

PREGNANCY OUTCOME AT MATERNAL AGE 40 AND OLDER

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SUMMARY

Objective: This case-control study was performed to compare the pregnancy outcomes of women aged 40 years and older with those of 20- to 30-year-old women.

Materials and Methods: Among 28,507 women who delivered in the Zeinabieh and Hafez hospitals affiliated to Shiraz University of Medical Sciences between September 2001 and October 2004, 574 women (2.01%) were 40 years old or older at the time of delivery. Eight cases were excluded because of multifetal pregnancies. From the 566 remaining cases, 200 women (case group) were selected by simple random sampling and their hospital admission charts were retrospectively reviewed. They were compared with 200 20- to 30-year-old mothers (control group).

Results: The mean age for the case group was 41.56 ± 2.06 years and that for the control group was 24.63 ± 2.89 years. The mean birth weight was $2,869 \pm 848$ g for the case group and $2,895 \pm 834$ g for the control group ($p=0.75$). The incidences of preeclampsia, gestational hypertension, cesarean delivery, abruptio placenta, preterm delivery, and 5-minute Apgar scores <7 were significantly higher in the older group ($p<0.05$). Some complications such as diabetes, chronic hypertension and perinatal mortality were more common in the older mothers, but the differences were not statistically significant. A comparison of complications with respect to parity showed that preterm birth ($p=0.002$) and low birth weight ($p=0.04$) occurred more frequently in primiparous older women. However, preeclampsia ($p=0.002$) and abruptio placenta ($p=0.012$) were more common in multiparous older women.

Conclusion: Maternal and neonatal complications increased in women aged 40 years and above, but neonatal outcomes were similar to those in the younger age group. [*Taiwan J Obstet Gynecol* 2008;47(3):318-321]

Key Words: advanced maternal age, low birth weight, parity, preeclampsia, pregnancy outcome

Introduction

Social trends in the past decades have encouraged women to delay their first pregnancies and some women continue childbearing beyond age 40. With the introduction of infertility treatments, women of almost all ages can sustain a pregnancy, even in postmenopausal states [1,2]. It is therefore expected that increasing numbers of women of advanced age will enter the obstetric population, requiring antenatal care and management.

Advanced maternal age has long been considered to be an obstetric risk factor, though several controversies exist in published reports [3]. Some authors have reported no significant differences in the obstetric outcomes [4], maternal and perinatal outcomes [5], birth weights, and gestational ages [6] between older and younger mothers, but these results are not supported by other studies [7,8].

This study was designed to compare the complications and pregnancy outcomes of women aged 40 years and above with women aged 20-30 years.

Materials and Methods

Between September 2001 and October 2004, 28,507 women delivered at gestational ages of >20 weeks in Zeinabieh and Hafez hospitals affiliated to Shiraz



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Table 1. Comparison of maternal and neonatal complications between women aged 40 years and older and those aged 20–30 years*

Variable	Women aged ≥ 40 years (n = 200)	Women aged 20–30 years (n = 200)	OR (95% CI)	p
Gestational hypertension	16 (8)	6 (3)	2.81 (1.07–7.34)	0.02
Preeclampsia	36 (18)	9 (4.5)	4.39 (2.05–9.37)	0.001
Chronic hypertension	6 (3)	2 (1)	3.06 (0.61–15.35)	0.142
Diabetes	11 (5.5)	4 (2)	2.85 (0.89–9.11)	0.065
Preterm birth	62 (31)	38 (19)	1.78 (1.12–2.83)	0.013
Post-term birth	3 (1.5)	9 (4.5)	0.323 (0.08–1.21)	0.079
Placental abruption	12 (6)	0 (0)	NA	0.001
Prolonged rupture of membranes	11 (5.5)	12 (6)	0.912 (0.393–2.11)	0.830
Cesarean delivery	116 (58)	71 (35.5)	2.50 (1.67–3.75)	0.001
Low birth weight	48 (24)	40 (20)	1.26 (0.78–2.03)	0.334
Macrosomia	12 (6)	6 (3)	2.06 (0.75–5.61)	0.148
1-minute Apgar score < 7	35 (17.5)	22 (11)	1.71 (0.96–3.04)	0.063
5-minute Apgar score < 7	25 (12.5)	13 (6.5)	2.05 (1.02–4.14)	0.041
Intrauterine fetal death	15 (7.5)	8 (4)	1.94 (0.80–4.69)	0.133
Primipara	28 (14)	125 (62.5)	0.09 (0.6–0.16)	0.001

*Data are presented as n (%). OR = odds ratio; CI = confidence interval; NA = not applicable.

