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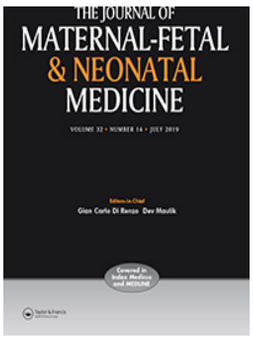

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Induction of labor in cases of late preterm isolated oligohydramnios: is it justified?

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ABSTRACT

Objectives: To analyze in a retrospective cohort study the outcomes of pregnancies with isolated oligohydramnios at the late preterm period (34–36.6 weeks of gestation).

Study design: This retrospective cohort study included three groups of women: (1) Women with isolated oligohydramnios whose pregnancy was managed conservatively ($n = 33$ births); (2) women with isolated oligohydramnios who were managed actively (i.e. induction of labor) ($n = 111$ births); and (3) a control group including women with normal amount of amniotic fluid who had a spontaneous late preterm delivery ($n = 10{,}445$ births). Maternal and fetal characteristics and obstetrics outcomes were collected from a computerized database of all deliveries at Soroka University Medical Center during the study period.

Results: Our cohort included 10,589 births. The rate of inducing labor was higher in the oligohydramnios groups compared to the controls ($p < .001$). There was an increase in the rate of cesarean section (CS) in the conservative treatment group ($p < .001$), compared with the other groups. Conservative management was associated with higher rates of maternal infection ($p = .026$), chorioamnionitis ($p = .01$), and transitory tachypnea of the newborn ($p = .02$). After controlling for confounding factors, mal presentation (OR = 19.9), and a prior CS (OR = 2.4) were independently associated with an increased risk for CS, while induction of labor was associated with a reduced risk for CS (OR = 0.28).

Conclusions: Women with late preterm isolated oligohydramnios had a higher rate of induction of labor than women with a normal amount of amniotic fluid. Induction of labor seems to be beneficial to both the neonate and the mother as seen by a lower rate of CS conducted in this group, as well as lower maternal and neonatal morbidity in comparison to the conservative group. Therefore, women with oligohydramnios at late preterm may benefit from induction of labor.

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Isolated oligohydramnios; induction of labor; cesarean section; neonatal and maternal complications

Introduction

The dynamics of the amniotic fluid volume (AFV) during gestation are complex and not entirely understood. Abnormal amounts of amniotic fluid in either direction might be associated with potentially deleterious effects on pregnancy outcomes [1]. Oligohydramnios is thought to complicate 0.5–5.5% of all pregnancies, depending on the definition that is used and the population under study [2–4]. The most commonly used definition for oligohydramnios is an amniotic fluid index (AFI) ≤ 5 cm or the largest vertical pocket measuring ≤ 2 cm [5].

Oligohydramnios without any evidence of anatomical, functional, or chromosomal abnormalities is termed as isolated oligohydramnios [6]. It is usually thought to result from hypoxemia that is most probably due to placental under perfusion that leads to decreased fetal urine production [7]. The correct management of isolated oligohydramnios (IO) is still debatable. During the 1980s, following reports that oligohydramnios is associated with increased risk of pregnancy adverse outcomes; induction of labor became the standard of care of these pregnancies [8]. However, since then controversy arose with regard to whether isolated oligohydramnios by itself has a potential impact on pregnancy

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outcome [9]. Several studies reported an increased risk for cesarean section (CS) due to nonreassuring fetal heart rate, lower Apgar scores, and a higher rate of neonatal intensive care unit admission (NICU) [10–12]. On the other hand, others suggested that perinatal outcome in cases of isolated oligohydramnios is comparable to that of pregnancies with normal amniotic fluid [6,13–16]. Furthermore, it has been suggested that the higher rate of adverse pregnancy outcomes in cases of isolated oligohydramnios results from the medical interventions (i.e. labor induction and CS) rather than the oligohydramnios by itself [17,18].

