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นิพนธ์ต้นฉบับ **Original Article**

Impact of Advanced Maternal Age on Pregnancy Outcome

ผลกระทบของมารดาที่มีอายุมากต่อผลลัพธ์ของการตั้งครรภ์

วีระเดช เฉลิมพลประภา พ.บ.,
ว.ว. สูติศาสตร์-นรีเวชวิทยา
กลุ่มงานสูติ-นรีเวชกรรม
โรงพยาบาลนครปฐม

Veeradej Chalermpolprapa M.D.,
Thai Board of Obstetrics and Gynecology
Division of Obstetrics and Gynecology
Nakhonpathom Hospital

ABSTRACT

Objectives : To determine maternal characteristics, antepartum complications, mode of delivery, indications for cesarean section, postpartum complications and neonatal outcomes in pregnant women aged 35 years or older.

Materials and methods : This was a retrospective cohort study. The labour records of 611 singleton pregnant women aged 35 years or older at the time of delivery who delivered in the labour room, Nakhonpathom hospital during October 1, 2008 - September 30, 2009 (study group) were reviewed and compared with a control group consisting of 3,498 singleton pregnant women aged 20-34 years at the time of delivery who delivered during the same period. The cases of delivering before 20 weeks gestation and of babies weighing < 500 gram were excluded from both groups.

Results : Compared with the younger control group, women aged 35 years or older had significantly higher risks of HIV seropositive, DM, heart diseases, chronic hypertension, preterm, postterm, placenta previa and mild PIH. They were also at significantly increased risks of cesarean section, breech assisting and vacuum extraction respectively. Most common indications for cesarean section in the older group were previous cesarean section, CPD and elective cesarean section respectively. In addition, the risks of puerperal infection, hysterectomy and rectal tear increased in the older group, including the risks of macrosomia, stillbirth, early neonatal death and low Apgar scores.

Conclusion : Advanced maternal age was associated with significantly elevated risks for pregnancy complications and adverse outcomes.

Key words : advanced maternal age, pregnancy outcome

บทคัดย่อ

วัตถุประสงค์ : เพื่อศึกษาลักษณะเฉพาะของมารดา ภาวะแทรกซ้อนก่อนคลอด วิธีการคลอด ข้อบ่งชี้ของการผ่าตัดคลอด ภาวะแทรกซ้อนหลังคลอดและผลลัพธ์ของทารกแรกคลอดในหญิงตั้งครรภ์ที่มีอายุตั้งแต่ 35 ปีขึ้นไป

วัสดุและวิธีการศึกษา : ศึกษาวิจัยเชิงวิเคราะห์ย้อนหลัง เปรียบเทียบเวชระเบียนของหญิงตั้งครรภ์เดี่ยวที่มีอายุขณะคลอดตั้งแต่ 35 ปีขึ้นไปที่มาคลอดที่โรงพยาบาลนครปฐม ระหว่างวันที่ 1 ตุลาคม 2551 จนถึง 30 กันยายน 2552 จำนวน 611 คน (กลุ่มศึกษา) กับกลุ่มควบคุมที่เป็นหญิงตั้งครรภ์เดี่ยวที่มีอายุขณะคลอด 20-34 ปีที่มาคลอดในระยะเวลาเดียวกันจำนวน 3,498 คน โดยคัดหญิงตั้งครรภ์ที่คลอดก่อนอายุครรภ์ 20 สัปดาห์หรือมีทารกแรกคลอดน้ำหนักน้อยกว่า 500 กรัมออกจากการศึกษาทั้งสองกลุ่ม

