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MATERNAL-FETAL MEDICINE

The impact of advanced maternal age on the outcome of twin pregnancies

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Abstract

Purpose To assess the effect of advanced maternal age on the obstetrics and neonatal outcome of twin pregnancies.

Methods A retrospective study of 716 dichorionic–diamniotic twin pregnancies delivered at our institute. The study population was divided into two groups: women aged 35–39 years (group A, $n = 142$) and women aged ≥ 40 years (Group B, $n = 48$). The control group consisted of women younger than 35 years (group C, $n = 516$).

Results The rate of cesarean section (CS) was significantly higher among women older than 35 years compared to the control group (A 76.8% and B 87.5% vs C 65.7%, $P = 0.001$). Women older than 35 years were also at higher risk for developing hypertensive disorders (A 7.0%, B 14.6%, vs C 5.4%, $P = 0.04$). On multivariate regression analysis, maternal age was found to be independently associated with a higher rate of CS (odds ratio vs reference group C: group A 1.6, 95% CI 1.08–2.6; group B 3.2, 95% CI 1.3–7.8). There was no difference between the groups in the rate of neonatal complications.

Conclusion Women with twin pregnancy, older than 35 years, have a significantly higher rate of CS and hypertensive disorder. This rate increases with maternal age, with no increased rate of neonatal complications.

Keywords Twin pregnancy · Advanced maternal age · Neonatal outcome

Introduction

The rate of multiple pregnancies has increased significantly during the last decades. The reason for this is that nowadays women delay their childbearing and many of them need assisted reproductive technology (ART) to conceive [1–3]. Higher rates of obstetrical and neonatal complications are associated with advanced maternal age in singleton pregnancies [4–6]. Multiple gestation poses an additional higher risk for adverse maternal and neonatal outcome [2, 3, 7]. Only few studies reported the effect of advanced maternal age on obstetrical and neonatal outcome in twin gestations. While some of the studies of twin pregnancies have demonstrated higher rates of cesarean section (CS), preeclampsia, and low birth weight [8–10], others found that advanced age has no adverse effect on obstetrical outcomes [11–13]. Except for the conflicting results, the studies did not report the rates of adverse outcomes during the neonatal period. The aim of the present study was to compare obstetrical and neonatal outcome between women with dichorionic–diamniotic twin pregnancies older than 35 years of age with women younger than 35 years of age.

Materials and methods

This is a retrospective, single center, cohort study. Medical records of all live diamniotic–dichorionic twin pregnancies, delivered after 24 weeks of gestation at our institute between January 2009 and December 2016 were reviewed. Known chromosomal abnormalities and fetal malformations were excluded. We reviewed maternal characteristics, pregnancy outcome, and pregnancy complications. Hypertensive disorders were defined as one of the following: preeclampsia, eclampsia, and gestational hypertension. Intrauterine growth restriction (IUGR) was defined as birth weight ≤ 10th percentile, according to gestational age at delivery, and preterm labor as delivery before 37 completed weeks. Neonatal data were obtained from the computerized pediatricians and neonatologists records. It included admissions to the neonatal

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intensive care unit (NICU), respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), neonatal sepsis, intraventricular hemorrhage (IVH), and neonatal death. The study population of women older than 35 years was divided into two groups: women aged 35–39 years (group A) and women aged ≥ 40 years (group B). The control group consisted of women younger than 35 years (group C).

Data were analyzed by the SPSS software, version 23 (IBM Inc.). Continuous variables are presented as mean ± SD or median and range, as appropriate. Categorical variables are presented as number (%). Continuous parameters were compared by Student's *t* test and categorical variables by chi-square test or Fisher exact test, as appropriate. *P* value < 0.05 was considered statistically significant.

The research protocol was approved by the local Institutional Review Board (Wolfson medical center ethics and research committee) before the study began, approval number WOMC-0125-15. Written informed consent was not needed, since the study based only on medical records, which were reviewed anonymously.

