

# Parity affects pregnancy outcomes in women 35 and older

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## Summary

**Purpose of investigation:** The objective of the study was to examine the impact of parity on pregnancy outcomes in women 35 years and older. **Methods:** The study was a retrospective cohort of singleton pregnancies of women aged  $\geq 35$  years old during the period 2004-2008. Women were divided in two groups: group 1 included primigravidas and group 2 those with at least one past labor. Epidemiological characteristics, obstetric and neonatal outcomes were analyzed using the *t* test and chi-square test. **Results:** 816 out of 5834 (14%) cases involved women aging  $\geq 35$  years, 234 (28.7%) of which were nulliparous and 582 (61.3%) multiparous. Rate of cesarean section was 2.4 fold higher for primigravidas ( $p < .0001$ ). Fetal distress, prolonged labor and Neonate Intensive Care Unit (NICU) admission were also significantly higher in group 1. **Conclusion:** Adverse pregnancy outcomes were increased in primigravidas of 35 years and older compared to multigravidas of the same age.

**Key words:** Older women; Obstetric outcomes; Neonatal morbidity.

## Introduction

It is a fact that women over the age of 35 retain a remarkable part of the total births in the developed world. Various reasons account for this contemporary phenomenon, the most important of which is delaying marriage due to advanced education and professional careers pursuits [1]. Subfertility is another factor responsible for delayed childbearing. This difficulty, however, has today been conquered by advances and wide availability of assisted reproductive technologies (ART), giving women the opportunity of pregnancy later in life [2, 3]. Second marriages as well as financial concerns may also contribute to the decision of giving birth over the age of 35 years [4, 5].

Numerous studies have been conducted to examine the impact of maternal age on pregnancy outcome. It has previously been shown that childbearing in advanced maternal age is accompanied by a high incidence of complications for both mother and fetus. This may be partially attributed to the fact that older women are more likely to suffer from diabetes mellitus, cardiovascular, neurological, renal, hypertensive and pulmonary disorders, aggravating pregnancy outcomes [6-9]. The overwhelming majority of the existing studies, though, compares pregnancies of younger and older women, demonstrating more unpropitious outcomes in the latter. Specifically, maternal morbidity by means of antepartum and intrapartum complications is reported to be elevated in older gravidas, while neonatal outcomes also appear to be negatively affected in the same population when compared to younger women [10-12].

Despite the plethora of studies investigating the association between maternal age and birth outcomes, there is a lack of evidence concerning the role of parity in obstet-

ric and neonatal outcomes, especially in those of older women. The aim of our study was to examine the impact of parity on pregnancy outcomes in women aged  $\geq 35$  years, a special population, where pregnancy is harder afforded and can be burdened by a plurality of difficulties in its progress.

## Materials and Methods

This was a retrospective cohort study of singleton pregnancies characterized by advanced maternal age, based on our institution's database during the period 2004-2008. Women aged  $\geq 35$  years old were exclusively enrolled in our study. Maternal and neonatal data was systematically recorded and verified by our institution's medical staff, reassuring the reliability of our statistical sample. Institutional Review Board approval was given to the present study.

The main aim of our study was to analyze the impact of parity on pregnancy outcomes. Therefore, women satisfying our inclusion criteria were divided in two groups: group 1 included nulliparous women and group 2 included women with at least one previous delivery. Mean maternal age and gestational week at delivery were the epidemiological aspects initially analyzed for each group. Along with epidemiological aspects, mode of delivery, rate of pregnancies achieved by in vitro fertilization (IVF) and maternal medical condition were additionally studied. Maternal pathologic conditions of interest to us included diabetes mellitus, hypertension, cardiovascular disorders, thalassemia and sickle cell anemia, whose rates were compared between both groups.

