

Perinatal Outcome of Pregnancies in Women Aged 40 and Over

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ABSTRACT

Perinatal outcome of pregnancies at forty and over was analyzed starting from the diagnosis of pregnancy to seven days following delivery. Retrospectively, pre-gestational health and reproduction status were dealt with, as well as the course of pregnancy, deliveries, and newborn children (study group). The control group was composed of pregnant women aged 20 to 29, who were identical to study group in terms of parity. Statistical data processing was done by means of χ^2 -test, and contingency 2×2 tables. The difference was significant if $p < 0.05$. Out of 2,099 diagnosed wanted pregnancies at forty and over, 415 (19.8%) had a miscarriage, in 33 (1.6%) an artificial abortion was performed after determining the fetus karyotype and 1,651 (78.2%) of pregnant women delivered. In 66.2% of pregnancies the fetus karyotype was determined and in 33 (2.5%) fetuses chromosomal abnormalities were found. Incidence of deliveries at 40 and over is 1.38%, which is a 35.6-percent increase in the last ten years. Nullipara and pluripara had an increase, and multipara had a decrease. Pre-gestational health and reproduction status in study group is lower than in control group. Complications during pregnancy: threatened abortion, EPH gestosis, placenta praevia, gestational diabetes, late fetal death are more frequent than in control group ($p < 0.05$). In intrapartum terms, more frequent were induction of delivery, meconium-stained amniotic fluid, fetal distress, operative vaginal deliveries, and Caesarian section ($p < 0.05$). In neonatal outcome there are more premature infant, there are more VLBW, LBW, SGA, newborn with low Apgar index values, and the total perinatal death is greater than in the control group ($p < 0.05$). In perinatal terms, (from the diagnosis to the seventh day following delivery) 1,617 children survived (77.0%), meaning that perinatal loss was 482 (23.0%). Authors conclude that pregnancy at 40 and over is a high-risk pregnancy. There is a high risk of pre-gestational and gestational complications, and perinatal loss is high. Therefore, those pregnancies are not desirable from the medical point of view.

Introduction

From the health, economic and social standpoint, the optimum age for childbirth is from the age of 20 to 29¹, however, this age limit may be moved to the age of 34². Advanced maternal age for delivery is 35^{3–5}, 40^{6–8} or 45^{9,10}. A gravide at 40 and over is high-risk due to numerous pre-gestational complications (with high blood pressure, obesity, uterus malformation, uterus myoma, previous spontaneous and artificial abortions^{8,11}, as well as gestational complications (spontaneous abortions, bleeding during pregnancy, chromosomal abnormalities, late fetal death, meconium-stained amniotic fluid, fetal distress, premature newborn, infant with low birth weight, children with low Apgar index^{2,8,11–24}.

Subjects and Methods

The retrograde study included single pregnancies of women aged 40 and above (study group) from January 1, 1979 to December 31, 1998 in Clinic for Clinic Obstetrics and Gynecology in Split and in the Gynecological and Obstetrical Department of Šibenik General Hospital. Study Group included 429 (26.0%) nullipara, 924 (56.0%) pluripara (two to four deliveries) and 298 (18.0%) multipara (five and more deliveries). Control group included 429 nullipara (the first one who delivered after nullipara from study group, aged between 20 and 29 was studied), 924 pluripara (two to four deliveries) (the first one after pluripara delivery from the study group was studied, at the age between 20 and 29), and 298 multipara (five and more deliveries – 134 aged between 20 and 29 and 164 aged 30 to 34). Control group obtained in such a way is identical with study group in terms of parity.

The data on spontaneous and artificial abortions were obtained from the medical case history of Gynecology Unit and Pro-

tolcol, and the data about pregnant women, pregnancy, delivery and newborn children from medical case history of Maternity Hospital. Health status prior to pregnancy was considered: high blood pressure (systolic ≥ 18.7 kPa and/or diastolic ≥ 11.9 kPa), heart problems, renal problems, diabetes type I, uterus myoma, previous spontaneous and artificial abortions, previous sterility or infertility treatment.