ผลการศึกษา : เมื่อเปรียบเทียบกับกลุ่มควบคุมที่มีอายุน้อยกว่า หญิงตั้งครรภ์ที่มีอายุตั้งแต่ 35 ปีขึ้นไปมีความเสี่ยงของการตรวจพบเลือดบวกเอชไอวี โรคเบาหวาน โรคหัวใจ โรคความดันโลหิตสูง คลอดก่อนกำหนด ตั้งครรภ์เกินกำหนด รกเกาะต่ำ และครรภ์เป็นพิษชนิดไม่รุนแรงสูงกว่า รวมทั้งยังมีความเสี่ยงสูงของการต้องผ่าตัดคลอด การช่วยคลอดท่าก้น และการช่วยคลอดโดยการใช้เครื่องดูดสูญญากาศ ตามลำดับ ส่วนใหญ่ข้อบ่งชี้ในการผ่าตัดคลอดในกลุ่มที่มีอายุมากกว่า คือ previous cesarean section, CPD และ elective cesarean section ตามลำดับ นอกจากนี้ยังมีความเสี่ยงต่อการติดเชื้อระยะหลังคลอด การถูกตัดมดลูกและการฉีกขาดของทวารหนัก รวมทั้งความเสี่ยงต่อ ทารกตัวโต ทารกตายคลอด ทารกเสียชีวิตหลังคลอด และ low Apgar scores สูงขึ้นในกลุ่มที่มีอายุมากกว่า

สรุป : หญิงตั้งครรภ์ที่มีอายุตั้งแต่ 35 ปีขึ้นไปมีความสัมพันธ์กับความเสี่ยงสูงที่จะเกิดภาวะแทรกซ้อนของการตั้งครรภ์และผลลัพธ์ของการตั้งครรภ์ที่ไม่ดี

คำสำคัญ : หญิงตั้งครรภ์ที่มีอายุมาก, ผลลัพธ์ของการตั้งครรภ์

Introduction

Many women today are delaying childbearing until they are in their late 30s. The reasons of the delay are multiple, including pursuance of professional careers and delaying of marriage.

Advanced maternal age, traditionally defined as aged 35 years or older, has been associated with increased obstetric morbidity and interventions. In addition, perinatal complications are reported to be higher in this patient population. It has been shown that pregnant women aged 35 years or older experienced increased risks of chromosomal abnormalities, spontaneous abortion, preterm delivery, prolonged labour, low birth weight, intrauterine fetal death, pregnancy induced hypertension, gestational diabetes and delivery by cesarean section. Thus, the impact of advanced maternal age on pregnancy outcomes has become important.

This study was conducted to evaluate the impact of the advanced maternal age on pregnancy outcomes.

Materials and methods

This was a retrospective cohort study. The labour records of 611 singleton pregnant women aged 35 years or older at the time of delivery who

delivered in the labour room, Nakhonpathom hospital during October 1, 2008 - September 30, 2009 (study group) were reviewed and compared with a control group consisting of 3,498 singleton pregnant women aged 20-34 years at the time of delivery who delivered during the same period. The cases delivering before 20 weeks gestation and of babies weighing < 500 gram. were excluded from the study.

The following data, including maternal characteristics, antepartum complications, mode of deliveries, indications for cesarean section, postpartum complications and neonatal outcomes, were collected and compared between two groups.

Statistical analysis was performed using the Chi-squared test, independent samples t-test. Relative risk (RR) and 95% confidence intervals (CI). Level of significance was set at $p < 0.05$. The soft wares used for statistical analysis were SPSS 15.0 for windows and OpenEpi version 2.3.

Results

The maternal characteristics of the two groups of pregnant women are shown in table 1. The gravida, para, numbers of antenatal care (ANC) visits and HIV seropositive were significantly higher in the study group compared with the control group. However, gestational age (GA) and hematocrit were not significantly different.

Table 2 shows antepartum complications. The study group significantly had more pre-existing diagnosis of diabetes mellitus, heart diseases, chronic hypertension and myoma uteri, but there were no significant difference in anemia and SLE between the two groups.