Results

A total of 716 women were included in the study: Group A consisted of 142 women, group B of 48 women, and group C (the control group) of 516 women. The rate of nulliparous women was significantly lower in the study groups than in the control group (A 32.4% and B 43.8% vs C 50.6%, $P = 0.001$). The rate of conception by in vitro fertilization (IVF) was significantly higher in the study groups, as compared to the control group (A 72.5% and B 81.3% vs C 59.3%, $P < 0.001$) (Table 1).

The rate of CS was significantly higher in the study groups, compared to the control group (A 76.8% and B 87.5% vs C 65.7%, $P = 0.001$) (Table 2). Most of the CSs were performed electively (A 66.9%, B 72.9%, C 59.1%, $P = 0.002$), and the most common indication for elective CS in all groups was non-vertex presentation of first or second twin (A 38%, B 31.6%, and C 29.2%). The rate of urgent CS was higher in groups A and B as compared to group C (A 9.9%, B 14.6%, C 6.6%, $P = 0.002$). However, the indications for urgent CS were similar between the groups.

Table 1 Background characteristics of the study groups and the control group

	Group A, $n = 142$	Group B, $n = 48$	Group C, $n = 516$	*P* value
Age, years	36.5 ± 1.3	42.7 ± 2.9	29.0 ± 3.5	< 0.001
Body mass index (BMI), kg/m^2	23.8 ± 4.9	25.4 ± 6.0	24.1 ± 5.0	0.35
Nulliparity	46 (32.4)	21 (43.8)	261 (50.6)	0.001
Smoking (yes)	1 (0.7)	0	8 (1.6)	0.52
Presentational diabetes mellitus	1 (0.7)	1 (2.1)	1 (0.2)	0.13
Chronic hypertension	1 (0.7)	1 (2.1)	3 (0.6)	0.49
In vitro fertilization (IVF)	103 (72.5)	39 (81.3)	306 (59.3)	< 0.001

Mean ± SD, or *n* (%)

Table 2 Pregnancy outcome and complications of the study groups and the control group

	Group A, $n = 142$	Group B, $n = 48$	Group C, $n = 516$	*P* value
Gestational age at delivery, weeks	35.8 ± 2.6	35.4 ± 3.0	35.8 ± 2.7	0.61
Birthweight, gram	2312 ± 504	2209 ± 630	2312 ± 545	0.44
Cesarean section	109 (76.8)	42 (87.5)	339 (65.7)	0.001
Elective cesarean section	95 (66.9)	35 (72.9)	305 (59.1)	0.002
Urgent cesarean section	14 (9.9)	7 (14.6)	34 (6.6)	0.002
Non-progressive labor	7 (4.9)	4 (8.3)	16 (3.1)	0.1
Non-reassuring fetal monitor	4 (2.8)	2 (4.2)	12 (2.3)	0.3
Placental abruption	3 (2.2)	1 (2.1)	6 (1.2)	0.4
Hypertensive disorders	10 (7.0)	7 (14.6)	28 (5.4)	0.04
Gestational diabetes mellitus	4 (2.8)	3 (6.3)	18 (3.5)	0.53
Intrauterine growth restriction	4 (2.8)	3 (6.3)	26 (5.0)	0.46
Preterm labor (GA < 37 weeks)	76 (53.5)	27 (56.3)	283 (54.8)	0.93
Preterm labor (GA < 34 weeks)	26 (18.3)	10 (20.8)	83 (16.1)	0.61
Preterm labor (GA < 28 weeks)	5 (3.5)	2 (4.2)	14 (2.7)	0.77

Mean ± SD, or *n* (%)

Advanced maternal age of women having a twin pregnancy was found to be independently associated with CS on multivariate regression analysis, after adjusting for nulliparity, IVF, and hypertensive disorders (odds ratio: group C = 1 (reference); group A 1.6, 95% CI 1.08–2.6; group B 3.2, 95% CI 1.3–7.8) (Fig. 1).