The diagnosis of oligohydramnios alters pregnancy management and may be an indication for delivery [19]. The issue of treating isolated oligohydramnios is still unclear, indeed, in a survey conducted among 632 members of the Society for Maternal-Fetal Medicine published in 2009, approximately 80% of the participants believed that induction of labor, in cases of isolated oligohydramnios, did not reduce perinatal morbidity, or they did not know whether it did. However, despite being unsure of its benefits, 96% of the practitioners leaned toward intervention in this setting [19]. Considering the fact that induction of labor at preterm (compared with induction at term) is complicated by an increased risk for prematurity-related complications [20] and by a higher rate of induction failure [21], it is important to delineate the risks of oligohydramnios and the benefits of prompt delivery [1,22].

We aimed to analyze in a retrospective cohort study the outcomes of pregnancies with isolated oligohydramnios at the late preterm period (34–36.6 weeks of gestation).

Materials and methods

Study population

This retrospective population-based cohort study included all singleton deliveries that occurred from 34 to 36.6 weeks of gestation at the Soroka University Medical Center (SUMC) between the years 1991–2011. SUMC is a tertiary medical center that serves the population of the Negev region and all hospital deliveries in this region take place in its labor and delivery suites. We excluded pregnancies complicated by any of the following conditions: preeclampsia, fetal anatomical malformations and chromosomal abnormalities, preterm prelabor rupture of membranes (PPROM), gestational diabetes mellitus, and fetal growth restriction.

Individual personal, obstetric and clinical data were collected from the electronic computerized database of SUMC. The information was captured from patient medical records and coded by trained secretaries according to the International Classification of Diseases, 9th edition (ICD-9) diagnosis. The study was approved by the Institutional Review Board Committee of SUMC.

We included all singleton pregnancies diagnosed with isolated oligohydramnios following a definition of amniotic fluid index [AFI] < 5 cm at $34+0$ to $36+6/7$ weeks of gestation after sonographic evaluation in the ultrasound unit of a university-affiliated tertiary hospital. Data were compared with a control group consisting of low-risk preterm pregnancies with normal levels of amniotic fluid (AFI 5–25 cm) based on sonographic evaluation in the same ultrasound unit, matched to the study group by gestational age.

The study population was divided into three groups based on the amount of amniotic fluid and the clinical management. (1) Conservative management (33 pregnancies) included women with isolated oligohydramnios that were followed as inpatients and were allowed to deliver spontaneously without medical intervention, aside inpatient surveillance of maternal, and fetal status; and (2) active management (111 pregnancies) included women that underwent induction of labor at the discretion of the attending physician. The control group included 10,445 low-risk late preterm pregnancies with normal amounts of amniotic fluid.

The outcomes tested in our study included mode of delivery, delivery complications (i.e. abruption, prolapse of cord) maternal infectious morbidity (chorioamnionitis – defined by its clinical criteria that includes fever, uterine fundal tenderness, maternal tachycardia $>$100/min, fetal tachycardia $>$160/min, and purulent or foul amniotic fluid [23,24], endometritis), and non-chorioamnionitis related infection perinatal outcome in terms of mortality, fetal status (nonreassuring fetal heart tracing) birth asphyxia, neonatal complications including neonatal infectious morbidity (sepsis, infection).

Statistical analysis

Categorical variables were analyzed using Pearson's chi-square and Fisher's exact tests. Normally distributed quantitative variables were analyzed with either *T*-test or one-way ANOVA. Not normally quantitative variables were processed using Mann–Whitney or Kruskal–Wallis tests.

Logistic regression was conducted to test the association between CS and the management options, including the three study groups. The models were adjusted for a history of CS, mal presentation, and nonreassuring fetal heart rate (NRFHR). We then

Table 1. Maternal demographic characteristics.

Characteristics	Control ($n = 10,445$)	Oligohydramnios		p Value
		Conservative management ($n = 33$)	Active management ($n = 111$)	
Maternal age	28.51 ± 6.2	28.3 ± 6.46	27.82 ± 6.4	.503
Ethnicity (Bedouin origin)	53.5 (5586)	48.5 (16)	59.5 (66)	.381
Gravidity	3 (1;21)	3 (1;14)	2 (1;11)	.015
Parity	3 (1;18)	2 (1;12)	2 (1;11)	.013
History of preterm deliveries	15.2 (1583)	12.4 (4)	10.8 (12)	.436
Infertility treatment	2.9 (306)	3 (1)	4.5 (5)	.452
History of SGA	0.1 (12)	0	0	.352

Data are presented as mean ± standard deviation, percentage (number), median (25–75 percentiles).
SGA: Small-for-gestational-age.