Obstetric outcomes and neonatal morbidity were then analyzed in groups 1 and 2. Analysis of obstetric outcomes involved rates of gestational diabetes, preeclampsia [defined as development of persistent blood pressure (more than 140/ 90 mm Hg) after 20 weeks of pregnancy (previously normotensive women), plus proteinuria ( $\geq 300$  mg of urinary protein per 24 h)], premature rupture of membranes (PROM), placenta previa, placenta accreta, placental abruption, chorioamnionitis, oligamnion, polyamnion, fetal distress [defined as a non-reassuring fetal heart rate (FHR) (tachycardia, bradycardia, late decelera-

tions)], malpresentation (noncephalic presentation), umbilical cord prolapse and prolonged labor (inadequate progress for three hours in nulliparous and two hours in multiparous women with documented uterine activity). Concerning neonatal morbidity, our study focused on the mean  $\pm$  standard deviation (SD) Apgar score in the 1<sup>st</sup> and 5<sup>th</sup> minute of life and the rate of neonates with an Apgar score  $\leq 4$  in the 1<sup>st</sup> minute and  $\leq 7$  in the 5<sup>th</sup> minute. Moreover, admission to the Neonate Intensive Care Unity (NICU) and need for emergency intubation (respiratory support) in the labor ward were studied. The rate of neonates characterized by low birth weight ( $< 2500$  g, LBW), very low birth weight ( $< 1500$  g, VLBW) and intrauterine growth retardation (IUGR) was also part of our study.

#### Statistical analysis

The Student's *t*-test was used for the different variables of the study with continuous data. Cross-tabulated data was compared with the chi-square and Fisher's exact test analysis. Additionally, odds ratio (OR) based on 95% confidence interval (CI) was also calculated for nominal data. All *p* values are 2-sided. A statistically significant difference was defined at *p*  $< .05$ . Statistical analysis was performed by using the Statistical Package for Social Sciences version 17.0 (SPSS Inc, Chicago, IL).

#### Results

During the study period, 816 out of 5,834 (14%) singleton pregnancies characterized by advanced maternal age ( $\geq 35$  years old) were delivered in our institution. Two hundred and thirty-four women (28.7%) of advanced maternal age were nulliparous (group 1), while 582 were (71.3%) multiparous (Group 2). Epidemiological analysis demonstrated that mean maternal age (mean  $\pm$  SD) was similar between the groups ( $37.7 \pm 2.7$  years vs  $37.4 \pm 2.2$  years, respectively), whereas mean gestational week at delivery (mean  $\pm$  SD) was higher for group 2 (group 1,  $37.2 \pm 3.6$  vs group 2,  $37.8 \pm 2.9$ , *p* = 0.03). Furthermore, rates of vaginal delivery, cesarean section (CS) and instrumental delivery (forceps/vacuum) were found to differ significantly between the two groups. Rate of vaginal delivery was significantly lower for nulliparous women (34.2%) compared with multiparous women (60.3%) [OR (95% CI): 2.93 (2.13-4.01)], whereas cesarean section and instrumental delivery were more frequent in the group of primigravidas (cesarean section - group 1; 55.1% vs  $\leq$  cesarean section - group 2; 33.7%) (instrumental delivery - group 1; 9.4% vs  $\leq$  instrumental delivery - group 2; 2.4%). Total cesarean section rate in the nulliparous group (55.1%) was analyzed in the following indications: 18.8% fetal distress, 6.5% prolonged labor, 7% malpresentation, 3.8% preeclampsia, 3% PROM, 2.6% placental abruption, 2.6% placenta previa, 2.4% IUGR, 1.7% diabetes mellitus, 6.7% others. Total cesarean section rate in the multiparous group (33.7%) was analyzed in the following indications: 16% previous cesarean section, 7.6% fetal distress, 4.5% malpresentation, 1.5% preeclampsia, 1.2% placenta previa, 0.9% placental abruption, 1.7% others. Moreover, pregnancies achieved by IVF were significantly higher in nulliparous (3.8%) versus multiparous mothers (0.3%) with OR (95% CI): 0.09 (0.02-0.40).

After the extraction of the IVF populations from each group, cesarean section rates remained significantly different between older primigravidas and multigravidas. None of the analyzed maternal medical conditions were found to be significantly different between the two groups. The epidemiological characteristics of the study are presented in Table 1.

