



Does parity affect pregnancy outcomes in the elderly gravida?

Gil Shechter-Maor^{1,2} · Dana Sadeh-Mestechkin^{1,2} · Yael Ganor Paz^{1,2} · Rivka Sukenik Halevy^{1,2,3} · Ofer Markovitch^{1,2} · Tal Biron-Shental^{1,2}

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Abstract

Purpose To identify whether older primiparas have more complications than do women who continue to deliver children into their late reproductive age. Patients of at least 35 years of age at delivery were included. Within this cohort, data from primiparous and multiparous women were compared.

Methods This retrospective study was based on electronic medical records from a single academic center, with more than 7000 deliveries annually. The impact of parity on maternal complications was assessed using a multivariate logistic regression model that adjusted for baseline maternal characteristics and medical history.

Results During the study period, there were 54 283 deliveries in our medical center. A total of 13,982 (25.7%) patients were at least 35 years old at delivery. The rate of twin pregnancy was higher in the primiparous group (1.9%) as compared to the multiparous group (0.8%, 95% CI 0.30–0.64, $P < 0.001$), as was the incidence of delivery prior to 34 weeks (6.1% of the primiparas versus 2.9% of the multiparas, $P < 0.001$, OR 2.16, 95% CI 1.75–2.68); hypertensive disorders (3.9% versus 1.7%, $P < 0.001$, 95% CI 0.33–0.57); diabetes (4.6% versus 3.2%, $P = 0.003$, 95% CI 0.55–0.88); and IUGR (10.5% versus 4.7%, $P < 0.001$, 95% CI 0.35–0.49), respectively. The increased risk for pre-term delivery, hypertensive disorders, diabetes, and IUGR was maintained after logistic regression analysis.

Conclusion We found that pregnancy complications typical to older parous women are significantly more common among primiparas, indicating that not only older age, but also having a first child relatively late in the reproductive period contributes to adverse pregnancy outcomes.

Keywords Advanced maternal age · Elderly gravida · Parity · Pregnancy complications · Pregnancy outcome · Primiparity

Introduction

In the last 30 years, child bearing in the later reproductive years has become increasingly common [1, 2]. Increased maternal age might be related to sociological and cultural changes of delayed marriage and parenthood, as well as a trend to protracting childbearing into the later years of fertility [3]. There is no universal definition for advanced reproductive age in women. The National Center for Health

Statistics evaluated maternal age at first delivery and categorized the upper age group as 35 and older. In Israel, where the study was performed, The Ministry of Health under guidelines consider patients age 35 and older as a high-risk group [4].

Advanced maternal age is associated with increased rates of pre-term delivery, gestational diabetes, and pre-eclampsia [1, 5–7], which can be related to higher maternal BMI and associated complications typical of the later years of fertility. Fetal complications, such as stillbirth, perinatal mortality, and low birth weights, increase with advanced maternal age, as well [1, 5–8].

The increasing incidence of advanced maternal age requires better understanding of the physiology and pathology of pregnancy in this population. Treatment protocols need to be developed to accommodate the associated risk factors.

✉ Gil Shechter-Maor
gilshec@gmail.com

¹ Department of Obstetrics and Gynecology, Meir Medical Center, Tel Aviv University, Tchernichovsky 59, 4428164 Kfar Saba, Israel

² Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

³ Genetics Institute, Meir Medical Center, Kfar Saba, Israel

Previous studies addressing maternal age and perinatal complications have compared outcomes among various maternal age groups [12]. Clinical experience has raised the question of whether complications are related to age or parity. The objective of the current study was to identify whether older primiparas have more complications than do women who continue to deliver children into late reproductive age.

Materials and methods

This retrospective study was based on electronic medical records from a single academic center, with more than 7000 deliveries annually and a level III neonatal intensive-care unit. Medical records were completed prospectively by trained midwives and obstetricians in the triage area and in the wards. Inclusion criteria were patients aged 35 years and older at delivery and gestational age at delivery of 23 weeks and above. Patients who delivered before 23 weeks + 0 days and patients with unknown or undocumented maternal age were excluded. Within this cohort, data from primiparous women (defined as first delivery at 24 weeks or more) and multiparous women (defined as patients with previous delivery at 24 weeks or more) were compared. Maternal demographics and medical status were evaluated.

Baseline demographic and pregnancy characteristics were compared between primiparous and multiparous patients; including maternal age, gravidity, chronic hypertension, pre-gestational diabetes, pregnancies associated with assisted reproductive technology (ART), and those conceived with donated ova.