The following pregnancy complications were dealt with: imminent abortion (less than 22 full weeks), vaginal bleeding ($\geq 23^{\text{rd}}$ week), placenta praevia, cervix incompetence, EPH gestosis (according to gestosis index), gestational diabetes (OGTT according to WHO criteria), excessive weight gain during pregnancy (≥ 18 kg), preterm premature rupture of membranes (PPROM), preterm labor, and late fetal death.

Among intrapartal complications, delivery induction was dealt with, prolonged delivery (≥ 13 hours), meconium-stained amniotic fluid, fetal distress (late deceleration, persistent tachycardia or bradycardia, operative vaginal delivery, Caesarian section, excessive bleeding during 3rd and 4th stage of labor (≥ 500 ml), lysis placentae and/or uterine exploration, injury of women in childbirth at vaginal delivery (symphysis rupture, diastase of symphysis, laceration of cervix, vagina rupture).

In neonatal outcome the following was established: sex of the newborn, incidence of VLBW (very low birth weight – under 1,500 g), LBW (low birth weight-less than 2,500 g), SGA (small for gestational age – less than 10 percentile for gestational age), LGA (large for gestational age – birth weight above 90 percentile for gestational age) and sex (26), preterm delivery (less 37 and less 32 completed weeks' gestation), low Apgar index in the first and fifth minutes. Fetal death is defined with weight of 500 g and over, perinatal

mortality is defined fetal death plus neonatal death (within the 7 days of life).

Statistical data processing was done by means of χ^2 test, 2×2 contingency table. The difference is considered significant if $p < 0.05$.

Results

Out of 2,099 diagnosed wanted pregnancies of women at 40 and above in 415 (19.8%) there was a spontaneous abortion, in 33 (1.6%) artificial abortion was carried out following determining the karyotype and 1,651 (78.2%) pregnant women delivered. In 1,327 (63.2%) of pregnant women in the study group karyotype of the fetus was determined and in 33 (2.5%) pregnancies were terminated due to fetuses chromosomal abnormalities. There is one chromosomal abnormality on 40.2 fetuses.

In a twenty-year period, there were 119,215 deliveries with one fetus and among them 1,651 (1.38%) were pregnant women aged 40 and over. In the period from 1979 to 1988 and from 1989 to 1998 the incidence of nullipara was 0.24%: 0.49% (increase of 104.2%; $p < 0.001$), pluripara 0.61%: 0.94% (increase of 54.0%; $p < 0.001$) and multipara 0.33%: 0.17% (decrease of 48.5%; $p < 0.001$). The total increase in the number of deliveries in the second decade was 35.6% (from 1.18% to 1.60%; $p < 0.001$) (Table 1).

Pre-gestational health and reproduction status of pregnant women from study group is less favorable than of the ones in the control group (Table 2).

Table 3 illustrates status during pregnancy. There were more threatened abortions, cervix incompetence, EPH gestosis, vaginal bleedings, placenta praevia carbohydrates metabolism disorders, and late fetal death in pregnant women in the study group ($p < 0.05$), whereas the incidence of weight gain (< 18 kg), PPROM, and preterm labor do not differ ($p < 0.05$).

In the study group there were more delivery inductions, meconium in amniotic fluid, fetal distress, operative vaginal deliveries, Caesarian sections, a greater number of pregnant women in the 3rd and 4th stage of labor lose more than 500 ml of blood, lysis placentae and/or exploration of uterus is more frequent and there were a greater number of pregnant women with injuries during delivery in comparison with the control group ($p < 0.05$) (Table 4).