Table 1. — Maternal characteristics by parity.

Characteristics	Nulliparous women (Group 1)	Multiparous women (Group 2)	Odds ratio (95% CI)	<i>p</i> value
Maternal age (mean $\pm$ SD)	$37.7 \pm 2.7$	$37.4 \pm 2.2$		NS <sup>§</sup>
Gestational week (mean $\pm$ SD)	$37.2 \pm 3.6$	$37.8 \pm 2.9$		.03 <sup>§</sup>
Mode of delivery				
Natural delivery, n (%)	80 (34.2)	351 (60.3)	0.34 (0.25-0.47)	$< .0001^*$
Cesarean section, n (%)	129 (55.1)	196 (33.7)	2.42 (1.78-3.30)	$< .0001^*$
Forceps/vacuum, n (%)	22 (9.4)	14 (2.4)	4.21 (2.11-8.38)	$< .0001^*$
In vitro fertilization (IVF)	9 (3.8)	2 (0.3)	11.60 (2.49-54.10)	$< .0001^*$
Maternal pathology				
Diabetes mellitus, n (%)	1 (0.4)	1 (0.7)	0.62 (0.07-5.58)	NS <sup>*</sup>
Hypertension, n (%)	2 (0.9)	11 (1.9)	0.45 (0.01-2.03)	NS <sup>*</sup>
Cardiovascular disorders, n (%)	0 (0)	1 (0.2)	1.00 (0.99-1.00)	NS <sup>*</sup>
Anemia*, n (%)	1 (0.4)	1 (0.3)	1.25 (0.11-13.79)	NS <sup>*</sup>

\*Thalassemia and sickle cell anemia; SD: standard deviation; NS: non significant; CI: confidence interval; <sup>§</sup> *p* value was calculated by the Student's *t*-test; <sup>\*</sup> *p* value was calculated by  $\chi^2$  and Fisher's exact test analysis.

Analysis of the obstetric outcomes yielded remarkable differences between primiparous and multiparous women. Fetal distress was observed much more frequently in group 1 (18.8%) than in group 2 (7.6%) (*p*  $< .0001$ ). Furthermore, labor was prolonged in 8.5% of nulliparous women and in 1.5% of multiparous women, which was significantly different (*p*  $< .0001$ ). Moreover, the rate of preeclampsia was 3.8% for primigravidas versus 1.5% for multigravidas indicating a significant trend (*p* = .06). Similarly, a trend was demonstrated concerning PROM (*p* = .08), placental abruption (*p* = .08), chorioamnionitis (*p* = .14) and malpresentation (*p* = .18). No significant difference was found in terms of gestational diabetes, placenta previa, placenta accreta, oligamnion, polyamnion and umbilical cord prolapse between nulliparous and multiparous women. The obstetric outcomes for groups 1 and 2 are presented in Table 2.

Finally, higher incidence of neonatal morbidity was observed in neonates of nulliparous women. Apgar score (mean  $\pm$  SD) in the 1<sup>st</sup> minute was significantly lower in neonates born by nulliparous women ( $7.1 \pm 1.9$ ) compared to those born by multiparous women ( $7.5 \pm 1.5$ ) for group 2, *p* = .01). A trend was also observed concerning the Apgar score in the 5<sup>th</sup> minute (*p* = .14) and the rate of neonates with a low Apgar score in the 1<sup>st</sup> minute (*p* = .16) and 5<sup>th</sup> minute (*p* = .13). Additionally, NICU admission was significantly higher in group 1 (20.5%) than the

