International Journal of Obstetrics and Gynecology ISSN 2736-1594 Vol. 8 (10), pp. 001-008, October, 2020. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research paper

Pregnancy outcome and neonatal health by mothers aged 40 years and over

Lorenza Driul[1*], Ambrogio P Londero[1*], Serena Bertozzi[2*], Laura Peressini[1], Michele Vanin[1], Vito D'Aietti[1], Arrigo Fruscalzo[3], Anna Biasioli[1], Stefania Salvador[1], Riccardo Furlan[4], Maria Maddalena Petrovec[1], Diego Marchesoni[1]

[1]Clinic of Obstetrics and Gynecology, AOU "S M della Misericordia", 33100 Udine, Italy
[2]Clinic of Surgical Semeiotics, AOU "S M della Misericordia", 33100 Udine, Italy
[3]Department of Obstetrics and Gynecology, Gesundheitszentrum Rheine - Mathias-Spital, Rheine, Germany
[4]Neonatology Department, AOU "S M della Misericordia", 33100 Udine, Italy

Accepted 04 July, 2020

This study was carried out to investigate obstetric outcomes in single pregnancies conceived by women older than 40 compared to those of their younger counterparts in a low natality setting with high mean age at first pregnancy. Data were collected about women who delivered in our Clinic between January and July 2005, excluding multiple pregnancies. Statistical analysis was performed using R (version 2.10.1), considering significant a p<0.05.We selected 688 women: 50 of them are 40 years or older and 638 are younger. Advanced age correlates with higher BMI (p=0.056) and seems to increase the risk of gestational hypertension (p<0.05) and gestational diabetes (p<0.05), cesarean sections (p<0.05) and vacuum extraction (p0.089), neonatal clavicle fracture (p<0.05) and perinatal mortality (p<0.05).Advanced age women have an increased risk of pregnancy complications, such as gestational hypertension and diabetes, neonatal clavicle fracture and perinatal death, and undergo more frequently cesarean sections.

Keywords: Advanced maternal age, pregnancy outcome, neonatal outcome, pregnancy related hypertensive disorders.

INTRODUCTION

A lot of studies indicate that delayed childbearing increases the risk for adverse perinatal outcomes, including preterm delivery, low birth weight and perinatal death (Nabukera et al., 2006; Astolfi et al., 2002; Breart, 1997; Berkowitz et al., 1990), particulary in primigravida (Delpisheh et al., 2008). A recent case-control study confirms the significantly higher perinatal mortality in primiparous women aged 35 and older (Tomic et al., 2008).

A systematic review stated that advanced aged mothers have an increased risk of stillbirth, although the magnitude and mechanisms of such risk remain unclear (Huang et al., 2008). Even the rate of cesarean sections increases proportionally with the maternal age (Kirchengast, 2007; Tebeu et al., 2007).

In women aged 35 and over there is a greater multiple pregnancies rate, also because they are more likely to use assisted reproductive technology (Suzuki and Miyake, 2008), and twin pregnancies are known to have a higher complication rate.

*Corresponding author E-mail: ambrogio.londero@gmail.com

ABBREVIATIONS LIST

BMI: Body mass index
CS: Cesarean section
GCT: Glucose challenge test
GDM: Gestational diabetes mellitus
IGT: Impaired glucose tolerance
IVF: In vitro fertilisation
IVH: Intraventicular haemorrage
LGA: Large for gestational age
NICU: Neonatal intensive care unit
OGTT: Oral glucose tolerance test
PRHDs: Pregnancy related hypertensive disorders
PROM: Premature rupture of membranes
ROP: Retinopathy of prematurity (ROP)
SGA: Small for gestational age
WHO: World Health Organisation

In Italy, there is a trend to increase the age at first pregnancy that was 25.2 years in 1981 and 28.2 years in 1996 (Sabbadini, 2001). In our Clinic between 2001 and 2006, the mean age at first pregnancy is 30.6 years (±5.22), and the women over 40 years represents about the 6% of cases. The steady increase in primiparous and multiparous women age raises questions concerning the possible increased obstetric risks and outcomes in such pregnancies.

In singleton pregnancies conceived by in vitro fertilisation (IVF), women aged 35 and over are more likely to be affected by pregnancy-induced hypertension, but there are no measurable differences in premature delivery or neonatal asphyxia, suggesting that obstetric complications in artificially conceived pregnancies do probably not depend on advanced maternal age (Suzuki and Miyake, 2008).

Older age at first delivery also correlates with higher risk of aneuploydia and chromosomal defects (Yoon et al., 1996), and White women aged over 40 seem to have a greater risk of neonatal congenital anomalies such as esophageal atresia (Oddsberg et al., 2008).