University of Medical Sciences. Among these were 574 mothers (2.01%) who were aged 40 years or above at the time of delivery. Eight of these older mothers had multifetal pregnancies and were excluded. Out of the remaining 566 older mothers, 200 cases were selected by simple random sampling and their obstetric charts were retrospectively reviewed (case group). They were compared with a control group consisting of 200 women with singleton pregnancies and aged from 20 to 30 years, who delivered immediately next to the women in the case group. These two groups were compared for the incidences of several complications including hypertensive disorders, diabetes, preterm delivery, placenta previa, abruptio placenta, cesarean delivery, and for neonatal outcomes such as preterm and post-term delivery, birth weight, Apgar score and perinatal death. To account for the effects of parity on these variables, the two groups were compared again after sub-classifying according to parity.

Preeclampsia was diagnosed when blood pressure was $\geq 140/90$ mmHg after 20 weeks gestation, in addition to the presence of proteinuria (urinary protein ≥ 300 mg in a 24-hour period or $\geq 1^+$ on urine dipstick) [9]. All types of glucose intolerance, diagnosed by abnormal fasting blood sugar or abnormal oral glucose tolerance tests, were classified together as diabetes. The diabetic mothers were classified according to the system recommended by the American College of Obstetricians and Gynecologists in 1986 [10]. Prolonged rupture of membranes was defined as rupture of membranes more than 18 hours before delivery. Occurrence of preterm delivery (birth prior to 37 completed weeks) and post-term

delivery (pregnancy continuing beyond 42 weeks), low birth weight (birth weight $\leq 2,500$ g), macrosomia (birth weight $\geq 4,500$ g) and low Apgar scores (Apgar score < 7) were compared between the groups [11].

Statistical analysis was performed using the Chi-squared test, *t* test and Fisher's exact test. Odds ratio (OR) and 95% confidence intervals (CI) are presented. Level of significance was set at $p < 0.05$.

Results

The mean age of women in the case group was 41.56 ± 2.06 years (range, 40–50 years) and that in the control group was 24.63 ± 2.89 years (range, 20–30 years) at the time of delivery. The mean birth weight was $2,869 \pm 848$ g for the case group and $2,895 \pm 834$ g for the control group ($p = 0.7$). Comparisons of maternal and neonatal complications are presented in Table 1.

Among the case group, there were 11 (5.5%) patients with diabetes: four (2%) with gestational diabetes class A₁, two (1%) with gestational diabetes class A₂ and five (2.5%) who were diagnosed with overt diabetes before pregnancy. Four patients (2%) from the control group developed diabetes: two gestational diabetes class A₁ and two class A₂.

The results showed that the frequencies of preeclampsia, gestational hypertension, cesarean delivery, placental abruption, preterm delivery, and 5-minute Apgar scores < 7 were significantly higher among mothers aged 40 years and older ($p < 0.05$). Although some complications such as diabetes, chronic hypertension, low birth

Table 2. Comparison of antepartum, intrapartum and neonatal complications between mothers aged 40 years and older and those aged 20–30 years according to their parity*

Variables	Primipara		<i>p</i>	Multipara		<i>p</i>
	≥ 40 years (<i>n</i> = 28)	20–30 years (<i>n</i> = 125)		≥ 40 years (<i>n</i> = 172)	20–30 years (<i>n</i> = 75)	
Gestational hypertension	2 (7.1)	3 (2.4)	0.227	14 (8.1)	3 (4)	0.237
Preeclampsia	4 (14.3)	6 (4.8)	0.86	32 (18.6)	3 (4)	0.002
Chronic hypertension	0 (0)	0 (0)	–	6 (3.5)	2 (2.7)	0.539
Diabetes	2 (7.1)	2 (1.6)	0.153	9 (5.2)	2 (2.6)	0.298
Preterm birth	13 (46.4)	22 (17.6)	0.002	49 (28.4)	16 (21.3)	0.3
Post-term birth	0 (0)	6 (4.8)	0.59	3 (1.7)	3 (4)	0.4
Placental abruption	0 (0)	0 (0)	–	12 (7)	0 (0)	0.012
Prolonged rupture of membranes	0 (0)	9 (7.2)	0.153	11 (6.4)	3 (4)	0.328
Cesarean delivery	17 (60.7)	41 (32.8)	0.001	99 (57.6)	30 (40)	0.001
Low birth weight	11 (39.2)	24 (19.2)	0.04	37 (21.5)	16 (21.3)	0.9
Macrosomia	0 (0)	4 (3.2)	0.44	12 (6.9)	2 (2.6)	0.23
1-minute Apgar score < 7	6 (21.4)	15 (12)	0.156	29 (16.9)	7 (9.3)	0.123
5-minute Apgar score < 7	5 (17.9)	9 (7.2)	0.086	20 (11.6)	4 (5.3)	0.125
Fetal death	2 (7.1)	5 (4)	0.377	13 (7.6)	3 (4)	0.227