The rate of hypertensive disorders was also significantly higher among women older than 35 years of age (A 7.0%, B 14.6%, vs C 5.4%, $P = 0.04$). The rates of preterm labor, gestational diabetes mellitus, and IUGR were similar between the groups (Table 2).

The mean duration of NICU hospitalization was significantly longer among twins born to women older than 35 years compared to twins of women in the control group (A 29 ± 25, B 31 ± 24 vs C 25 ± 22 days; $P = 0.01$). There was no difference between the groups in the rate of other neonatal complications such as RDS, the need for phototherapy treatment, neonatal hypoglycemia, neonatal sepsis, NEC, IVH, and neonatal death (Table 3). The rate of composite outcome among neonates of women who underwent urgent CS was higher in the study groups (more substantially in group B), as compared to group C (A 2.8%, B 10.4% vs C 2.1%, $P < 0.001$). Overall, there were five cases of neonatal death (one in group B and four in group C), all of them were related to neonatal complications of extreme prematurity (between 24 and 27 weeks) that included RDS, fourth degree IVH, and NEC (Table 4).

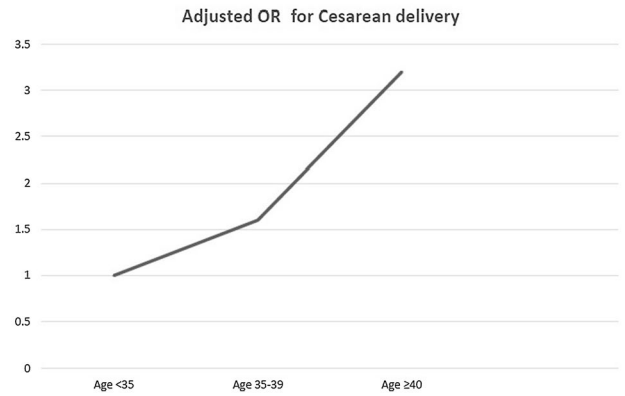

Fig. 1 Adjusted odd ratio and 95% confidence interval for cesarean delivery

Discussion

Our findings suggest that among women with twin pregnancies, the rates of CS, hypertensive disorders, and mean duration of neonatal hospitalization in NICU are higher among women older than 35 years compared to younger women.

In accordance with the previous studies [8, 10–13], we have found that CS is the most prevalent mode of delivery of twin pregnancy in women with advanced maternal age. Most of the CSs were performed electively in these women. This finding could be partially attributed to our departmental protocol [9], by which in cases of a non-vertex second twin,

Table 4 Adjusted odds ratio and 95% confidence interval for cesarean delivery

Age group	Adjusted OR (95% CI)[a]	*P* value
Group C	1 (reference)	
Group A	1.6 (1.08–2.6)	0.02
Group B	3.2 (1.3–7.8)	0.01

[a]Adjusted for nulliparity, IVF, and hypertensive disorders

Table 3 Neonatal complications of the study groups and the control group

	Group A, $n = 281$	Group B, $n = 96$	Group C, $n = 1028$	*P* value
NICU admission rate	41 (14.6)	19 (19.8)	182 (17.7)	0.4
Mean NICU admission, days	29 ± 25	31 ± 24	25 ± 22	0.01
Respiratory distress syndrome	10 (7.0)	5 (10.4)	51 (9.9)	0.56
Phototherapy treatment	19 (13.4)	10 (20.8)	98 (19.0)	0.26
Neonatal hypoglycemia	11 (7.7)	1 (2.1)	29 (5.6)	0.32
Neonatal sepsis	0	0	4 (0.8)	0.47
Necrotizing enterocolitis	0	1 (2.1)	2 (0.4)	0.15
Intraventricular hemorrhage	1 (0.7)	0	8 (1.6)	0.52
Neonatal death	0	1 (2.1)	4 (0.8)	0.31
Composite outcome[a]	26 (18.3)	12 (25.0)	119 (23.1)	0.43
Composite outcome in urgent CS	8 (2.8)	10 (10.4)	22 (2.1)	< 0.001