Although, in previous studies infants born to mothers over the age of 40 currently are about 3% of total births, they represent 5% of those requiring neonatal intensive care (Battin et al., 2007). Fortunately, the increasing frequency of advanced age pregnancies is accompanied by an improvement in perinatal care, making advanced maternal age every time more compatible with successful pregnancies (Topalovska et al., 2006).

The aim of this study is to highlight the effects of maternal age on obstetric and perinatal outcome, investigating single pregnancies conceived by women older than 40, compared to those of their younger counterparts in a lowest-low fertility setting with high mean age at first pregnancy.

MATERIALS AND METHODS

We retrospectively analysed the clinical database of our clinic, which is a third level obstetric care department with neonatal intensive care unit (NICU) facility. We selected with chronological continuity, a group of women who delivered between January and July 2005, excluding multiple pregnancies and incomplete records, and divided them into two groups based on the age at delivery, considering advanced aged women those aged 40 and older.

Considered personal data are maternal age and BMI, alcohol assumption, tobacco smoke during pregnancy or during the year before pregnancy, parity and eventual medical-assisted procreation. Collected obstetric data concern weight gain during pregnancy, mode of delivery, duration of first and second labour stages and blood loss during delivery in case of vaginal delivery, duration of surgery in case of cesarean section, days of hospitalization after delivery.

We considered the following pregnancy and neonatal outcomes: pregnancy-related hypertensive disorders (PRHDs), abnormalities of glucose tolerance, placenta previa, abruptio placentae, neonatal weight, length, cranial circumference, intrauterine growth restriction (IUGR), small for gestational age (SGA), large for gestational age (LGA), gestational age at birth, preterm delivery, premature rupture of membranes (PROM), sex, Apgar score, respiratory distress syndrome (RDS), oxygen therapy, necrotizing enterocolitis, intraventicular hemorrhage (IVH), retinopathy of prematurity (ROP), neonatal scalp trauma, neonatal clavicle fracture, neonatal hypoglycemia, foetal acute suffering during labour, days of hospitalization, neonatal congenital malformations, and perinatal death.

We considered as pregnancy-related hypertensive disorders (PRHDs) pre- eclampsia, gestational hypertension, pre-eclampsia superimposed on chronic hypertension, and eclampsia. Pre-eclampsia is defined by increased blood pressure accompanied by proteinuria. Diagnostic blood pressure increases are either a systolic blood pressure of greater than or equal to 140 mm Hg or a diastolic blood pressure of greater than or equal to 90 mm Hg. Proteinuria is defined as the urinary excretion of 0.3 g protein or greater in a 24-hour period (this usually correlates with 30 mg/dL or greater in a random urine determination). Gestational hypertension is defined as the same as pre-eclampsia, but without proteinuria, and eclampsia is defined as the same as pre-eclampsia, but with convulsions. Chronic hypertension is defined as hypertension present before the 20th gestational week (Lowe et al., 2009).

Abnormalities of glucose tolerance were diagnosed through a two-step approach: an initial screening by measuring the plasma or serum glucose concentration 1 h after a 50-g oral glucose load (glucose challenge test - GCT) and a consequent diagnostic 100-g oral glucose tolerance test (OGTT) on that subset of women exceeding the glucose threshold value of 140 mg/dl. Gestational diabetes mellitus (GDM) is diagnosed if two or more of the venous plasma concentrations exceeded the following threshold values by 100-g OGTT: fasting 95 mg/dl, 1st-hour 180 mg/dl, 2nd-hour 155 mg/dl, 3rd-hour 140 mg/dl. For the diagnosis of impaired glucose tolerance (IGT) only one glucose venous plasma concentration must be met or exceeded the previous threshold values (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2003).

In this study, we define IUGR as the sonographic finding of delayed foetal growth under the 10th centile for estimated weight (using Hadlock formula) associated with the increased impedence index of umbilical artery over the 90th centile, and a post-partum confirmation with a foetal weight under the 10th centile at birth. In this study, SGA is defined as the neonatal weight under the 10th centile, and LGA as the neonatal weight over the 90th centile. Preterm delivery is considered while happening before the 37th gestational week.

The term placenta previa refers to a placenta that overlies or is proximate to the internal orifice of the cervix: complete if the placenta completely covers the internal orifice, partial if the placenta partially covers it, marginal if the placenta just lies within 2cm from it, but does not cover it. Abruptio placentae refers to the premature separation of the normally implanted placenta from the uterus.