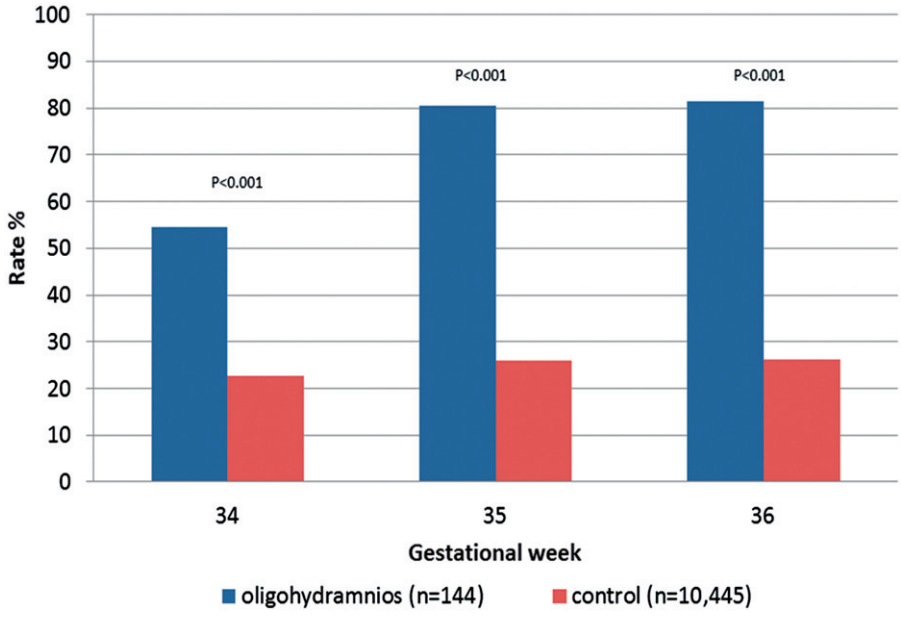

Figure 1. Induction of labor rate according to gestational age at delivery.

repeated our models only among deliveries with isolated oligohydramnios. The statistical analyses were performed using IBM Statistics SPSS (version 20), and statistical significance was determined as p value $<.05$.

Results

Of the total 14,080 late preterm births that underwent sonographic evaluation during the study period, 10,589 pregnancies met the inclusion criteria. 144 (1.5%) women had isolated oligohydramnios and were divided into two groups: Conservative management 22.9% (33/144) and active management 77.1% (111/144) pregnancies.

Table 1 presents the demographic characteristics of the patients included in our study. Women in the control group had a higher median gravidity ($p = .015$) and parity ($p = .013$) compared to the active management group. No significant differences were found among the study groups regarding maternal age, ethnicity, history of preterm deliveries or small-for-gestational-age neonates, and the use of assisted reproductive technologies.

Women with oligohydramnios had a higher rate of labor induction than those in the control group (77 versus 25% respectively; $p < .001$) (Figure 1). The study examined four different modes of inducing labor: transcervical Foley Catheter, oxytocin, prostaglandin, and amniotomy. Transcervical Foley Catheter was the preferred method in the active management group (52.3%); while the use of amniotomy was more prevalent in the control group (7%). In both the groups, oxytocin was used for induction and augmentation (active-74.8%, control-18.3%). Women in the isolated oligohydramnios group who were managed conservatively had a higher rate of CS compared to the other study groups ($p < .001$) (Figure 2). Women in the conservation management group had a higher rate of chorioamnionitis ($p = .01$) and maternal infection ($p = .026$) than those in the control group. Other maternal complications did not differ between the groups (Table 2).

