

Pregnancy Outcome After Age 50

Michal J. Simchen, MD, Yoav Yinon, MD, Orit Moran, MD, Eyal Schiff, MD, and Eyal Sivan, MD

OBJECTIVE: To evaluate pregnancy complications occurring after age 50.

METHODS: We compared the pregnancy outcomes of women aged 50–64 years with those aged 45–49 years and with the general population.

RESULTS: During 5 years from January 1, 1999, to June 30, 2004, 123 women aged 45 years and older gave birth. Fifty-five percent were nulliparous, 24 of 123 were aged 50–64 years, and 99 of 123 women were aged 45–49 years. All women older than age 50 conceived via in vitro fertilization with oocyte donation. For these 123 women, the overall mean gestational age at delivery was 37.6 ± 2.6 weeks. The mean birth weight was $2,684 \pm 754$ g, significantly lower than the general population, and the incidences of multifetal pregnancies, diabetes, and hypertension were high. Women aged 50 years and older were more likely to be hospitalized during pregnancy than women younger than 50 years (63% versus 22%, $P < .001$). Neonatal outcome was generally good. Women aged 50 years and older gave birth to significantly more low birth weight babies than those younger than age 50 years (61% versus 32%, $P = .002$). Gestational age and birth weight were both significantly lower for singletons and multiples in women older than age 50 years compared with those younger than age 50 years (gestational age of singletons 36.9 versus 38.4 weeks, $P = .005$; birth weight of singletons 2,694 versus 3,027 g, $P = .019$; gestational age of multiples 35.1 versus 36.4 weeks, $P = .01$; birth weight of multiples 1,976 versus 2,310 g, $P = .038$, respectively).

CONCLUSION: Pregnant women aged 50–64 years have increased risks of preterm birth, low birth weight babies, diabetes mellitus, hypertension, and hospitalization.

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From the Department of Obstetrics and Gynecology, Sheba Medical Center, Tel Hashomer, Israel.

Corresponding author: Michal J. Simchen, MD, Department of Obstetrics and Gynecology, Sheba Medical Center, Tel Hashomer, 52621, Israel; e-mail: michal.simchen@sheba.health.gov.il.

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During the last 3 decades, an increasing number of women in the developed world have been electing to delay childbearing until after age 35–40 years. It is a well-established fact that fecundity decreases and the risk for miscarriage increases with age. However, the enormous advances in reproductive medicine have compensated, to some extent, for this natural decrease in fecundity, and with oocyte donation even postmenopausal women may become pregnant.

The influence of advanced maternal age and delayed childbearing on perinatal outcome has been studied before, but most studies have evaluated outcome in women aged 35 years or older. It has previously been shown that pregnant women aged 35 years or older experience an increased risk of intrauterine fetal death, pregnancy-induced hypertension, gestational diabetes, and cesarean delivery.^{1,2} There is some information in the medical literature regarding the older pregnant population, but this refers mainly to women in their 40s.^{3–5}

In the present study, our interest lay in investigating whether there is a difference in the rate of complications between women conceiving in the fifth decade of life (what has been traditionally considered the extreme end of fertility) and women conceiving later, mainly through artificial fertilization. Our aim was to estimate whether women aged 50 years and more face unique pregnancy complications, when compared with women in their late 40s, to enable health care providers to counsel these older women better before undertaking a pregnancy.

MATERIALS AND METHODS

Detailed information was collected regarding all pregnant women who were at least 45 years of age at the time of delivery, between January 1, 1999, and June 30, 2004, who gave birth at the Chaim Sheba Medical Center, Tel Hashomer, Israel. Data extracted included maternal age, gravidity, parity, gestational age at delivery, birth weight, birth weight percentile, number of fetuses, mode of conception, mode of delivery, complications of pregnancy (including hy-



pertension, diabetes, and postpartum complications, among others), and need for hospitalization during pregnancy. For the purpose of a normal comparison group, we extracted data from a computer database on all deliveries that took place at Chaim Sheba Medical Center during a 6-month period, between July 1, 2003, and December 31, 2003. The information in this database is entered prospectively by the obstetrician responsible for the laboring woman's medical care and includes maternal demographics, obstetric history, labor and delivery events, and immediate neonatal outcome.