Perinatal death is based on the WHO definition, and includes the stillbirth and the neonatal death in the first week of life (Richardus et al., 1998). Acute suffering during labour in this work is intended as the presence of an abnormal CTG trace and the confirmation of neonatal suffering after cesarean section with a neonatal lactate more than 5 mmol/l. The delivery complications we focused on are operative delivery (in our case performed by vacuum extraction), cesarean section, cesarean section after labour initiation, labour induction, ante-partum and post-partum hemorrhage. As ante-partum hemorrhage we considered any bleeding from the vagina after the 24th week of pregnancy, and as postpartum hemorrhage (PPH) any blood loss greater than 500 mL during a vaginal delivery or greater than 1,000 mL by a cesarean delivery, considering only early PPH (within 24 hours of delivery).

The pregnancy management in our clinic overlays on the Italian Society of Obstetrics and Gynecology Guidelines. Women hospitalized for threatened preterm labour are treated with a single course of betametasone prophylaxis, and tocolisys with ritodrine or

Table 1. Mothers' characteristics. Mean ±sd, t test and chi-square test where appropriate.

	< 40 years old	**40 years old**	**p**
Age (years)	31.16 (±4.84)	41 (±1.46)	<0.05
BMI (Kg/m²)	22.32 (±3.69)	23.62 (±4.6)	0.056
Weight gain (Kg)	12.87 (±5.28)	13.7 (±5.03)	0.269
Gravida			
0	44.2% (282/638)	18% (9/50)	<0.05
2	48.9% (312/638)	50% (25/50)	0.881
>2	6.9% (44/638)	32% (16/50)	<0.05
Parity			
0	51.88% (331/638)	32% (16/50)	<0.05
2	46.55% (297/638)	58% (29/50)	0.118
>2	1.57% (10/638)	10% (5/50)	<0.05
Medical-assisted reproduction	0.63% (4/638)	0% (0/50)	0.574
Alcool assumption during pregnancy	23.67% (151/638)	22% (11/50)	0.789
Tobacco smoke during pregnancy	5.49% (35/638)	8% (4/50)	0.459
Tobacco smoke the year before pregnancy	25.24% (161/638)	34% (17/50)	0.173
Chronic hypertension	2.04% (13/638)	4% (2/50)	0.360
Type I diabetes mellitus	0.63% (4/638)	0% (0/50)	0.574

atosiban. Women with a single previous cesarean section have the possibility to undergo a trial of labour only after 24 months and in absence of associated risk factors, in the other cases a caesarean section is indicated. Gestational diabetes treated with insulin therapy without complications are induced at 38 gestational weeks and the patients treated only with diet at 40 gestational weeks. All foetuses in breech presentation are delivered by cesarean section.

Because of its retrospective organisation, this study did not require the official approval of our Institutional Review Board, which is used just to be informed about the protocols of retrospective studies, but not to submit them to approval.

Statistical analysis was performed using R (version 2.10.1) and considering statistically significant a p<0.05. Data was analysed using bivariate methods, such as t-test and Wilcoxon test for continuous variables and chi-sqare-test or Fisher exact test for dicotomic data, and also multivariate logistic regressions were performed.

RESULTS

Women included in our study are 688: 50 of them are aged 40 years and over, with a mean age of 41 years (±1.00), and 638 are younger than 40 years, with a mean age of 31 years (±6.00) (table 1).

Parity in younger women is significantly lower than in older ones, with a mean number of previous deliveries of 0.60 (±0.47) vs 1.18 (±1.44) (p<0.05), and a mean number of previous pregnancies respectively of 0.89 (±0.70) and 1.98 (±1.77) (p<0.05). Moreover, nulliparity is a significantly more frequent condition in younger women (51.88% vs 32%, p<0.05) (table 1).

Difference of BMI between the two groups is near to significance (p=0.056) with a mean value of 22.32 Kg/m^2 (±3.29) in the younger group and 23.62 Kg/m^2 (±4.40) in the older one (table 1).

Also duration of labour stages results significantly different between younger and older women (p<0.05), lasting about 353 minutes the first stage and 40 minutes the second stage in younger women, and respectively about 200 and 25 minutes in the older ones (p<0.05) (table 2).

The pregnancy complications we found significantly correlated with advanced maternal age (p<0.05) are gestational hypertension and gestational diabetes. Even if without statistical significance, advanced maternal age seems to increase the risk of PRHDs in general (p<0.068) and IGT (p<0.082) (table 2). In particular, gestational hypertension affected the 2.19% (14/638) of younger women and 8% (4/50) of the older ones (p<0.05).

By multivariate logistic regression, the age older than 40 years does not significantly increase the risk of PRHDs (OR 2.73, CI95% 0.88 - 8.54, p0.083), adjusted for glucose metabolism disorders in pregnancy, parity, BMI, weight gain during pregnancy, tobacco smoke during pregnancy, and medically assisted reproduction techniques (figure 1). Taking in consideration only the gestational hypertension, the adjusted odds ratio results to be 3.13 (CI95% 0.96 - 10.26, p0.059).