Table 2. — *Obstetric outcomes of nulliparous and multiparous women.*

Obstetric outcomes	Nulliparous women (Group 1) n = 234	Multiparous women (Group 2) n = 582	Odds ratio (95% CI)	p value
Gestational diabetes	4 (1.7)	5 (0.9)	2.00 (0.53- 7.54)	NS*
Preeclampsia	9 (3.8)	9 (1.5)	2.54 (0.99- 6.49)	NS**
PROM	10 (4.3)	11 (1.9)	2.31 (0.97- 5.53)	NS*
Placenta previa	6 (2.6)	7 (1.2)	2.16 (0.71- 6.50)	NS*
Placenta accreta	1 (0.4)	2 (0.3)	1.25 (0.11-13.79)	NS*
Placental abruption	6 (2.6)	5 (0.9)	3.04 (0.91-10.05)	NS**
Chorioamnionitis	3 (1.3)	2 (0.3)	3.77 (0.63-22.69)	NS**
Oligamnion	2 (0.9)	2 (0.3)	2.50 (0.35-17.85)	NS*
Polyamnion	1 (0.4)	3 (0.5)	0.82 (0.09- 8.00)	NS*
Fetal distress	44 (18.8)	44 (7.6)	2.83 (1.80- 4.43)	< .0001*
Malpresentation	22 (9.4)	38 (6.5)	1.49 (0.86- 2.57)	NS**
Umbilical cord prolapse	0 (0)	2 (0.3)	1.00 (0.99- 1.00)	NS*
Prolonged labor	20 (8.5)	9 (1.5)	5.95 (2.67-13.27)	< .0001*

NS\*: value of trend ( $p < .2$ ), PROM: premature rupture of membranes, NS: non significant, CI: confidence interval; +  $p$  value was calculated by  $\chi^2$  and Fisher's exact test analysis.

Table 3. — *Neonatal outcomes of nulliparous and multiparous women.*

Neonatal outcomes	Nulliparous women (Group 1) n = 234	Multiparous women (Group 2) n = 582	Odds ratio (95% CI)	p value
NS-LBW, n (%)	46 (19.7)	82 (14.1)	1.49 (1.00-2.22)	NS*+
VLBW, n (%)	21 (9.0)	26 (4.5)	2.10 (1.16-5.82)	.02+
IUGR, n (%)	8 (3.4)	8 (1.4)	2.54 (0.94-6.85)	NS*+
Apgar score (mean $\pm$ SD)				
1 min	7.1 $\pm$ 1.9	7.5 $\pm$ 1.5		.01 <sup>‡</sup>
5 min	8.5 $\pm$ 1.6	8.6 $\pm$ 1.4		NS <sup>‡</sup>
1 min $\leq$ 4, n (%)	20 (8.6)	33 (5.7)	1.56 (0.88-2.78)	NS**
5 min $\leq$ 7, n (%)	18 (7.7)	29 (5.0)	1.59 (0.86-2.92)	NS**
Emergency intubation, n (%)	5 (2.1)	11 (1.9)	1.13 (0.39-3.30)	NS*
NICU admission, n (%)	48 (20.5)	80 (13.7)	1.62 (1.09-2.40)	.02+

NS\*: value of trend ( $p < .2$ ); LBW: low birth weight; VLBW: very low birth weight; NICU: Neonatal Intensive Care Unit; SD: standard deviation; NS: non significant; CI: confidence interval.

<sup>‡</sup>  $p$  value was calculated by the Student's  $t$ -test.

\*  $p$  value was calculated by  $\chi^2$  and Fisher's exact test analysis.

respective rate observed in group 2 (13.7%) ( $p = .02$ ). On the contrary, frequency of emergency intubation did not differ between the two groups. Neonates born by primigravidas were also characterized by significantly higher rates of VLBW ( $p = .02$ ), as well as by a trend concerning LBW and IUGR ( $p = .06$ ) ( $p = .09$ ). Neonatal characteristics for both nulliparous and multiparous women are presented in Table 3.

## Discussion

In spite of the extended literature regarding the relation of advanced maternal age to adverse obstetric outcomes, there is lack of evidence concerning the role of parity in this prominent issue. To our knowledge, parity has mainly been studied in terms of comparison of pregnancy outcomes between younger and older women [1, 2, 13]. In the present study we examined a population of gravidas over the critical age of 35 years, focusing on the potential effect parity has on their pregnancy outcomes. Indeed, the beneficial impact of a previous labor on both maternal and neonatal characteristics was demonstrated.