Table 5 shows neonatal outcome. There were more VLBW, LBW, SGA, prematurely born infant (up to 37th week), newborn with low Apgar index values and perinatal mortality was higher in the study group, whereas there were more LGA in the control group, and newborn with Apgar index 7 in the 5th minute and less and early neonatal death does not differ ($p < 0.05$). Out of 1,651 deliveries at the age of 40 and over there were 19 late

TABLE 1
INCIDENCE OF DELIVERIES AT 40 AND OVER. TOTAL NUMBER OF DELIVERIES IN
THE PERIOD 1979–1988 = 60,591 AND IN 1989–1998 = 58,624

Parity	Period 1979–1988	Period 1989–1998	p
Nullipara	144 (0.24%)	285 (0.49%)	< 0.001
Pluripara	371 (0.61%)	553 (0.94%)	< 0.001
Multipara	199 (0.33%)	99 (0.17%)	< 0.001
Total	714 (1.18%)	937 (1.60%)	< 0.001

TABLE 2
PRE-GESTATIONAL AND REPRODUCTIVE STATUS

Status	Study group	Control group	p
	N = 1,651	N = 1,651	
High blood pressure	32 (1.9%)	12 (0.7%)	< 0.01
Heart problem	48 (2.9%)	33 (2.0%)	ns
Stright renal problem	18 (1.1%)	15 (0.9%)	ns
Diabetes type I	13 (0.8%)	6 (0.4%)	ns
Uterus malformations	32 (1.9%)	15 (0.9%)	< 0.05
Uterus myoma	85 (5.1%)	21 (1.3%)	< 0.001
Previous spontaneous abortions	314 (19.0%)	134 (8.1%)	< 0.001
Previous artificial abortions	159 (9.6%)	74 (4.3%)	< 0.001
Treated for sterility and infert.	188 (11.4%)	99 (6.0%)	< 0.001

TABLE 3
HEALTH STATUS DURING PREGNANCY

Status	Study group	Control group	p
	N = 1,651	N = 1,651	
Threatened abortion	245 (14.8%)	118 (7.1%)	< 0.001
Incompetentio cervicis	69 (4.2%)	44 (2.7%)	< 0.001
EPH gestosis index:			
1–4	153 (9.3%)	101 (6.1%)	< 0.001
5–7	71 (4.3%)	26 (1.6%)	< 0.001
≥ 8	25 (1.5%)	12 (0.7%)	< 0.05
Vaginal bleeding	123 (7.5%)	64 (3.9%)	< 0.001
Placenta praevia	27 (1.6%)	8 (0.5%)	< 0.001
Glucose intolerance	N = 709	N = 592	
	71 (10.0%)	32 (5.4%)	< 0.01
Gestational diabetes	75 (10.6%)	33 (5.6%)	< 0.001
Weight gain over 18 kg	N = 1,146	N = 1,090	
	127 (11.1%)	128 (11.7%)	ns
PPROM	51 (3.1%)	43 (2.6%)	ns
Preterm labor	59 (3.6%)	50 (3.0%)	ns
Late fetal death	19 (1.15%)	5 (0.3%)	< 0.01

PPROM = preterm premature rupture of membranes

fetal deaths (1.15%), there were 15 early neonatal deaths (0.91%), so that the total perinatal mortality was 2.06%. Out of 2,099 diagnosed wanted pregnancies at 40 and over perinatal loss was 23.0%.

Discussion

Emancipation of women – education, employment, career – in the last decades led to postponement of maternity, which

TABLE 4
INTRAPARTAL COMPLICATIONS

Complication	Study group	Control group	p
	N = 1,651	N = 1,651	
Induction of labor	N = 1,425	N = 1,633	
	252 (17.7%)	180 (11.0%)	< 0.001
Prolonged delivery (≥ 13 hours)	22 (1.5%)	32 (2.0%)	ns
Meconium-stained amniotic fluid	220 (13.2%)	130 (7.9%)	< 0.001
Fetal distress	121 (7.3%)	90 (5.5%)	< 0.05
Operative vaginal delivery	N = 1,187	N = 1,540	
	128 (10.8%)	101 (6.6%)	< 0.001
Caesarian section			
Primary	226 (13.7%)	18 (1.1%)	< 0.001
Secondary	238 (14.4%)	93 (5.6%)	< 0.001
Blood loss in 3 rd and 4 th gestational ages (≥ 500 ml)	66 (5.6%)	34 (2.2%)	< 0.001
Lysis placentae or uterus exploration	68 (5.7%)	38 (2.5%)	< 0.001
Injury of women in labor during vaginal delivery	52 (4.4%)	33 (2.1%)	< 0.001