Small for gestational age (SGA) was defined as birth weight below the 10th percentile for gestational age according to accepted tables,^{6,7} pregestational diabetes and gestational diabetes mellitus, as well as hypertensive complications of pregnancy, were defined according to criteria of the American College of Obstetricians and Gynecologists (ACOG).^{8,9}

Two sets of comparisons were performed. In the first comparison, we investigated labor and delivery characteristics of our older pregnant cohort and compared them with the general laboring population at our medical center. In the second set of comparisons, we performed subgroup analysis on two age groups within our older cohort. This was done to investigate whether there is a difference in specific risks with advancing maternal age and to determine the nature of those risks. Women were therefore classified into two groups for the sake of comparisons: group 1 included women between 45 and 49 years of age, and group 2 included women aged 50 years and more. Institutional review board approval for the collection of data was obtained from the Helsinki Ethics Board.

Statistical analysis was performed with SigmaStat 1.0 software (Jandel Engineering Ltd, Linslade, Bedfordshire, UK). Categorical data were compared using the Pearson χ^2 test and Fisher exact test, as appropriate. Continuous variables were compared using the Student *t* test when data were normally

distributed and the Mann-Whitney rank sum test when not normally distributed. $P \leq .05$ was considered statistically significant.

RESULTS

Between January 1, 1999, and June 30, 2004, 123 women who were 45 years of age or older gave birth at our labor and delivery suite at Sheba Medical Center, Tel Hashomer, Israel. With an annual delivery rate of 10,000–11,000 deliveries, this represents 0.2% of the total deliveries at that time period at our institution.

During a 6-month representative comparison period between July and December 2003, 5,162 women gave birth at our center. We used the data from these deliveries to serve as a comparison base for our study group, and the data are presented in Table 1.

Of the 123 study women, 67 women (55%) conceived by means of assisted reproductive techniques. Additionally, 67 women (55%) were also nulliparous, compared with only 40% of women in our general population who were nulliparous. This would reflect the very high rate of assisted reproductive techniques (ART) in our older study group, although not all study women who benefited from ART were necessarily nulliparous.

The mean maternal age at delivery of our elderly study group was 47.7 ± 3.8 years (range 45–64 years), compared with 30.3 ± 5.1 years in our general population. The mean gestational age at delivery was 37.6 ± 2.6 weeks (range 28–42 weeks), compared with 39.5 ± 2.0 weeks in our general population. The mean birth weight was $2,684 \pm 754$ g, compared with $3,175 \pm 571$ g in our general population. All of these differences were highly statistically significant.

Of the 123 study women, 28 (23%) had a multifetal pregnancy (27 twins, 1 triplet), compared with a 3% multifetal pregnancies rate in the general population ($P < .001$). The rate of preterm delivery was also very high in our study group, compared

Table 1. Obstetric Characteristics of Study Group and Comparison Group

	Study Group – All (n=123)	Comparison Group (n=5,162)	<i>P</i>
Maternal age (y, mean±SD)	47.7±3.8	30.3±5.1	<.001
Primiparity (%)	55	40	.001
Gestational age (wk, mean±SD)	37.6±2.6	39.5±2.0	<.001
Birth weight (g, mean±SD)	2,684±754	3,175±571	<.001
Multifetal pregnancies [% (n)]	23 (28)	3 (172)	<.001
Delivery [% (n)]			
34 weeks or less	14 (17)	3 (134)	<.001
32 weeks or less	5 (6)	1 (58)	<.001

SD, standard deviation.



with the general population, with 14% of pregnancies ending at or before 34 weeks of gestation and 5% ending at or before 32 weeks of gestation (compared with 3% and 1% in the general population, respectively, $P<.001$). When only singletons were analyzed, the preterm birth rate (at or before 34 weeks of gestation) was 11% in the study group and 2% in the general population ($P<.001$). The information regarding pregnancy outcome in the study group ($n=123$) and the general population comparison group is presented in Table 1.

To further delineate the different complications arising with pregnancy in very advanced maternal age, we divided our study cohort into two age groups. Women aged 45–49 were termed group 1, and women aged 50 years and more were designated group 2.

Of 123 women aged 45 years or more, 99 women were between 45 and 49 years of age (median 46 years) at the time of delivery, and 50 of these 99 (50%) women were nulliparous. Forty-three women (43%) conceived by means of in vitro fertilization, whereas 13 (13%) required ovum donation.

Twenty-four of 123 women were aged 50 years or more (median age 52, range 50–64 years). All of these women (100%) conceived by means of assisted reproductive techniques with ovum donation and came to our clinic after completion of the first trimester. Seventeen of 24 women (71%) were nulliparous.