The other antepartum complications such as preterm delivery, postterm, placenta previa and mild PIH were significantly higher in the study group compared with the control group , but there were no significant difference in abruptio placenta, PROM, IUGR, severe PIH, eclampsia, oligohydramnios and polyhydramnios between the two groups.

Normal delivery was the most common mode of delivery in both groups. (47.30% in the study group vs 58.40% in the control group). Cesarean section was the second most common mode of delivery in both groups. (47.14% in the study group vs 39.25% in the control group). Normal delivery was significantly lower in the study group compared with the control group, whereas cesarean section and vacuum extraction were significantly higher in the study group compared with the control group. However, there was no significant difference in forceps extraction between the two groups. (Table 3).

Previous cesarean section was the most common indication for cesarean section in both groups (35.76% in the study group vs 31.83% in the control group). CPD and elective cesarean section were the most common indication for primary cesarean section in the study group. (22.57% and 13.89% respectively), whereas CPD and breech presentation were the most common indication for primary cesarean section in the control group (28.91% and 9.98% respectively). CPD was signifi cantly lower and elective cesarean section was significantly higher in the study group compared with the control group. (Table 4)

Puerperal infection, rectal tear and hysterectomy were significantly higher in the study group

Table 1 Comparison of maternal characteristics between pregnant women aged ≥ 35 years and those aged 20-34 years

Maternal characteristics	Study group N = 611	Control group N = 3,498	p-value
Age (years)	37.72 ± 2.52	26.50 ± 4.08	.000*
Gravida	3.72 ± 1.18	2.89 ± 0.92	.000*
Para	3.42 ± 0.99	2.72 ± 0.84	.000*
GA (weeks)	37.88 ± 2.02	38.13 ± 2.27	.868
Number of antenatal care (ANC) visits	8.02 ± 3.56	8.29 ± 3.13	.016*
HIV seropositive	13 (2.13%)	21 (0.60%)	.000*
Hct (%)	34.00 ± 6.36	34.21 ± 5.74	.239

* Indicates difference is statistically significant ($p < .05$).

compared with the control group, but there were no significant difference in postpartum hemorrhage (PPH), retained placenta and perineal hematoma between the two groups. (Table 5)

The neonatal outcomes such as body weight (BW), macrosomia, stillbirth, early neonatal death, 1 and 5 minute Apgar scores = 1-3, 1 and 5 minute Apgar scores = 4-7 were significantly higher in the study group compared with the control group, but there were no significant difference in low birth weight (LBW), fetal anomalies and hydrops fetalis between the two groups. (Table 6)

Discussion

Advanced maternal age in pregnancy refers to a pregnant woman whose age is 35 years or older. Successful pregnancy outcomes occur in women with advanced maternal age but there is an increased risk of infertility and pregnancy complications. This study demonstrated only pregnant women aged 35 years or older who delivered after 20 weeks gestation and of babies weighing > 500 gram, so there was not any data about abortion because most abortion occurs in the first trimester for women of all ages. Pregnant women with advanced maternal age had an increased risk of spontaneous abortion or miscarriage due to the decline in egg or ovocyte quality as well as changes in uterine and hormonal function.

The maternal characteristics of both groups of women showed that there were pregnant women with advanced maternal age infected with HIV more than the control group and had numbers of antenatal care visits less than the control group.

Table 2 Comparison of antepartum complications between pregnant women aged ≥ 35 years and those aged 20-34 years