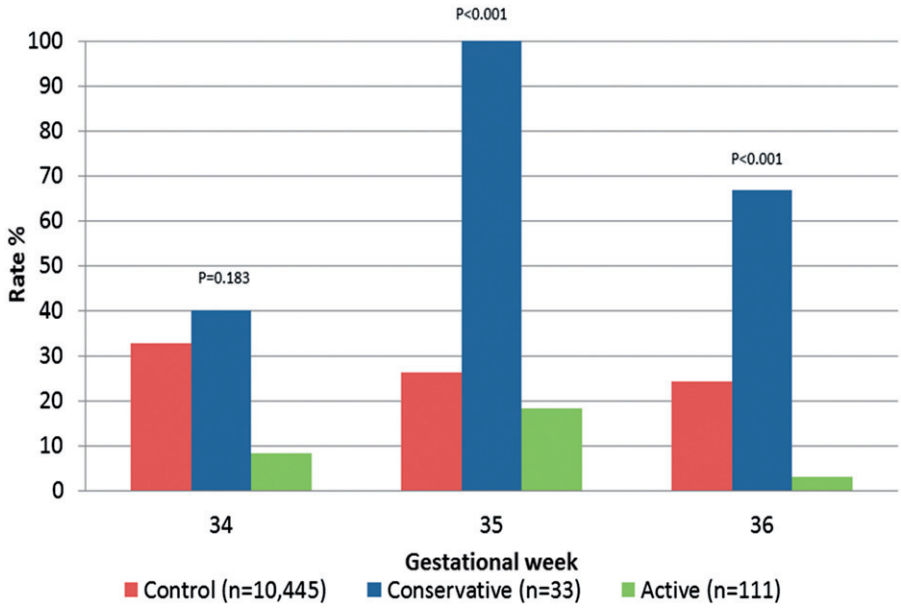

Figure 2. Cesarean section rate according to gestational age at delivery.

Table 2. Pregnancy characteristics and complications.

		Oligohydramnios		
Characteristics	Control ($n = 10,445$)	Conservative management ($n = 33$)	Active management ($n = 111$)	p Value
Mode of delivery				
Cesarean section	25.8 (2690)	66.7 (22)	8.1 (9)	<.001
Vacuum delivery	1.8 (192)	0 (0)	0.9 (1)	.851
Vaginal delivery	72.4 (7562)	33.3 (11)	91 (101)	<.001
Mode of induction				
Transcervical Foley Catheter (Embrey)	4.5 (468)	0 (0)	52.3 (58)	<.001
Oxytocin	18.3 (1909)	0 (0)	74.8 (83)	<.001
Prostaglandin	2.9 (301)	0 (0)	21.6 (24)	<.001
Amniotomy	7 (735)	0 (0)	22.5 (25)	<.001
Interval to delivery	0 (0–1)	7 (4.5–14)	2 (1–5)	<.001
Blood transfusion	2.8 (289)	0 (0)	1.8 (2)	.909
Maternal anemia	3.6 (381)	3 (1)	5.4 (6)	.454
Chorioamnionitis	1.8 (190)	9.1 (3)	3.6 (4)	.01
Infection	8.6 (903)	21.2 (7)	11.7 (13)	.026
Incomplete placenta	1.2 (121)	0 (0)	0.9 (1)	1
Adherent placenta	0.8 (83)	0 (0)	0.9 (1)	.685
Maternal bleeding	0.5 (48)	0 (0)	0	1
Hysterectomy	0.1 (6)	0 (0)	0	1
Rupture of uterus	0.1 (15)	0 (0)	0	1
Placental abruption	2.4 (251)	6.1 (2)	0.9 (1)	.185

Data are presented as percentage (number), median (25–75 percentiles).

Neonatal outcome is presented in Table 3. The rate of Apgar score <5 at 1 min and <7 at 5 minutes, neonatal acidosis, birth asphyxia, and mortality did not differ among the study groups. Neonates of women in the conservative group had higher rate of Transient Tachypnea of the Newborn (TTN) ($p = .028$) and longer period of hospitalization ($p = .002$) compared to the other two groups. In comparison to the control group, neonates of women who were managed conservatively had a lower mean birthweight ($p < .001$), and those of women who were managed actively had a higher rate of SGA neonates ($p < .001$). The rate of neonatal fever was higher in neonates of women who were included in the active management group in comparison to the other study groups ($p = .038$) (Table 3).