More women were nulliparous among the older group 2 women, although this was not quite statistically significant ($P=.07$). This reflects the decision to delay the onset of childbearing in this population.

Overall, 151 infants were born in our cohort of women aged 45 years or more, 118 in group 1 and 33

in group 2. Neonatal outcome was good, with no significant neonatal complications, with the exception of one intrauterine death of a severely growth-restricted twin in group 1.

The overall rate of multifetal pregnancies was 23% (compared with 3% in our general population, Table 1). Twenty women (20%) in group 1 had multifetal (twins) pregnancies, whereas eight women (33%) in group 2 had multifetal pregnancies: seven twins and one set of triplets.

Women in group 2 gave birth significantly earlier than women in group 1 (mean gestational age 36.3 ± 2.4 versus 37.9 ± 2.6 weeks, $P=.006$). This difference persisted even when singleton and multiple pregnancies were analyzed separately. Mean gestational age at delivery was lower for group 2 than for group 1 (gestational age of singletons 36.9 weeks versus 38.4 weeks, $P=.005$; gestational age of multiples 35.1 versus 36.4 weeks, respectively, $P=.01$, Table 2).

Furthermore, infants born to women in group 2 were significantly smaller than those in group 1 (birth weight $2,324\pm 589$ g versus $2,784\pm 766$ g, respectively, $P=.002$). Moreover, women aged 50 years or older gave birth to significantly more low birth weight infants (birth weight less than 2,500 g) (61% in group 2 versus 32% in group 1, $P=.002$) and SGA infants (less than the 10th percentile in birth weight) (49% in group 2 versus 30% in group 1, $P=.04$). Here again, the observed differences in birth weight persisted when analyzed separately for singletons and multiple pregnancies (birth weight of group 2 singletons 2,694 g versus 3,027 g in group 1, $P=.019$; birth weight of group 2 multiples 1,976 g versus 2,310 g in group 1, $P=.038$, respectively).

Table 2. Pregnancy Outcome in Elderly Pregnant Women

Outcome	Group 1 Age 45–49 (n=118)	Group 2 Age 50+ (n=33)	P
GA at delivery (wk)	37.9±2.6	36.3±2.4	.006
Multiple pregnancy	20 (20)	33 (8)	.17
GA singletons (wk)	38.4±2.7	36.9±2.4	.005
GA multiples (wk)	36.4±1.6	35.0±1.8	.01
Birth weight (g)	2,784±766	2,324±589	.002
BW singletons (g)	3,027±739	2,694±499	.019
BW multiples (g)	2,310±577	1,976±442	.038
Delivery			
34 weeks or less	9 (11)	18 (6)	.15
32 weeks or less	3 (4)	6 (2)	.48
SGA	30 (35)	49 (16)	.04
LBW (less than 2,500 g)	32 (38)	61 (20)	.003
VLBW (less than 1,500 g)	5 (6)	9 (3)	.40

GA, gestational age; BW, birth weight; SGA, small for gestational age; LBW, low birth weight; VLBW, very low birth weight. Data are expressed as mean±standard deviation or % (n).



As previously mentioned, the rate of clinically significant preterm birth before 32–34 weeks of gestation was high in our cohort. Seventeen of 123 women (14%) gave birth before or at 34 completed weeks, and six of 123 (5%) delivered before or at 32 weeks, both significantly higher than that observed in the general population (Table 1). It is interesting to note that the preterm birth rate in women aged 50 years or more was almost twice that of women aged 45–49 years, although this was not statistically significant. The information regarding pregnancy outcome by subgroup analysis is summarized in Table 2.

The overall incidence of diabetes and hypertension was very high in our cohort, 21% and 28%, respectively, and similar between groups 1 and 2, although more women in group 2 suffered from pregestational diabetes. Additionally, older women were more likely to be hospitalized during pregnancy (63% versus 22%, $P < .001$). Indications for hospitalization included vaginal bleeding, hypertensive complications, and premature contractions. In addition, one woman with pre-existing polycystic kidneys and pregestational diabetes was hospitalized for mild renal failure and hypertension, one woman for acute renal failure and lung congestion with acute respiratory failure, and one woman with increased liver enzymes and abdominal edema that resolved with supportive care, all in group 2. All women in group 2 gave birth by cesarean delivery, whereas 21 of 99 women in group 1 delivered vaginally. The information regarding maternal complications is summarized in Table 3.