*Data are presented as *n* (%).

weight, macrosomia, and perinatal mortality were more frequently seen among older mothers, the differences were not statistically significant.

The older mothers had a mean gravidity of 4.88 ± 2.7 as compared with 1.79 ± 1.07 for the control group ($p = 0.001$). Twenty-eight (14%) of the women in the older group were primiparous as compared with 125 (62.5%) in the younger group ($p = 0.001$). Comparison of the complications between the primiparous and multiparous women in the two groups is presented in Table 2.

Preeclampsia (OR, 5.48; 95% CI, 1.62–18.5; $p = 0.002$) and abruptio placenta (OR, not applicable; $p = 0.012$) were more frequent among the multiparous older mothers, but the rates of preterm birth (OR, 4.05; 95% CI, 1.69–9.7; $p = 0.002$) and low birth weight (OR, 2.72; 95% CI, 1.13–6.5; $p = 0.04$) were higher among primiparous older mothers. The rates of cesarean delivery were significantly higher in both primiparous ($p = 0.001$) and multiparous ($p = 0.001$) women in the advanced age group, as compared with the younger group. No maternal mortality was seen in this study.

Discussion

The greater risks of chromosomal abnormalities, spontaneous abortions, hypertensive disorders and diabetes occurring in pregnancies in mothers of advanced ages are widely accepted. However, there remains disagreement concerning some aspects of perinatal and maternal

outcomes. These discrepancies seem to be partly due to differing definitions of “advanced age”; most of the previous research has been done on mothers aged > 35 years [12–14], but some recently published studies have considered 40 years to be the cut-off age [5,8,15,16].

In this study, a higher incidence of maternal medical diseases such as hypertensive disorders and diabetes was seen among the advanced age mothers than among the younger mothers. Gestational hypertension (2.8-fold), preeclampsia (4.3-fold), chronic hypertension (3-fold) and diabetes (2.8-fold) were diagnosed more frequently among the case group. Many other reports confirm these findings [5,15,17]. The diabetics in the control group were diagnosed during pregnancy as having gestational diabetes class A₁ and A₂. However, almost half of the diabetic mothers in the older group were diagnosed before pregnancy. In this survey, all kinds of hypertensive disorders were more frequently seen in the multiparous women in the advanced age group.

In general, increased vascular endothelial changes with aging are suggested to be responsible for the increased risk of medical and chronic diseases in the older population [1].

This study showed that both multiparous and nulliparous mothers aged 40 and older had a higher risk for cesarean delivery ($p = 0.001$), possibly due to deterioration of uterine activity with age [18]. Diabetes and hypertension, as predisposing factors for macrosomia and low birth weight, are also contributing factors for cesarean deliveries. A lower threshold of obstetricians for

performing cesarean sections in older women, referred as “precious baby syndrome”, has also been proposed in many reports [3,19].

In the present study, abruptio placenta was more frequent among the older group, which could be related to the higher incidence of hypertensive disorders in these women. Preterm birth ($p=0.002$) and low birth weight ($p=0.04$) were more frequently seen among nulliparous women aged 40 years and older. This finding may be related to the underlying maternal and fetal complications seen in the older mothers, such as hypertensive diseases, diabetes, intrauterine growth restriction or fetal distress. The correlation between advanced maternal age and low birth weight may be due to age-related changes in the uterine vasculature [20].

In this study, macrosomia was more frequent among the multiparous older women, but the difference was not significant ($p=0.2$).