Antepartum complications	Study group N = 611	Control group N = 3,498	RR & CI
Anemia	69 (11.29%)	399 (11.41%)	0.99 (0.78-1.26)
DM	22 (3.60%)	26 (0.74%)	4.84 (2.764-8.49) *
Heart disease	4 (0.65%)	5 (0.14%)	4.58 (1.23-17.01) *
Chronic hypertension	26 (4.26%)	23 (0.66%)	6.47 (3.72-11.27) *
SLE	2 (0.33%)	3 (0.09%)	3.82 (0.64-22.79)
Preterm delivery	102 (16.69%)	391 (11.18%)	1.49 (1.22-1.83) *
Postterm	13 (2.13%)	17 (0.49) %	4.38 (2.14-8.97) *
Placenta previa	7 (1.15%)	12 (0.34%)	3.34 (1.32-8.45) *
Abruptio placenta	2 (0.33%)	9 (0.26%)	1.27 (0.28-5.87)
Myoma uteri	3 (0.49%)	1 (0.03%)	17.18 (1.79-164.8) *
PROM	12 (1.96%)	62 (1.77%)	1.11 (0.61-2.04)
IUGR	2 (0.33%)	7 (0.20%)	1.64 (0.34-7.86)
Mild PIH	28 (4.58%)	63 (1.80%)	2.54 (1.64-3.94) *
Severe PIH	19 (3.11%)	66 (1.89%)	1.65 (0.99-2.73)
Eclampsia	1 (0.16%)	3 (0.09%)	1.91 (0.19-18.31)
Oligohydramnios	12 (1.96%)	39 (1.11%)	1.76 (0.93-3.35)
Polyhydramnios	4 (0.65%)	11 (0.31%)	2.08 (0.67-6.52)

* Indicates difference is statistically significant ($p < .05$).

Therefore , pregnant women with advanced maternal age might have poor health status and lack of interest in caring during pregnancy which had the impact on pregnancy outcomes.

The results of this study confirmed many of the earlier studies [1-5]. Medical associated diseases such as chronic hypertension, DM and heart diseases occurred in higher frequencies in pregnant women with advanced maternal age. Incidence of chronic hypertension increased 6.47 fold in pregnant women with advanced maternal age, compared with the control group. While DM and heart diseases increased 4.84-fold and 4.58-fold respectively in pregnant women with advanced maternal age, compared with the control group. All of these medical complications had the impact on pregnancy outcome. Chronic

Table 3 Comparison of mode of delivery between pregnant women aged ≥ 35 years and those aged 20-34 years

Mode of delivery	Study group N = 611	Control group N = 3,498	RR & CI
Breech assisting	5 (0.82%)	9 (0.26%)	3.18 (1.07-9.46) *
Cesarean section	288 (47.14%)	1,373 (39.25%)	1.20 (1.09-1.32) *
Forceps extraction	4 (0.65%)	8 (0.23%)	2.86 (0.86-9.48)
Normal labour	289 (47.30%)	2,043 (58.40%)	0.81 (0.74-0.88) *
Vacuum extraction	25 (4.09%)	65 (1.86%)	2.20 (1.4-3.46) *

* Indicates difference is statistically significant ($p < .05$).

hypertension could complicate pregnancies by restricting fetal growth and might necessitate premature delivery. DM as predisposing factor for macrosomia, was also a contributing factor for cesarean deliveries. In this study, macrosomia increased 1.65-fold in pregnant women with advanced maternal age which was consistent with the studies of Spellacy et al[1], Jacobsson et al[3] and Ziadeh et al [6].

Preterm delivery increased 1.49-fold in pregnant women with advanced maternal age which was consistent with the studies of Jacobsson et al [3], Jahromi et al[7], Edge et al[8] and Prysak et al[9]. Placenta previa increased 3.34-fold in pregnant women with advanced maternal age, consistent with the studies of Spellacy et al[1], Ziadeh S. et al[6], Blanco et al[10] and Gilbert WM. et al [11]. The increased risk of placenta previa might be secondary to the relationship between aging and progressive vascular endothelial damage. Unlike the other studies, this study did not find the statistically significant association between pregnant women with advanced maternal age and increased risk for abruptio placenta, despite chronic hypertension has been suggested to be a risk factor for abruptio placenta. There is also a general agreement that the frequency of abruptio placenta increases in pregnant women with hypertension and superimposed preeclampsia. Due to the small amount of pregnant women diagnosed with abruptio placenta may be the cause of statistical insignificance, especially in posterior placenta that could be difficult to diagnose. The incidence of PIH, especially in mild PIH, was significantly higher in pregnant women with advanced maternal age but not in severe PIH and eclampsia. This result was consistent with Ziadeh et al[12] and Cleary-Goldman et al [13].