TABLE 5
NEONATAL OUTCOME

	Study group	Control group	p
	N = 1,651	N = 1,651	
Male	878 (53.2%)	838 (50.8%)	ns
Birth weight (g)			
VLBW	27 (1.6%)	10 (0.6%)	< 0.01
LBW	96 (5.8%)	54 (3.3%)	< 0.001
SGA	118 (7.1%)	57 (3.5%)	< 0.001
LGA	155 (9.4%)	232 (14.1%)	< 0.001
Delivery:			
< 37 weeks	207 (12.5%)	98 (5.9%)	< 0.001
< 32 weeks	36 (2.2%)	25 (1.5%)	ns
Low Apgar	N = 1,632	N = 1,646	
At 1 min ≤ 4	32 (2.0%)	18 (1.1%)	< 0.05
At 5 min ≤ 7	22 (1.4%)	12 (0.7%)	ns
Early neonatal death	15 (0.91%)	13 (0.78%)	ns
Perinatal mortality	34 (2.06%)	18 (1.09%)	< 0.05

VLBW = very low birth weight; LBW = low birth weight; SGA = small for gestational age; LGA = large for gestational age

resulted in the increase in pregnancies at 40 and over. The incidence of those preg-

nancies was from 0.7% to 2.1%^{2,3,8,12,13,17,22}. In our research in the last ten years

there has been an increase of 35.6% (from 1.18% to 1.60%). There has been an increase in nullipara (by 104.2%) and pluripara (by 54.0%), whereas in multipara there has been a decrease of 48.5%. The majority of authors^{8,11,18,22,26,27} found an increase in the number of nullipara and pluripara, whereas multipara deliveries have been reduced (8,26%). In 63.5% of pregnant women fetus karyotype has been determined and in 2.5% fetuses chromosomal abnormalities were found (one chromosomal abnormality on 40.2 fetuses), which indicates that it is necessary to determine karyotype^{2,14,17,23}.

With the increase in age, pre-gestational health and reproduction status has deteriorated, due to initial degenerative changes and initial hormonal disbalance, which has to reflect in perinatal outcome^{11,18}. In pregnant women from the study group there is a high risk of spontaneous abortions^{8,23,28}. During pregnancy there are numerous complications (EPH gestosis, vaginal bleeding, placenta praevia, gestational diabetes, late fetal death), which indicates high risk of this age group^{5,8,11–13,18,20,22,23,29,31}. Disorder of health and reproduction status prior to pregnancy and many complications are only an introduction into expected complications during delivery. High incidence of delivery induction, meconium-stained amniotic fluid, fetal distress, operative vaginal deliveries, primary and secondary Caesarian sections^{8,11,12,17,22,29,31,32}.

More often, there is an incidence of lysis placentae and/or exploration of uterus, loss of blood in the 3rd and 4th stage of labor above 500 ml and injuries of delivery tracts^{8,12}, however, there are authors^{11,27,32} who do not have such findings. Pregnant women aged 40 and over more frequently deliver male children^{8,31}. Advanced maternal age has influence on neonatal outcome¹³. This group of pregnant women has a high risk of VLBW, LBW, premature infants, and newborn with low Apgar index values^{2,5,11,12,14,17–19,31}, whereas there are fewer LGA children^{11,14,18}. The increase in age of gravida is accompanied by risk of unexplained fetal death²¹ and early neonatal death^{2,11,14}. There is a high incidence of late fetal death^{12,14,16,20} and early neonatal death^{2,14}, which makes perinatal death twice^{14,19} and three times²⁶ as high.