DISCUSSION

During the past 2–3 decades, a remarkable shift in demographics has occurred in the industrialized world, with a sharp increase in the proportion of women giving birth after the age of 40 years. The mean maternal age at the birth of the first child increased from 21.4 to 24.9 years in the United States and from 25.6 to 28.0 years in Japan between 1970 and 2000.¹⁰

In the present study, we focused our attention on a previously understudied group of pregnant women, those aged 45 years of age and older. Furthermore, what is unique in our study is the attempt to specifically focus on women at the extreme end of the reproductive potential, perimenopausal women aged 50 years or more, in whom pregnancy was previously seldom observed.

Several points emerge from our study. First, it is encouraging to see that pregnancy outcome in our older population was generally good. Most of our cohort tolerated pregnancy well, although hospitalization during pregnancy was common—over 30% of our cohort members required hospitalization during their pregnancy. When considering women in the elderly group—50 years or older—the rate of hospitalization was extremely high, with nearly two thirds of women spending at least part of their pregnancy as inpatients. This could be related, at least in part, to physician stress and patient stress.

Our study population, as a whole, is a significantly high-risk group, with an extremely high rate of pregnancy complications such as diabetes and hypertension. The increased incidence of complications due to diabetes and hypertensive disorders of pregnancy among older women has been previously published and is well established.^{11,12}

Preterm birth is another significant complication of pregnancy in the older population, even when controlling for the effect of multifetal pregnancies. Of women who completed the first trimester, the overall rate of preterm birth was extremely high, with 14% of women giving birth before 34 weeks and 5% before 32 weeks of gestation. Nevertheless, there were no cases of extreme prematurity, and mean gestational age at delivery approached term.

Advanced maternal age has been associated by several investigators with adverse pregnancy outcomes such as increased perinatal mortality,^{13,14} preterm delivery, low birth weight, and SGA age infants.^{15–17} On the

Table 3. Maternal Complications in Women Aged 45 and More

	Group 1 Age 45–49 (n=99)	Group 2 Age 50+ (n=24)	P
Maternal age (y, mean±SD)	46.1±1.3	54±4.4	<.001
Nulliparity	50 (50)	71 (17)	.07
Cesarean delivery	68 (68)	100 (24)	.001
Diabetes	19 (19)	29 (7)	.28
Pregestational DM	1 (1)	8 (2)	.04
Hypertension	27 (27)	33 (8)	.55
Severe hypertensive complications	11 (11)	4 (1)	.30
Hospitalization during pregnancy	22 (22)	63 (15)	<.001

SD, standard deviation; DM, diabetes mellitus.

Data are expressed as % (n), except where otherwise indicated.



other hand, other investigators^{12,18} have found no difference.

Several hospital-based studies have investigated women aged 45 years or older.^{3,19} Dildy et al¹⁹ reported on maternal and neonatal outcome of women 45–47 years of age, predominantly grand multiparous women, among whom the main problems encountered were cesarean delivery, high aneuploidy rate, and associated medical complications such as diabetes and hypertension. In the report by Dulitzki et al,³ the mean maternal age in the study group was 45 years, and most women were multiparous. This is a very different population from the one presented in our study of older, primarily primiparous women in the perimenopausal period.

Paulson et al¹² and Sauer et al²⁰ also reported on the reproductive outcome of women between 50–54 years of age using ovum donation and reported good pregnancy outcome, notwithstanding high rates of maternal complications, mainly pregnancy-induced hypertension.

Our findings in the present study were somewhat disturbing. We found a significantly higher rate of low birth weight and SGA infants in the older group (aged 50 years or older) when compared with women aged 45–49 years. Additionally, older women delivered at an earlier gestational age and had smaller babies, even when singletons and twins were analyzed separately. This would potentially place these infants at increased risk of prematurity-related and SGA-related complications, both short term and in the long run.

Women in industrialized societies are progressively delaying the age of first pregnancy, and as a result, more and more of these pregnancies are achieved by means of assisted reproductive technologies. The emergence of ovum donation as an alternative to aging ovaries and ova has opened the door for women at more advanced ages to conceive. There are tremendous ethical issues involved in fertility treatments in women of advanced age, but these are outside the scope of this study. The aim of the present study was to investigate whether there is a difference in pregnancy outcome for women in their sixth and even seventh decade, when compared with women aged 45 years, and to put these in the context of the general population of pregnant women. This information may be used for more accurate consultation with women who are contemplating pregnancy after the age of 50 years.

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