Maternal complications between the two groups were compared, including twin pregnancies; hypertensive complications (chronic hypertension, gestational hypertension, pre-eclampsia, and HELLP syndrome); diabetic disorders (diabetes mellitus types 1 and 2 and gestational diabetes); intrauterine growth restriction (IUGR), defined as birth weight below the 10th percentile; and gestational age at delivery, including pre-term deliveries (defined as delivery before 37 completed weeks of gestation). Secondary analyses of early pre-term delivery (before completed 34 weeks of gestation), neonatal birth weight, stillbirths, and Apgar scores were also conducted.

Multivariate logistic regression models adjusted for baseline maternal characteristics and medical parameters were performed. Parameters that were significantly different between the study groups in the univariate analysis and that can have an effect on the outcomes measured were included. The parameters included were ART, hypertensive disorders, twin pregnancy, induction of labor, IUGR, type of delivery, postpartum hemorrhage, delivery before 34 weeks, gestational diabetes, and pre-eclampsia. The effect of parity on

obstetrical complications was assessed with estimated odds ratios (OR) and 95% confidence intervals (CI).

The study was approved by the local hospital ethical committee.

Results

During the study period, there were 54 283 deliveries in our medical center. A total of 13,982 (25.7%) of these patients were at least 35 years old at the time of delivery. The age distribution of the cohort is presented in Fig. 1 by the groups of primiparous and multiparous mothers. Among the study cohort, 1994 (14.3%) mothers were primiparous and 11,988 (85.7%) were multiparous.

We compared maternal baseline characteristics for the two groups (Table 1). The average age of the primiparous group was 37.5 ± 2.9 years and 37.6 ± 2.3 years in the multiparas group ($P = 0.233$). It was the first pregnancy for 67.7% of the patients in the primiparous group. The percentage of patients with pre-gestational diabetes was the same in both groups, but the prevalence of chronic hypertension was higher in the primiparous group (Table 1).

More pregnancies were conceived by ART among the primiparous group as compared to the multiparous group (4% versus 0.6%, respectively, $P < 0.001$). Egg donation was more frequent in the primiparous group, as well.

There was no difference in gestational age at delivery between the primiparous and multiparous groups (38.6 ± 2.51 weeks and 38.7 ± 1.9 weeks, respectively). However, the newborns of the primiparous had significantly lower mean birthweights (3022 g) versus 3254 g for the multiparous. Gender distributions were similar (Table 2).

The rate of twin pregnancy was higher in the primiparous group as compared to the multiparous group (1.9% versus 0.8%, respectively; $P < 0.001$) Table 2.

Pre-term delivery was also more common among the primiparas. The difference was maintained for delivery prior to 34 weeks, which occurred among 6.1% of the primiparas versus 2.9% of the multiparas ($P < 0.001$; Table 2).

Obstetric complications are shown in Table 2. Primiparas had significantly higher incidence of hypertensive disorders (3.9% versus 1.7%, $P < 0.001$) and gestational diabetes (4.6% versus 3.2%, $P = 0.003$), as compared to multiparas. The rate of IUGR was also increased in the primiparous group (10.5% versus 4.7%, respectively, $P < 0.001$).

The percentage of newborns with 5 min Apgar scores ≤ 7 was higher among the primiparas (1.7% versus 0.8%, $P < 0.001$), as was stillbirths (0.9% versus 0.5%, $P = 0.035$; Table 2).

Primiparas were more likely to undergo labor induction (19.6% versus 9.4%, $P < 0.001$) for a variety of medical indications. During labor, internal fetal monitoring was used