This study showed that a 5-minute Apgar score <7 , which is considered to be a good indicator of long-term outcome, was twice as common in the older mothers ($p=0.04$). Additionally, the results showed a 1.8-fold increase in perinatal mortality in the older group, although the difference was not statistically significant ($p=0.13$). This finding is supported by other reports [13,17]. Hypertensive disorders may contribute to increased perinatal mortality caused by extreme prematurity and growth restriction. The failure of the uterine vasculature to adapt satisfactorily to the increased hemodynamic demands of pregnancy has also been suggested as a cause of fetal death in older women [13].

In conclusion, significantly higher incidences of complications, such as preeclampsia, gestational hypertension, abruptio placenta, cesarean delivery, preterm birth and lower Apgar scores, were seen in pregnant women aged 40 years and older. However, the overall neonatal outcomes were similar in the older and younger groups in this study. Although modern obstetric management and intensive perinatal care and monitoring have increased the probability of an acceptable outcome, health care providers should be prepared to counsel women of advanced age about the increased risk of pregnancy complications.

References

- Eisenberg VH, Schenker JG. Pregnancy in the older woman: scientific and ethical aspects. *Int J Gynaecol Obstet* 1997;56:163-9.
- Antinori S, Gholami GH, Versaci C, et al. Obstetric and perinatal outcome in menopausal women: a 12-year clinical study. *Reprod Biomed Online* 2003;6:257-61.
- Carolan M. The graying of the obstetric population: implications for the older mother. *J Obstet Gynecol Neonatal Nurs* 2003;32:19-27.
- Smit Y, Scherjon SA, Treffers PE. Elderly nulliparae in midwifery care in Amsterdam. *Midwifery* 1997;13:73-7.
- Diejomaoh MFE, Al-Shamali IA, Al-Kandari F, Al-Qenae M, Mohd AT. The reproductive performance of women at 40 years and over. *Eur J Obstet Gynecol Reprod Biol* 2006;126:33-8.
- Achanna S, Monga D. Performance of elderly primigravidae in Kelantan. *Med J Malaysia* 1995;50:37-41.
- Kirchengast S, Hartmann B. Advanced maternal age is not only associated with newborn somatometrics but also with the mode of delivery. *Ann Hum Biol* 2003;30:1-12.
- Ziadeh S, Yahaya A. Pregnancy outcome at age 40 and older. *Arch Gynecol Obstet* 2001;265:30-3.
- Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. Hypertensive disorders in pregnancy. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. *Williams Obstetrics*, 22nd edition. New York: McGraw-Hill, 2005:762-808.
- Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. Diabetes. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. *Williams Obstetrics*, 22nd edition. New York: McGraw-Hill, 2005:1169-87.
- Wright LL, Vohr BR, Fanaroff AA. Perinatal-neonatal epidemiology. In: Taeusch HW, Ballard RA, Gleason CA, eds. *Avery's Diseases of the Newborn*, 8th edition. Philadelphia: Elsevier Saunders, 2005:1-8.
- Prysak M, Lorenz RP, Kisly A. Pregnancy outcome in nulliparous women 35 years and older. *Obstet Gynecol* 1995;85:65-70.
- Fretts RC, Schmittiel J, McLean FH, Usher RH, Goldman MB. Increased maternal age and the risk of fetal death. *N Engl J Med* 1995;333:953-7.
- Tough SC, Newburn-Cook C, Johnston DW, Svenson LW, Rose S, Belik J. Delayed childbearing and its impact on population rate changes in lower birth weight, multiple birth, and preterm delivery. *Pediatrics* 2002;109:399-403.
- Scholz HS, Haas J, Petru E. Do primiparas aged 40 years or older carry an increased obstetric risk? *Prev Med* 1999;29:263-6.
- Gilbert WM, Nesbitt TS, Danielsen B. Childbearing beyond age 40: pregnancy outcome in 24,032 cases. *Obstet Gynecol* 1999;93:9-14.
- Miller DA. Is advanced maternal age an independent risk factor for uteroplacental insufficiency? *Am J Obstet Gynecol* 2005;192:1974-82.
- Jolly M, Sebire N, Harris J, Robinson S, Regan L. The risks associated with pregnancy in women aged 35 years or older. *Hum Reprod* 2000;15:2433-7.
- Papapetros I. Obstetric intervention among private and public patients in Australia. Intervention relates more to age than to having private insurance. *BMJ* 2001;322:430-1.
- Aldous MB, Edmonson MB. Maternal age at first childbirth and risk of low birth weight and preterm delivery in Washington State. *JAMA* 1993;270:2574-7.