presence of polyhydramnios, gestational age at delivery, the presence of congenital malformations, grand multiparity, birthweight and induction of labor retained statistical significance as independent risks factors for perinatal mortality (Table 3). In this model, severe PIH and nulliparity were protective factors for perinatal mortality. To further explore the significance of the high odds ratio of induction of labor as a predictor for perinatal mortality, the same logistic regression model

Table 2
Clinical and perinatal characteristics according to the amniotic fluid volume and presence or absence of congenital malformations

Variables	Excluding congenital malformations			Including congenital malformations		
	Normal amniotic fluid ($n = 3818$)	Increased amniotic fluid ($n = 142$)	Significance	Normal amniotic fluid ($n = 4001$)	Increased amniotic fluid ($n = 210$)	Significance
Gestational age (week ± S.D.)	33.9 ± 3.04	33.6 ± 3.16	NS	33 ± 3.1	33.1 ± 3.2	NS
Birthweight (g ± S.D.)	2190 ± 636	2410 ± 893	NS	2163 ± 641	2186 ± 890	NS
Apgar 1 min (n)						
≤7	823 (21.6%)	48 (33.8%)	$P<0.001$	892 (22.3%)	89 (42.4%)	$P<0.00001$
≤3	332 (8.7%)	21 (14.8%)	$P<0.02$	375 (9.4%)	50 (23.8%)	$P<0.00001$
Apgar 5 min (n)						
≤7	326 (8.5%)	22 (15.5%)	$P<0.01$	363 (9.1%)	56 (26.7%)	$P<0.00001$
≤3	164 (4.3%)	8 (5.6%)	NS	184 (4.6%)	32 (15.2%)	$P<0.00001$
Antepartum fetal death (n)	165 (4.3%)	14 (9.9%)	$P<0.002$	190 (4.7%)	31 (14.8%)	$P<0.00001$
Intrapartum fetal death (n)	32 (0.8%)	3 (2.1%)	NS	43 (1.1%)	9 (4.3%)	$P<0.00001$
Neonatal death (n)	186 (4.9%)	13 (9.2%)	$P<0.05$	226 (5.6%)	47 (22.4%)	$P<0.001$
Previous Cesarean section (n)	479 (12.5%)	30 (21.1%)	$P<0.005$	505 (12.6%)	34 (16.2%)	NS
LGA neonates (n)	77 (2.0%)	27 (19.0%)	$P<0.00001$	82 (2.1%)	31 (14.8%)	$P<0.00001$
SGA neonates (n)	184 (4.8%)	6 (4.2%)	NS	211 (5.3%)	13 (6.2%)	NS
Prolapse of cord (n)	30 (0.8%)	2 (1.4%)	NS	30 (0.7%)	2 (1.0%)	NS
Cervical incompetence (n)	101 (2.6%)	6 (4.2%)	NS	104 (2.6%)	6 (2.9%)	NS
Cesarean section (n)	895 (23.4%)	46 (32.4%)	$P<0.02$	947 (23.7%)	58 (27.6%)	NS
Induction of labor (n)	334 (8.7%)	25 (17.6%)	$P<0.0005$	115 (2.9%)	11 (5.2%)	0.05
Meconium (n)	186 (4.9%)	8 (5.6%)	NS	204 (5.1%)	14 (6.7%)	NS
Fetal distress (n)	278 (7.3%)	15 (10.6%)	NS	297 (7.4%)	21 (10.0%)	NS
Abruptio placenta (n)	158 (4.1%)	10 (7%)	NS	164 (4.1%)	15 (7.1%)	$P<0.05$
Malpresentation (n)	463 (12.1%)	28 (19.7%)	$P<0.01$	497 (12.4%)	37 (17.6%)	<0.05
Clinical chorioamnionitis (n)	110 (2.9%)	4 (2.8%)	NS	117 (2.9%)	4 (1.9%)	NS
Postpartum hemorrhage (n)	16 (0.4%)	1 (0.7%)	NS	17 (0.4%)	1 (0.5%)	NS

NS, not significant; S.D., standard deviation of the mean; PIH, pregnancy induced hypertension; LGA, large for gestational age; SGA, small for gestational age.

was used to investigate the relationship with perinatal mortality excluding stillbirth (intrapartum and postpartum mortality only) as outcome variable. The odds ratio of polyhydramnios raised from 5.79 to 6.83 while the odds ratio of induction of labor was lower (2.64 vs. 13.75) but still significant (Table 3), and the presence of severe PIH became not significant.