We then evaluated potential risk factors for CS among the study population. Malpresentation was found to be statistically higher in the conservative group compared to the control group ($p = .001$). The rate of meconium-stained amniotic fluid rate was higher in the active group ($p = .007$) (Table 4).

Table 3. Neonatal characteristics and complications.

		Oligohydramnios		
Characteristics	Control ($n = 10,445$)	Conservative management ($n = 33$)	Active management ($n = 111$)	p Value
Gestational age (weeks)	3635.49 ± 0.0715	3535.15 ± 0.87	3635.49 ± 0.686	.052
Birthweight (g)	2646 ± 434.562	2371.33 ± 334.053	2392 ± 365.6	<.001
Apgar $1' < 5$	6.4 (665)	3 (1)	5.4 (6)	.650
Apgar $5' < 7$	4.2 (442)	3 (1)	5.4 (6)	.817
pH < 7	0 (0)	0 (0)	0 (0)	n/a
Neonatal gender (Male)	53.4 (5578)	63.6 (21)	46.8 (52)	.194
SGA	3.7 (390)	3 (1)	12.6 (14)	<.001
AGA	81 (8461)	93.9 (31)	83.8 (93)	<.001
LGA	12.3 (1282)	0 (0)	0.9 (1)	<.001
APD	1.3 (137)	0 (0)	3.6 (4)	.128
IPD	0 (0)	0 (0)	0 (0)	n/a
PPD	0.3 (29)	0 (0)	0.9 (1)	.337
Jaundice	19 (1924)	21.9 (7)	22.5 (25)	.586
Fever	19 (1930)	12.5 (4)	27.9 (31)	.038
Transient tachypnea of the newborn	7.7 (776)	18.8 (6)	4.5 (5)	.028
Hypoglycemia	5.1 (520)	12.5 (4)	6.3 (7)	.147
Respiratory distress syndrome	2 (202)	0 (0)	2.7 (3)	.732
Blood transfusion	1.6 (159)	0 (0)	2.7 (3)	.553
Asphyxia	1.8 (182)	6.2 (2)	2.7 (3)	.089
Antibiotics transfusion	20.5 (2080)	18.8 (6)	18.9 (21)	.891
Hemolytic disorder	0.5 (48)	0 (0)	0.9 (1)	.497
Acidosis	1.7 (175)	0 (0)	0.9 (1)	1
Chorioamnionitis affecting fetus	0.1 (9)	0 (0)	0	1
Anemia	0.2 (16)	0 (0)	0	1
Cardiogenic shock	0	0 (0)	0	1
Infection	0.4 (38)	0 (0)	0	1
Hospitalization (days)	3 (0; 30)	5 [1,14]	2 (0; 25)	.002

Data are presented as mean ± standard deviation, percentage (number), median (25–75 percentiles).
SGA: small-for-gestational-age; AGA: appropriate for gestational age; LGA: large-for-gestational-age; APD, antepartum death; IPD: intrapartum death; PPD: postpartum death; n/a: not applicable.

Table 4. Risk factors and indications for cesarean delivery.

		Oligohydramnios		
Characteristics	Control ($n = 10,445$)	Conservative management ($n = 33$)	Active management ($n = 9$)	p Value
Past cesarean section	11.5 (309)	9.1 (2)	11.1 (1)	1
Malpresentation	27.4 (737)	63.6 (14)	22.2 (2)	.001
Arrest of dilatation	3.9 (104)	0 (0)	11.1 (1)	.334
Arrest of descent	0.6 (16)	0 (0)	0	1
NRFHR	5.8 (156)	9.1 (2)	0	.633
Placental abruption	6.5 (174)	4.5 (1)	11.1(1)	.544
Umbilical cord prolapse	1.4 (39)	0 (0)	11.1 (1)	.161
Meconium-stained amniotic fluid	4.5 (120)	0 (0)	33.3 (3)	.007

Data are presented as percentage (number).
NRFHR: nonreassuring fetal heart rate.