In this study, postterm increased 4.38-fold in pregnant women with advanced maternal age. Unlike the other studies, Ziadeh S. et al[6] and

Table 4 Comparison of indications for cesarean section between pregnant women aged ≥ 35 years and those aged 20-34 years

Indications for cesarean section	Study group N = 288	Control group N = 1,373	RR & CI
Abruptio placenta	1 (0.35%)	5 (0.36%)	0.95 (0.11-8.13)
Placenta previa	7 (2.43%)	12 (0.87%)	2.78 (1.11-7.00) *
Previous cesarean section	103 (35.76%)	437 (31.83%)	1.12 (0.95-1.34)
CPD	65 (22.57%)	397 (28.91%)	0.78 (0.62-0.98) *
Breech presentation	26 (9.03%)	137 (9.98%)	0.90 (0.61-1.35)
Elective cesarean section	40 (13.89%)	116 (8.45%)	1.64 (1.18-2.30) *
Fetal distress	11 (3.82%)	73 (5.32%)	0.72 (0.39-1.34)
Oligohydramnios	7 (2.43%)	29 (2.11%)	1.15 (0.51-2.60)
Thick meconium stained	3 (1.04%)	17 (1.24%)	0.84 (0.25-2.85)
Severe PIH	9 (3.13%)	31 (2.26%)	1.38 (0.67-2.88)
Eclampsia	0	2 (0.15%)	
Failed induction	11 (3.82%)	62 (4.52%)	0.85 (0.45-1.59)
Unfavorable cervix	0	17 (1.24%)	
Others	5 (1.73%)	38 (2.76%)	0.63 (0.25-1.58)

* Indicates difference is statistically significant ($p < .05$).

Gilbert WM.[11] demonstrated that postterm has decreased. Postterm is associated with increased fetal, neonatal and maternal complications. Induction of labour prior to 42 weeks gestation after cervix is ripe, is the most decisive treatment. In addition, pregnant women should be encouraged to acknowledge the important of antenatal care as well as to confirm the estimated date of delivery by ultrasound. All of these methods can reduce postterm.

As with prior studies[6, 10, 1], this study demonstrated that rate of cesarean section, breech assisting and vacuum extraction were significantly higher in pregnant women with advanced maternal age. Older women might be at increased risks for abnormalities of the course of labour, perhaps secondary to the physiology of aging as well as decreased myometrial efficiency. Diabetes and hypertension, as predisposing factors for macrosomia and low birth weight, are also contributing factors for cesarean deliveries. Nonetheless, maternal age alone may be a factor influencing both patients and physicians decision making especially in the elderly primigravida[14,15]

Table 5 Comparison of postpartum complications between pregnant women aged ≥ 35 years and those aged 20-34 years

Postpartum complications	Study group N = 611	Control group N = 3,498	RR & CI
PPH	4 (0.65%)	16 (0.46%)	1.43 (0.48-4.27)
Retained placenta	4 (0.65%)	9 (0.26%)	2.54 (0.79-8.24)
Perineal hematoma	3 (0.49%)	7 (0.20%)	2.45 (0.64-9.46)
Puerperal infection	9 (1.47%)	16 (0.46%)	3.22 (1.43-7.25) *
Hysterectomy	2 (0.33%)	1 (0.03%)	11.45 (1.04-126.1) *
Rectal tear	4 (0.65%)	3 (0.09%)	7.63 (1.71-34.02) *

* Indicates difference is statistically significant ($p < .05$).

because elective cesarean section increased 1.64-fold in pregnant women with advanced maternal age.