When the occurrence of intrapartum morbidity was analyzed a significant relationship was found with all the independent variables except for a history of previous perinatal death and induction of labor. (OR: gestational age = 0.85 (CI 0.83–0.86), $P < 0.0001$; presence of congenital malformations = 1.77 (CI 1.39–2.25), $P < 0.00001$; grand multiparity = 1.21 (CI 1.04–1.42), $P < 0.02$; birtweight (100 g increments) = 0.89 (CI 0.88–0.90), $P < 0.0001$; fetal malpresentation during labor = 11.2 (CI 8.88–14.16), $P < 0.00001$; severe PIH = 4.09 (CI 3.17–5. 29), $P < 0.00001$; diabetes = 1.57 (CI 1.27–1.94), $P < 0.0001$; maternal age greater than 35 = 1.41 (CI 1.22–2.64), $P < 0.0001$; polyhydramnios = 2.21 (CI 1.53–2.6), $P < 0.00001$]). When these covariates were entered simultaneously into a multiple logistic model, polyhydramnios, severe PIH, diabetes, birtweight, fetal malpresentation, maternal age greater than 35 years, nulliparity, congenital malformation and gestational age at delivery were significantly correlated with the occurrence of intrapartum morbidity. (Table 4) Unlike the association found with perinatal mortality, when intrapartum morbidity is examined, induction of labor and grand multiparity were not significant.

Table 3
Relationship of various independent variables with the occurrence of perinatal mortality

Independent variable	Total cases			Excluding cases with antepartum death		
	OR	95% CI	Significance	OR	95% CI	Significance
Polyhydramnios	5.79	3.68–9.11	$P<0.00001$	6.82	3.97–11.73	$P<0.00001$
Gestational age at delivery (weeks)[b]	0.76	0.71–0.82	$P<0.00001$	0.66	0.61–0.73	$P<0.00001$
Congenital malformations	7.91	5.31–11.78	$P<0.00001$	11.99	7.61–18.92	$P<0.00001$
Severe PIH	0.31	0.18–0.54	$P<0.00001$	0.52	0.26–1.07	NS
Grand multiparity[a]	2.32	1.60–3.37	$P<0.00001$	2.34	1.47–3.74	$P=0.004$
Birthweight (100 g increments)	0.87	0.84–0.90	$P<0.00001$	0.92	0.86–0.97	$P=0.004$
Induction of labor	13.75	9.51–19.89	$P<0.0001$	2.64	1.39–5.06	$P=0.03$
Nulliparity	0.69	0.51–0.95	$P=0.02$	0.73	0.49–1.08	NS
Previous perinatal death	1.75	0.85–3.57	NS	1.38	0.59–3.23	NS
Maternal age[a]	0.79	0.54–1.16	NS	0.69	0.49–1.08	NS
Fetal malpresentation	1.25	0.89–1.75	NS	1.25	0.85–1.86	NS
Diabetes	0.69	0.38–1.24	NS	0.84	0.4–1.67	NS

NS, Not significant; PIH, pregnancy induced hypertension.
[a] Variables were dichotomized: grand multiparity (<5 children vs. ≥5 children), maternal age (<35 years vs. ≥35 years).
[b] Variables were entered as continuous values.

4. Comment

The results of our study indicate that the prevalence of polyhydramnios is significantly higher in patients with preterm delivery than in those with term delivery (5% vs. 1.9%). Overall, the prevalence of polyhydramnios during the study period was 2.1%. This rate is similar to that previously reported by other investigators using similar semiquantitative sonographic techniques [15–17]. However, when increased amniotic fluid volume is defined under weaker criteria, the rate of polyhydramnios has been reported to be up to 8.2% [18]. The high prevalence of polyhydramnios in patients who deliver prematurely is of particular interest since both conditions have a synergic negative effect on pregnancy outcome [1–3,10,19].