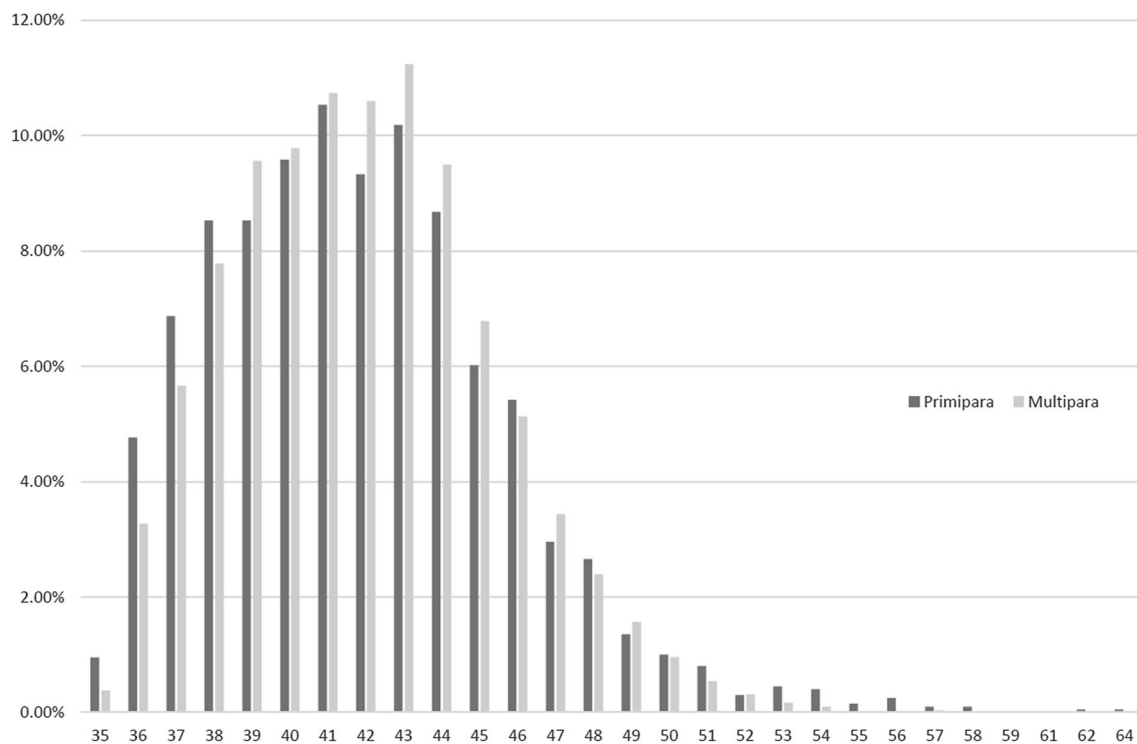


Fig. 1 Age distribution by parity

Table 1 Maternal characteristics

Characteristic	Primiparous N= 1994	Multiparous N= 11,988	P value (95% confidence interval)
Age, years mean \pm SD (range)	37.5 \pm 2.87 (35–58)	37.6 \pm 2.33 (35–59)	0.233
Gravidity Mean \pm SD (range)	1.5 \pm 0.894 (1–13)	3.9 \pm 1.776 (2–17)	< 0.001
Primigravida, n (%)	1351 (67.7)	0	< 0.001 (18.22–21.18)
Chronic HTN, n (%)	22 (1.1)	77 (0.6)	0.023 (0.36–0.93)
Pre-gestational diabetes, n (%)	1 (0.1)	15 (0.1)	0.717 (0.33–18.913)
Conceived using ART, n (%)	80 (4)	71 (0.6)	< 0.000 (0.10–0.19)
Egg donation, n (%)	24 (1.2)	22 (0.2)	< 0.001 (0.08–0.27)

more often in the primiparous group (12.1% versus 6.2%, $P < 0.001$).

Cesarean sections were more common among the primiparous group (35% versus 23%), as were operative vaginal deliveries (22.7% versus 4.7%). Postpartum hemorrhage (PPH) was more common, as well (Table 2).

To determine whether there was an independent association between parity in older gravidas and adverse pregnancy outcomes, a logistic regression analysis for pregnancy outcomes and delivery complications that varied

between the groups was performed. The rate of ART, twin pregnancies, hypertensive disorders, gestational diabetes, IUGR, induction of labor, mode of delivery, PPH, and delivery before 34 weeks were included in the logistic regression analysis. ART was found to have an effect on the obstetrical complications. The significantly increased risks in primiparous pregnancies for IUGR, induction of labor, delivery before 34 weeks, PPH, and cesarean section or operative vaginal delivery were maintained (Table 3).