We constructed a logistical regression model to assess the association between the management of late preterm pregnancies complicated with oligohydramnios and the risk for CS, as compared to the control group. Conservative management of oligohydramnios in late preterm was associated with an independent higher risk for CS (OR 2.43; CI 1–5.85) and active management of isolated oligohydramnios at late preterm was associated with a lower risk for CS (OR 0.28; CI 0.13–0.59), compared to the control group (Table 5). When repeating the model only among women with isolated oligohydramnios we found that active management was independently associated with a substantially lower risk for CS (OR 0.9; CI 0.02–0.28), compared to conservative management (Table 6).

Discussion

Our findings suggest that active management (i.e. induction of labor) of women diagnosed with late preterm isolated oligohydramnios is associated with reduced rate of CS and maternal and neonatal complications in comparison to the conservative management. We also found that neonates of women in the conservative group had higher rates of TTN and longer hospitalization as compared to the active management and the control group. Nevertheless, neonates in the

Table 5. Multivariate assessment of risk factors for cesarean section in the whole study population.

Variable	Adjusted OR (95%CI)
Conservative management of oligohydramnios	2.43 [1–5.85]
Active management of oligohydramnios	0.28 [0.13–0.59]
Past cesarean section	8.07 [6.48–10.04]
Malpresentation	19.91 [16.64–23.81]
NRFHR	n/a
Meconium-stained amniotic fluid	n/a

n/a: not applicable; NRFHR: nonreassuring fetal heart rate.

Table 6. Multivariate assessment of risk factors for cesarean section related only to the isolated oligohydramnios group.

Variable	Adjusted OR (95%CI)
Active management of oligohydramnios	0.19 [0.02–0.28]
Past cesarean section	2.04 [0.22–18.85]
Malpresentation	7.5 [1.73–32.42]
NRFHR	n/a
Meconium-stained amniotic fluid	n/a

n/a: not applicable; NRFHR: Nonreassuring fetal heart rate.

induction of labor group had a higher rate of SGA and febrile morbidity.

A wide variation exists in the documented prevalence of oligohydramnios beyond 34 weeks of gestation that ranges from 0.5% to even 40% [25]. This variation might be due to several factors such as (1) characteristics of the studied population; (2) technical parameters implemented; (3) associated medical conditions; (4) medical center in which the examination was performed (tertiary versus primary care centers); (5) gestational age at time of examination; (6) altitude; and (7) maternal hydration status [26–32]. The reported prevalence of isolated oligohydramnios is 0.75% of all pregnancies [13]. In our study including late preterm pregnancies, this prevalence reached 1.5%.

Oligohydramnios may portend a significant potential of fetal jeopardy, especially at the late preterm period [27]. Some studies demonstrated an association between isolate oligohydramnios during the late preterm period and small for gestational age (SGA) fetuses that are not detected before delivery [33,34]. This raises concern about the mechanism that led to the reduction in the amount of amniotic fluid – perhaps there is an underlying placental under perfusion that its only clinical presentation is a reduction in amniotic fluid volume [35]. Indeed, we also observed a higher rate of SGA neonates in the isolate oligohydramnios group, and it seems that these fetuses were more prone to induction of labor even in the absence of the prenatal diagnosis of fetal growth restriction.

The diagnosis of oligohydramnios alters pregnancy and delivery management. Therefore, in most medical centers the generally accepted protocol isolated oligohydramnios at term is the induction of labor. This approach has been currently challenged since apparently, it raises the risk of obstetric intervention without improving the related adverse perinatal outcome [9,13,34,36]. The American College of Obstetrics and Gynecologists (ACOG) points out the lack of convincing data to support labor induction to isolate oligohydramnios in the absence of other risk factors for adverse perinatal outcome. However, ACOG does not provide a firm definition regarding the optimal timing of delivery in such patients [1,37]. The results regarding the effect of labor induction on the risk of CS are conflicting. While some suggested that labor induction is associated with increased risk for CS [6,10,38], others failed to detect such an association [39–42]. Moreover, there are reports suggesting that among women who undergo induction of labor wherein the preliminary increased for CS that is not attributed to the etiology of induction than the procedure itself. In our study, induction of labor of patients with isolated oligohydramnios was associated with an independently decreased risk for CS after controlling for confounding factors such as prior CS and mal presentation. This finding could be due to a negative effect of prolonged oligohydramnios on the course of delivery (in the conservative management group) but it also might be attributed to the underlying mechanism leading to reduced production of amniotic fluid in these fetuses. Targeted studies of placental histology and a long-term outcome of these neonates are lacking.