Conclusion

Gravida aged 40 and over has a high risk of spontaneous abortions, chromosomal abnormalities, EPH gestosis, placenta praevia, late fetal death, meconium-stained amniotic fluid, operative vaginal deliveries, Caesarian sections, premature labor, VLBW, LBW, and SGA children, and children with low Apgar index values. Perinatal loss (from diagnosing to 7th day after delivery) is 23.0%. Pregnancy at 40 and above is not desirable from the medical point of view.

REFERENCES

1. DOTT, A. B., A. T. FORT, *Am. J. Obstet. Gynecol.*, 125 (1976) 532. — 2. FRIEDE, A., W. BALDWIN, P. H. RHODES, J. W. BUEHLER, L. T. STRAUSS, *Obstet. Gynecol.*, 72 (1988) 152. — 3. GRIMES, D. A., G. K. GROSS, *Obstet. Gynecol.*, 58 (1981) 164. — 4. STEIN, A., *Nurse. Midwife*, 28 (1983) 17. — 5. ALES, K. L., M. L. DRUZIN, D. L. SANTINI, *Surgery. Obstet. Gynecol.*, 171 (1990) 209. — 6. KANAJOJA, P., O. WINDHOLM, *Obstet. Gynecol.*, 51 (1978) 47. — 7. POSNER, L. B., *Obstet. Gynecol.*, 17 (1961) 194. — 8.

MIKULANDRA, F., I. MERLAK, M. PERIŠA, D. ŠIKIĆ, J. JERKOVIĆ, *Jugosl. Ginek. Perinatol.*, 3 (1991) 11. — 9. STATON, E.F., *Am. J. Obstet. Gynecol.*, 71 (1956) 270. — 10. KUSHNER, D., *Med. Ann. D.C.*, 43 (1974) 491. — 11. BIANCO, A., J. STONE, L. LYNCH, R. LAPINSKI, G. BERKOWITZ, R. L. BERKOWITZ, *Obstet. Gynecol.*, 87 (1996) 917. — 12. ZIADEH, S., A. YAHAYA, *Arch. Gynecol. Obstet.*, 265 (2001) 30. — 13. KIRZ, D.S., W. DORCHESTER, R.K. FREEMAN, *Am. J. Obstet. Gynecol.*, 152 (1985) 7. —

14. MIKULANDRA, F., M. PERIŠA, I. MERLAK, D. ŠIKIĆ, J. JERKOVIĆ, Arhiv. zašt. majke djeteta, 35 (1991) 93. — 15. MIKULANDRA, F., I. BANOVIĆ, I. TADIN, Z. ZAKANJ, J. GRGURIĆ, M. PERIŠA, E. STOINI, T. MILETIĆ, K. MIKULANDRA, A. MRDEŽA, Med. Jad., 31 (2001) 17. — 16. FRETTS, R. C., J. SCHMITTDIEL, F. H. MCLEAN, R. H. USHER, M. B. GOLDMAN, N. Engl. J. Med., 333 (1995) 953. — 17. EKBLAD, U., T. VILPA, Ann. Chir. Gynaecol., 208 Suppl. (1994) 68. — 18. VERCELLINI, P., G. ZULIANI, M. T. ROGNONY, L. TRESPIDI, S. OLDANI, A. CARDINALE, Eur. J. Obstet. Gynecol. Reprod. Biol., 48 (1993) 191. — 19. PUGLIESE, A., D. VICEDOMINI, A. D. ARSIERI, Minerva. Gynaecol., 49 (1997) 81. — 20. RAGOSCH, V., H. ALTINOZ, H. HUNDERTMARK, M. ENTEZAMI, Z. Geburtshilfe. Neonatol., 201 (1997) 86. — 21. FRETTS, R. C., R. H. USHER, Obstet. Gynecol., 89 (1997) 40. — 22. GILBERT, W. M., T. S. NESBITT, B. DANIELSEN, Obstet. Gynecol., 93 (1999) 9. — 23. Scholz, H. S., J. Haas, E. Petru, Prev. Med., 29 (1999) 263. — 24. MIKULANDRA, F., M. PERIŠA, I. TADIN, D. KARELOVIĆ, M. JUNAČKOVIĆ, Ž. DUBOVIČAK, T. MILETIĆ, K. MIKULANDRA, Gynaecol. Perinatol., 10 Suppl. 1 (2001) 126. — 25. THOMSON, A. M., W. Z. BILLEWITZ, F. E. HYTTEN, J. Obstet. Gynecol. Br. Comm., 75 (1968) 903. — 26. DARBOIS, Y., M. C. BOULANGER, Rev. Fr. Gynecol. Obstet., 85 (1990) 158. — 27. HEIMANN, F., D. MESSERER, J. BALTZER, Geburtshilfe. Frauenheilkd., 53 (1993) 411. — 28. MULACHI, R., J. F. KNAGGS, Am. J. Obstet. Gynecol., 101 (1968) 844. — 29. Lagrew, D. C., M. A. MORGAN, K. NAKAMOTO, N. LAGREW, J. Perinatol., 16 (1996) 256. — 30. CHAN, B. C. P., T. T. LAO, Hum. Reprod., 14 (1999) 833. — 31. SPELLACY, W. N., S. J. MILLER, A. WINEGAR, Obstet. Gynecol., 68 (1986) 452. — 32. WONG, S. F., L. C. HO, Aus. NZJ. Obstet. Gynaecol., 38 (1998) 388.