Older women may be at risk for malpresentation of fetus[6,11]. Cesarean births were the most often to be performed while vaginal breech births were unlikely because breech presentation may associated with risk of cord prolapse and head entrapment. In contrast, incidence of breech assisting in this study was significantly higher in pregnant women with advanced maternal age, compared with the control group. This could be explained that women with advanced maternal age were more likely to have small infants and their cervix was fully dilate while they were admitted. Thus, there was not enough time to delivery by cesarean section.

In regard to postpartum complications, pregnant women with advanced maternal age had significantly higher incidence of puerperal infection, hysterectomy and rectal tear. This could be explained by the fact that pregnant women with advanced maternal age were found to have significantly increased incidence of cesarean section, operative vaginal delivery, HIV seropostive and macrosomia which were known predisposing factors to these complications. While the incidence of postpartum hemorrhage, retained placenta and perineal hematoma were likely to increase but they were not statistically significant.

In this study, neonatal complications were largely increased in the pregnant women with advanced maternal age such as stillbirth, early neonatal death and low Apgar scores. These results were consistent with those reported in the prior studies which cited increases in perinatal morbidity and mortality.[1,3,5,16] There are several possible rea-

Table 6 Comparison of neonatal outcomes between pregnant women aged ≥ 35 years and those aged 20-34 years

Neonatal outcomes	Study group N = 611	Control group N = 3,498	RR & CI
BW (gm)	3,053.66 ± 595.86	3,043.56 ± 514.13	.000*
LBW	82 (13.42%)	381 (10.89%)	1.23 (0.99-1.54)
Macrosomia	21 (3.44%)	73 (2.09%)	1.65 (1.02-2.66) *
Stillbirth	8 (1.31%)	17 (0.49%)	2.69 (1.17-6.22) *
Early neonatal death	6 (0.98%)	7 (0.20%)	4.91 (1.66-14.55) *
Fetal anomaly	1 (0.16%)	5 (0.14%)	1.15 (0.13-9.78)
Hydrops fetalis	3 (0.49%)	4 (0.11%)	4.29 (0.96-19.14)
1-minute Apgar scores = 1-3	8 (1.31%)	14 (0.40%)	3.27 (1.38-7.77) *
1-minute Apgar scores = 4-7	23 (3.76%)	79 (2.26%)	1.67 (1.06-2.63) *
5-minute Apgar scores = 1-3	4 (0.65%)	4 (0.11%)	5.73 (1.44-22.83) *
5-minute Apgar scores = 4-7	11 (1.80%)	22 (0.63%)	2.86 (1.39-5.87) *

* Indicates difference is statistically significant ($p < .05$).

sons for the excess risks of adverse birth outcomes among older pregnant women. For instance, a higher prevalence of medical diseases, preterm, postterm, placenta previa, myoma uteri and pregnancy induced hypertension can contribute to higher rates of adverse outcomes in neonates. In contrast, some studies had reported no adverse neonatal outcomes associated with pregnancy in older women.[6,9,10,17]

In this study, there were some potential confounding factors that could affect neonatal outcomes such as HIV infection and postterm. These factors were more likely to produce biased results. Thus, potential confounding factors must be controlled to ensure accurate results. Cnattingius et al [18], Kristensen et al[19] and Yu et al [20] had demonstrated that obesity in mothers was the potential confounding factor that affected neonatal outcomes clearly. In addition, the other potential confounding factors to the relationship between advancing maternal age and neonatal outcomes including race, parity, level of education, marital status, smoking, history of medical problems, previous adverse pregnancy outcome and history of assisted conception must be controlled to ensure accurate results too.

Conclusion

This study has demonstrated that advanced maternal age was associated with significantly elevated risks for pregnancy complications and adverse pregnancy outcomes. Some risks associated with advanced maternal age could be managed effectively with good antepartum, intrapartum, postpartum and neonatal care to ensure good maternal and fetal outcomes.

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