Several studies reported that isolated oligohydramnios is associated with increased rate of obstetrical interventions, which result in higher rates of adverse perinatal outcome [43]. A meta-analysis conducted to evaluate isolated oligohydramnios at term demonstrated such an association, without lowering the risk of adverse perinatal outcomes [6]. Similarly, Chauhan et al. in a meta-analysis of 10,551 patients demonstrated that antepartum diagnosis of oligohydramnios at term was associated with a significantly increased risk of CS due to nonreassuring fetal status [10]. Casey et al. retrospectively analyzed 6423 patients with oligohydramnios (defined by an AFI <5 cm) who underwent clinically indicated antepartum ultrasonography (i.e. uncertain gestational age, suspected deviant fetal growth or anomalies) beyond 34 weeks of gestation and concluded that oligohydramnios was significantly associated with increased risk for induction of labor, stillbirth, NRFHR, admission to NICU, meconium aspiration syndrome, and neonatal death [9,38]. However, as only cases with a clinical indication for sonographic examination were included in that study, a selection

bias may have influenced the results. In order to avoid the confounding effect of placental-mediated complication (preeclampsia, fetal growth restriction) we excluded all these patients from our study. Nevertheless, we were still able to demonstrate a beneficial effect for active management of patients with isolated oligohydramnios at the late preterm period over a conservative approach.

Contradictory to our results Melamed et al. reported a higher rate of adverse neonatal outcome in pregnancies complicated by isolated oligohydramnios before 37 gestational weeks and suggested that it is related to the higher rate of iatrogenic interventions and confounders rather than to the presence of isolated oligohydramnios *per se* [40]. However, our findings that isolated oligohydramnios is less frequently associated with significant adverse perinatal outcome are consistent with the findings of several other studies [13,17,44]. Rainford et al. in a cohort of 332 women at term without risk factors, compared perinatal outcomes in women with AFI $\leq$5 cm or $>$5 cm. They found no differences in the rates of operative delivery or Apgar scores, although meconium-stained AF was more frequent in women with low AF volume [44]. Manzanares and Zhang et al. also reported that pregnancies with isolated oligohydramnios had perinatal outcomes similar to pregnancies with a normal amount of AF index [13,18]. These observations strengthen the claim that oligohydramnios by itself may not be associated with a poor neonatal outcome.

The strength of our study is that it is based on a large, detailed, and accurate database of pregnancies, deliveries, and neonates. The comprehensive database allowed us to determine reliably the relationship between isolated oligohydramnios and multiple outcomes of interest. The study has several limitations. These include (1) its retrospective design which prevented us gathering information regarding certain confounders, such as data on the precise AFI and lack of validation of the diagnosis by other means; and (2) the long period of the study (20 years), this time frame is both an advantage and disadvantage. During this prolonged period of time aspects of the medical practice obviously have changed and the studied population experienced a different prenatal and antenatal care. Nevertheless, the current study included a large number of participants and aimed to address isolated oligohydramnios during the late preterm period, that only very few studies examined before; (3) we evaluated only infants born at late preterm and therefore our results are not applicable to pregnancies with isolated oligohydramnios at term.

Conclusions

In conclusion, induction of labor in pregnancies with late onset oligohydramnios (34–36.6 weeks) seems a reasonable option that is safe both for the mother and her offspring. Moreover, it is associated with lower risk of CS, an assumption that should be verified by other large-scale prospective studies.

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Disclosure statement

The authors report no conflicts of interest.

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