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PERINATALNI ISHOD TRUDNOĆA U ŽENA STARIH 40 GODINA I VIŠE

S A Ž E T A K

U radu je analiziran perinatalni ishod trudnoća dijagnosticiranih do 7 dana nakon poroda u žena starih 40 godina i više. Pregestacijsko zdravlje, reprodukcijski status, tijek trudnoće, porod i novorođenačko razdoblje analizirani su retrospektivno (ispitivana skupina). Kontrolnu skupinu činile su trudnice u dobi od 20 do 29 godina, koje su u pogledu pariteta bile identične sa ispitivanom skupinom. Statistički podaci obrađeni su pomoću χ^2 -testa i 2×2 tablica kontingencije. Statistički značajna razlika je $p < 0.05$. Od ukupno 2.099 dijagnosticiranih željenih trudnoća u žena starih 40 godina i više, u 415 (19.8%) je učinjen pobačaj, nakon učinjene kariotipizacije fetusa arteficijelni pobačaj učinjen je u 33 (1.6%), a 1.651 (78.2%) trudnica je rodilo. Kariotipizacija fetusa učinjena je u 66.2% trudnoća, a abnormalnosti kromosoma nađene su u 33 (2.5%) fetusa. Incidencija poroda u žena starih 40 godina i više iznosi 1.38%, što je u posljednjih deset godina porast od 35.6%. U nulipara i pluripara zabilježen je porast, dok se u multipara bilježi pad incidencije. Pregestacijsko zdravlje i reprodukcijski status u ispitivanoj skupini lošiji je nego u kontrolnoj skupini. Komplikacije tijekom trudnoće: prijeteći pobačaj, EPH gestoze, placenta previja, gestacijski dijabetes i kasna fetalna smrt češći su nego u kontrolnoj skupini ($p < 0.05$). Intrapartalno su zabilježeni češće indukcije poroda, mekonijska plodna voda, fetalni distress, operacijski vaginalni porodi i carski rez ($p < 0.05$). U neonatalnom periodu češće su zabilježeni prijevremena novo-

rođenčad, VLBW, LBW, SGA, novorođenčad s niskim vrijednostima Apgar indeksa, a i perinatalna smrtnost veća je nego u kontrolnoj skupini ($p < 0.05$). Perinatalno razdoblje (od trenutka dijagnosticiranja trudnoće do 7 dana nakon poroda) preživjelo je 1.617 (77.0%), što znači da je perinatalni gubitak 482 (23.0%) djece. Trudnoća u žene stare 40 i više godina je visoko rizična. Postoji visok rizik pregestacijskih i gestacijskih komplikacija. Perinatalni je gubitak visok. S medicinskog stajališta takve se trudnoće ne preporučuju.