Table 4
Relationship of various independent variables with the occurrence of intrapartum morbidity

Independent variable	OR	95% CI	Significance
Polyhydramnios	2.79	1.94–4.03	$P<0.00001$
Severe PIH	6.92	5.05–9.49	$P<0.00001$
Diabetes	2.32	1.75–3.07	$P<0.00001$
Birthweight (100 g increments)	0.91	0.90–0.93	$P<0.00001$
Fetal malpresentation	10.37	8.09–13.29	$P<0.00001$
Maternal age[a]	1.44	1.16–1.8	$P=0.001$
Nulliparity	0.75	0.63–0.91	$P=0.003$
Congenital malformations	1.63	1.17–2.30	$P=0.042$
Gestational age at delivery (weeks)[b]	0.95	0.91–1	$P=0.045$
Grand multiparity[a]	1.07	0.85–1.36	NS
Induction of labor	0.76	0.56–1.05	NS
Previous perinatal death	0.92	0.57–1.52	NS

NS, not significant; PIH, pregnancy induced hypertension.
[a] Variables were dichotomized: grand multiparity (<5 children vs. ≥5 children), maternal age (<35 years vs. ≥35 years).
[b] Variables were entered as continuous values.

The present study indicates that preterm parturition complicated by polyhydramnios is associated with a significant increased risk for perinatal mortality and intrapartum morbidity. These findings remain significant after adjusting for conditions known to be strongly associated with intrapartum morbidity and mortality (Tables 3 and 4). Diabetes mellitus is a common complication of pregnancy, traditionally associated with polyhydramnios and adverse perinatal outcome [20]. Indeed, we found among patients with polyhydramnios, a significantly higher incidence of diabetes (both A and B-R) than among those with normal amniotic fluid (Table 1). However, the presence of diabetes was not associated with higher perinatal mortality in the multivariate model. A possible explanation can be the intense surveillance of maternal glycemic status and fetal well being during pregnancy and delivery in our institution.

An interesting finding of this study is the higher risk for perinatal mortality observed in newborns delivered following an induction of labor. It is clear that this increased risk may be partially explained by the indications that lead to induction of labor. Any induction of labor in patients at a gestational age less than 37 weeks has an intrinsic high risk of perinatal mortality and morbidity and therefore termination of pregnancy is the optimal compromise between fetal survival and maternal well being.

We did not find a relationship between the presence of severe PIH and both intra- and postpartum mortality whereas severe PIH had, after fetal malpresentation, the strongest relationship with the occurrence of intrapartum complications (OR = 6.92) among the variables

that we considered of value in determining an increased intrapartum morbidity. The reason for this is that conditions such as abruptio placenta, postpartum hemorrhage, fetal distress and the need for a cesarean section (e.g. intra uterine growth retardation, poor uteroplacental perfusion) are complications more frequently associated with the delivery of patients with severe PIH than that of normotensive women [21]. Patients with severe PIH were strictly monitored immediately after admission, and treated with antihypertensive and anticonvulsant agents. The treatment of the mother and the intensive neonatal care of the newborns are the most probable explanations for the absence of a relation between severe PIH and intra- and postpartum mortality.

The major finding of this study is that, in patients with preterm parturition, polyhydramnios is the second most important variable, after congenital malformation, that contributes to intra- and post-partum mortality. Indeed, polyhydramnios increases the risk of perinatal mortality of almost 6-fold when other important causes are adjusted for (Table 3). Additionally, polyhydramnios remains a strong contributor to intrapartum morbidity with an OR of 2.8 after correcting for other potential variables (Table 4). Future studies are needed to explore the etiology and the mechanisms responsible for the negative effects that polyhydramnios has on the outcome of preterm parturition. Furthermore, a different approach to the management of patients with preterm delivery and pohyhydramnios is needed. Anecdotal studies have demonstrated that repeated evacuative amniocenteses are useful to prolong the duration of pregnancy [22–24]. Other investigators have administered indomethacin and achieved a significant decrease in the amount of amniotic fluid [25,26]. Nevertheless, the risks associated with these modalities of treatment (e.g. abruptio placenta, rupture of membranes, narrowing of the ductus arteriosus, renal impairment) have not been fully investigated.

In conclusion, our study clearly demonstrates that polyhydramnios in preterm parturition plays a major role in determining perinatal mortality and intrapartum complications. We have shown that the damaging effect of polyhydramnios is not a secondary phenomenon related to other types of maternal pathologic conditions traditionally linked to perinatal morbidity and mortality. The possibility of treatment of patients presenting with idiopathic polyhydramnios in the second half of pregnancy has to be investigated in the hope of improving maternal and perinatal outcome.

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