Table 2 Maternal and neonatal characteristics of elderly gravida by parity

Variable	Primiparous <i>n</i> (%)	Multiparous <i>n</i> (%)	Crude <i>P</i> value (95% Confidence interval)
Neonatal characteristics			
Twins, <i>n</i> (%)	37 (1.9%)	99 (0.8%)	< 0.001 (0.30–0.64)
Hypertensive disorders	77 (3.9)	208 (1.7)	< 0.001 (0.33–0.57)
Gestational diabetes	91 (4.6)	388 (3.2)	0.003 (0.55–0.88)
IUGR	209 (10.5)	564 (4.7)	< 0.001 (0.35–0.49)
Induction of labor, <i>n</i> (%)	391 (19.6)	1123 (9.4)	< 0.001 (0.37–0.48)
Gestational age at delivery, weeks (range)	38.6 ± 2.51 (25–43)	38.7 ± 1.90 (20–43)	0.266
Delivery before 34 weeks	122 (6.1)	350 (2.9)	< 0.001 (1.75–2.67)
Operative vaginal delivery, <i>n</i> (%)	453 (22.7)	564 (4.7)	< 0.001 (0.14–0.19)
Cesarean delivery, <i>n</i> (%)	699 (35)	2784 (23)	< 0.001 (1.61–1.97)
Postpartum hemorrhage, <i>n</i> (%)	19 (1)	44 (0.4)	< 0.001 (0.22–0.65)
Neonatal characteristics			
Birth weight, g (range), SD	3042 ± 577 (370–6320)	3249 ± 530 (263–5960)	0.0001
Stillbirth, <i>n</i> (%)	18 (0.9)	62 (0.5)	0.035 (0.33–0.96)
Apgar 5' ≤ 6 <i>n</i> (%)	33 (1.7)	97 (0.8)	< 0.001 (1.38–3.06)

Table 3 Multivariate regression analysis for obstetrical complications

Variable	Adjusted <i>P</i> value (95% confidence interval)	Adjusted OR	95% CI for OR	
			Lower	Upper
ART	0.000	5.484	3.846	7.820
Hypertensive disorders	0.092	1.330	0.954	1.854
Twins	0.051	0.641	0.411	1.002
Apgar 5' < 7	0.618	0.882	0.538	1.445
Induction of labor	0.000	2.566	2.249	2.928
Intrauterine growth restriction	0.000	1.849	1.535	2.226
Mode of delivery	0.000	3.589	3.242	3.974
Postpartum hemorrhage	0.001	2.689	1.494	4.839
Delivery < 34 weeks	0.006	0.709	0.555	0.906
Gestational diabetes	0.844	0.975	0.757	1.255
Pre-eclampsia	0.708	1.137	0.580	2.230

The parameters included in the multivariate regression analysis were ART, hypertensive disorders, twin pregnancy, induction of labor, IUGR, type of delivery, postpartum hemorrhage, delivery before 34 weeks, gestational diabetes, and pre-eclampsia

Discussion

Pregnancy at an advanced maternal age has become increasingly popular. This phenomenon is accompanied

by the potential complications of pre-eclampsia, diabetes, and cesarean delivery. Previous studies have examined the effect of fetal sex and ART together with advanced maternal age on pregnancy outcomes and complications [9, 10].

The current study evaluated the effects of parity on pregnancy-related complications in parturients at advanced maternal age. Our aim was to differentiate obstetric complications that are specific to older primigravidas from complications that are common to older gravidas.

Older gravidas are at increased risk for obstetric and perinatal complications, such as stillbirth, IUGR, gestational diabetes, pre-eclampsia, and cesarean section [11, 12]. We found that pregnancy complications typical to older parous women are significantly more common among primiparas, indicating that not just older age, but having a first child relatively late in the reproductive period contributes to adverse pregnancy outcomes. In addition, multiparity appears to be protective from some of the complications attributed to older maternal age.

The novelty of the current study is that it examined perinatal complications of advanced maternal age from the perspective of parity. It is well established that pregnancy complications such as pre-eclampsia, IUGR, pre-term delivery, and cesarean deliveries are related to primiparity, whereas others such as PPH are related to multiparity. Apgar scores and intrauterine fetal demise are not related to parity [13–17].

Reports differentiating older primiparas from multiparas are scarce. In our study population, we found that advanced maternal age in a first delivery carried increased risks for maternal hypertensive disorders, diabetes, IUGR, and pre-term delivery when compared to advanced maternal age in a multiparous woman. We found that among women ≥ 35 years of age, primiparas tended to have twins and deliver smaller babies more often than did multiparas of the same age, even after adjusting for the number of fetuses. Furthermore, they had higher rates of induced labor, operative vaginal delivery, cesarean delivery, and PPH. When trying to explain these findings, each obstetric outcome or complication should be addressed separately.

Our observation of increased rates of twins among the primiparous with advanced maternal age is probably due to the use of ART, including egg donation in this group. Our findings are in agreement with the previous reports regarding women electing to postpone their (first) pregnancies, implying an effect of advanced maternal age on fertility [18].