Mean ± SD, or *n* (%)

NICU neonatal intensive care unit, *CS* cesarean section

[a]Composite outcome include any of the above: respiratory distress syndrome, phototherapy treatment, neonatal hypoglycemia, neonatal sepsis, necrotizing enterocolitis, intraventricular hemorrhage, neonatal death

women are offered to choose liberally an elective CS. It may also be attributed to the wish of older women to deliver safely by CS [4, 6]. Although the rate of urgent CS was significantly higher in the study groups A and B, as compared to group C, the indications for urgent CS were similar between the groups. This higher rate of urgent CS in women with advanced maternal age may be explained by the effect of maternal age on decision making during active labor, as it is reported to be associated with a higher rate of maternal and perinatal complications in singleton pregnancies [14].

We found a significantly higher rate of hypertensive disorders in the study groups of women older than 35 years compared to the control group of younger women. It reached nearly 15% in women older than 40 years. Fox et al. [10] have studied twin pregnancies outcomes of women older than 45 years, and found a threefold higher rate of preeclampsia, as compared to our results. This difference could be explained both by the higher age of the population (≥ 45 years), as well as the high proportion of egg donation (95%), in this study. These two findings are known risk factors for hypertensive disorders [15–17]. The number of women in our study older than 45 years was too small to make such a comparison. However, our data indicate that even women older than 40 years have a higher rate of hypertensive disorders compared to younger women. Other studies have failed to show increased rate of hypertensive disorders [8, 12, 18], and it probably related to younger maternal age (mean age of 35) in the studies' populations.

Although the mean duration of NICU admission was longer in the study groups compared to the control group, the rates of neonatal admissions, and neonatal adverse outcomes were similar between the groups. The results are not surprising, since the rates of prematurity and IUGR (the major causes for neonatal morbidities) were also similar between the groups. The longer duration of NICU admission might be explained by the higher rate of composite outcome of neonates delivered by urgent CS in the study groups. Neonatal complications have been rarely studied in the previous reports. Few have investigated birth weight and the rates of neonatal deaths. To the best of our knowledge, the rates of neonatal morbidity have so far not been studied at all. Prapas et al. [12] compared twin pregnancies in women ≥ 35 years of age to women younger than 35 years, and concluded that advanced maternal age seems to have no effect on the perinatal outcomes. Our results strengthen this conclusion, and extend it to the neonatal period as well.

Older maternal age carries a higher risk for preterm labor and IUGR in singleton pregnancies [16]. Regarding twin pregnancies, this association is controversial. Amelia et al. [19] reported that the risk for preterm birth increased slightly for women ≥ 40 years. In contrast, Sarka et al. [8] did not find any differences regarding the rates of preterm birth, between different age groups. Yet, they did find higher rate of IUGR among women older than 35 years. In contrary, according to our results, and in accordance with a study conducted by Suzuki et al. [11], the rates of both preterm labor and IUGR are not significantly different among older women with twin gestation when compared to younger women.

The limitations of our study are inherent in its retrospective nature and the small sample size of the older group. The strengths of our study are the uniform management of all pregnancies, including the neonatal care in one tertiary medical center. Moreover, to the best of our knowledge, this is the first study that investigates the effect of advanced maternal age on neonatal complications rates, in twin pregnancies.

In conclusion, according to our data, dichorionic–diamniotic twin pregnancies of women with advanced maternal age are associated with higher rates of CS, hypertensive disorders, and longer duration of NICU admission. Other neonatal outcomes in women with twin pregnancies aged 35 years or older are similar to those of younger women.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required.

Human and animal rights statement This article does not contain any studies with animals performed by any of the authors.

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