Our study showed a significantly raised level of intrapartum complications in older nulliparous women, including fetal distress, malpresentation and prolonged labor. Similarly to our results, Ziadeh *et al.*, found an increased incidence of these complications in gravidas of 40 years or older with no previous births [2]. Augmentation of malpresentation rates and prolonged labor is also mentioned by Gilbert *et al.* in the same population category [1].

The analysis of our data demonstrated a slight supremacy of aged primigravidas as far as antepartum complications are concerned. Preeclampsia, PROM, chorioamnionitis and placental abruption rates were augmented in the nulliparous population, but not significantly. Other studies have also reported increased rates of such complications in older primigravidas in comparison with those having at least one previous labor [1, 2]. However, our findings conflict with those of Bianco *et al.* where PROM and placental abruption appear to occur more often in mature multiparous women [13]. Furthermore, despite the repeated references in published articles outlining the relationship between multiparity and high risk for placenta previa, such an observation can not be confirmed by the present study [1].

One of the most remarkable differences between older nulliparous and multiparous women was the significantly elevated rates of cesarean section and operative vaginal delivery in the first group. The higher incidence of cesarean delivery in aged primigravidas has been pointed in previous studies [14-16]. Main *et al.* showed an almost 4-fold and 2-fold increase in cesarean section and operative vaginal delivery rates, respectively, for mature primigravidas in comparison with younger primigravidas [4]. Others observed a slow progress of labor in older nulliparous women due to insufficient uterine activity as a result of a combination of their advanced age and the lack of a previous delivery [16, 17]. This reduced uterine contractility in parallel with the higher rate of intrapartum complications that we observed, may offer a plausible explanation to the increased rates of cesarean section in older nulliparous mothers.

Another parameter affecting rates of cesarean delivery in primigravidas aging  $\geq 35$  years old may be physician anxiety concerning the outcome of such pregnancies. This may often influence an obstetrician's decision to perform cesarean section in such cases, in an attempt to alleviate the likelihood of adverse outcomes [18-21]. The higher incidence of IVF in older nulliparous women causes additional anguish to the physician for excellent birth outcomes, which may lead to a decision of cesarean section earlier than usual [22-24]. This fact could further explain the higher rate of cesarean delivery in our aged primigravidas, who also presented higher rates of IVF. However, excluding the IVF population from our analysis, rate of cesarean section remained significantly higher in the primiparous women compared to the multiparous group.

The demonstrated surcharge of intrapartum and antepartum complications in older primigravidas resulted

in an elevated number of adverse neonatal outcomes. Rates of both low birth weight and VLBW infants were remarkably higher in the nulliparous group, corroborating the current literature. Delphisheh *et al.* similarly showed that these birth outcomes differed significantly between primiparas and multiparas of 40 years and older [20]. Further analysis of neonatal characteristics revealed increased incidence of low Apgar scores in aged primigravidas, as has previously been shown by published reports [2, 13]. An additional important difference in infant birth outcomes was the significantly higher incidence of NICU admission in the nulliparous mothers of our study, reflecting once more their augmented obstetric complications. According to Bianco *et al.* an alternative explanation to this finding may alert physicians to pay attention to these peculiar pregnancies [2, 13].

The present data was not without deficiencies. A potential confounder to our results may be the small sample of the study. However, our outcomes are in accordance with other studies, including sizable populations. Another factor possibly biasing the conclusions of our analysis was non-consideration of epidural analgesia, which has been mentioned to affect rates of cesarean section and duration of labor [25]. Lack of information related to maternal height, weight nutritional and financial status could also limit our findings. Nevertheless, inclusion of such epidemiological characteristics, as well as information concerning mode of analgesia, is not a common practice among the rest of published reports considering pregnancy outcomes in older gravidas.

## Conclusion

In conclusion, the present study showed increased adverse pregnancy outcomes for primiparous women of 35 years or older in comparison with multigravidas of the same age. Both obstetric and neonatal characteristics were negatively affected in the nulliparous population, demonstrating the beneficial role of a previous labor in prevention of adverse pregnancy outcomes.

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