Second, the management of older parturients requires treating pre-existing comorbidities, coping with complications during pregnancy, delivery, and postpartum. Chronic diseases such as arthritis, hypertension, and diabetes are more common among these patients [19]. Our observation of increased rates of diabetes and hypertension in pregnancy among older primiparous patients indicates that this group requires a special attention when planning and consulting with them regarding pregnancy.

Third, we observed that primiparas had higher rates of IUGR compared to multiparous. IUGR occurs more

frequently among primiparous regardless of age [21]. Here, we found an apparent additive influence of primiparity and advanced maternal age and demonstrated that IUGR is even more common when an older woman is delivering her first child. These patients require a special attention.

It is well established that some pregnancy complications attributed to primiparity also occur more often among women with advanced maternal age, such as pre-term birth, low birth weight, and perinatal mortality [20]. In our study, pre-term births were more frequent among primiparous when compared to the multiparous group. The rate of delivery before 34 weeks in the group of older multiparas was similar to that of the general population [21]. Due to the limitations of our database, we could not identify spontaneous pre-term births, but we can still conclude that older primigravidas have increased risk for pre-term birth before 34 weeks of gestation.

In addition, primiparas underwent induction of labor more often than multiparas did. Unfortunately, we do not have information regarding the indications for induction. However, according to our protocols, inductions are performed for medical indications only (maternal age is not considered an indication) and not due to maternal request. The primiparous in our study population had higher rates of hypertension and diabetes. Therefore, we speculate that these were the most likely indications for labor induction.

Primiparas with advanced maternal age in our study had higher rates of cesarean deliveries and operative vaginal deliveries, as compared to multiparas and to the general population. Since maternal age or request is not indications for a specific mode of delivery in our institution, these deliveries can be attributed to higher rates of pregnancy complications among this group of patients. Interestingly, parturients with advanced maternal age are more likely to deliver by cesarean section; however, most women who attempt a trial of labor, deliver vaginally [21]. These data raise the question of whether increased rates of cesarean deliveries for older primiparous are age related or are iatrogenic, caused by physicians' attitudes towards the mode of delivery among this group. It is well accepted that patients who are at an advanced age and pregnant are at higher risk for complications, but management protocols for these patients are not well established. Avoiding complications such as stillbirth and pre-eclampsia by early induction is part of routine management guidelines [22, 23], and was not found to increase the rates of cesarean sections and operative vaginal delivery for this age group [23, 24]. This observation of increased rates of cesarean section and induction of labor in the older primiparous group might be due to increased anxiety of the patient and her obstetrician, because she is older and delivering her first child. Our observation of increased use of internal

fetal monitoring in the older primiparous patients might also represent a higher index of suspicion for non-reassuring fetal heart rate in this group.

We observed more cases of PPH among the primiparas as compared to the multiparas. Given previous studies regarding increased incidence of PPH among multigravida deliveries [23], our results were surprising. We may attribute increased rates of PPH among primiparas to prolonged labors and increased rates of labor induction with long periods of oxytocin administration.

A major strength of this study is the large sample size. To the best of our knowledge, it is the largest to date to evaluate the effect of parity on outcomes of pregnancies with advanced maternal age. The study population is homogenous in that all patients were followed, treated, and delivered in one medical center using the same medical approach and protocols. In addition, uniform diagnostic and procedural codes were used.

The study is not without limitations. As it is retrospective, data collection bias might have occurred, as it was based on a computerized database that was prospectively collected. Thus, some information was not available for all patients in the cohort. Also, it was based on ICD9 diagnostic coding that might be inaccurate in some cases. Therefore, large prospective studies are indicated to obtain a better perspective on the effects of maternal age and pregnancy outcomes in relation to parity.

The literature discussing the influence of age on pregnancy complications and outcomes is broad. The contribution of the current study is that it differentiates between older primigravidas and multigravidas. According to our results, the pregnancy complications and adverse outcomes evaluated were increased in the primiparous group when compared to the multiparous women. The difference in pregnancy complications between the two groups might indicate the need for different treatment protocols for each group, focusing on older primigravidas as patients with potentially increased risk in pregnancy.

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Compliance with ethical standards

Conflict of interest The authors report no conflict of interest.

Ethical approval The Meir Medical Center Ethics Committee reviewed and approved the study. The study data were obtained from the hospital database and informed consent was not required.

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