Moreover, the age older than 40 represents no significant risk factor for GDM OR 3.08 (CI95% 0.93 - 10.19, p0.066), corrected for parity, BMI, weight gain during pregnancy, tobacco smoke during pregnancy. Anyway, in the same model, pre-gravidic BMI results to be an independent risk factor for GDM (OR 1.12, CI95% 1.02 - 1.23, p<0.05).

Taking in account the mode of delivery, cesarean section (p<0.05) and operative intervention by vacuum

Table 2.Course of pregnancy and delivery characteristics. Median (interquartile range), Wilcoxon test, Chi-square test and Fisher exact test where appropriate.

	< 40 years old	40 years old	p
PRHDs	2.82% (18/638)	8% (4/50)	0.068
Heparin prophylaxis	2.51% (16/637)	6% (3/50)	0.148
Impaired glucose tolerance	1.1% (7/638)	4% (2/50)	0.082
Gestational diabetes mellitus	2.35% (15/638)	8% (4/50)	<0.05
Postnatal hospitalization (days)	4.52 (±2.85)	5.16 (±3.41)	0.203
Medical induction of labour	7.05% (45/638)	4% (2/50)	0.410
I delivery stage (minutes)	280 (150-450)	165 (97.5-225)	<0.05
II delivery stage (minutes)	29 (15-53)	18.5 (10-29.5)	<0.05
Spontaneous delivery	56.74% (362/638)	56% (28/50)	0.919
Vacuum assisted extraction	8.93% (57/638)	2% (1/50)	0.089
Caesarean section without labour	18.81% (120/638)	34% (17/50)	<0.05
Caesarean section during labour	8.78% (56/638)	10% (5/50)	0.770
Cervical dilatation at CS	4.8 (±1.44)	4.98 (±0.71)	0.366
Placenta previa	0.78% (5/638)	2% (1/50)	0.373
Abruptio placentae	0.63% (4/638)	0% (0/50)	0.574
Blood loss peri-partum	200 (100-300)	250 (200-400)	0.119
Ante-partum haemorrhage	1.57% (10/638)	0% (0/50)	0.373
Post-partum haemorrhage	0.78% (5/638)	0% (0/50)	0.530

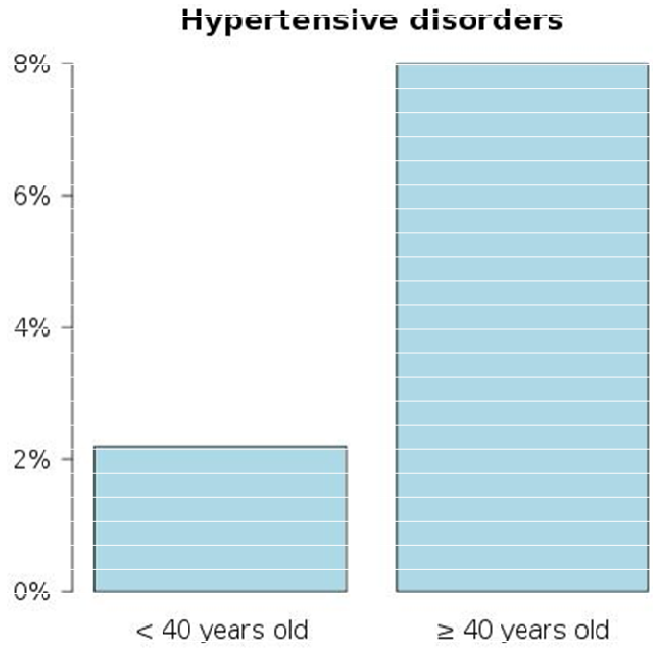

Figure 1. Hypertensive disorders during pregnancy and their prevalence in the two different aged groups of women

extraction (p0.089) result more frequently performed in women aged 40 and over. By multivariate analysis, adjusted for glucose metabolism disorders in pregnancy, chronic hypertension, PRHDs, ante-partum hemorrhage, placenta previa, parity, medical induction of labour, BMI, weight gain during pregnancy, tobacco smoke during pregnancy, and medically assisted reproduction techniques, the age over than 40 seems to be an independent risk factor for caesarean section (OR 2.2, CI95% 1.14 - 4.24, p<0.05) but not for operative delivery.

By multivariate analysis, newborn of women over than 40 have a higher incidence of clavicle fracture (OR 6.99,

Table 3. Neonate characteristics and outcomes. Mean (±sd), t-test, Chi-square test and Fisher exact test where appropriate.

	< 40 years old	40 years old	p
Gestational age at birth (weeks)	38.76 (±2.28)	38.82 (±1.49)	0.785
Pre-term delivery			
<34 weeks	3.92% (25/638)	2% (1/50)	0.493
34-37 weeks	4.55% (29/638)	6% (3/50)	0.638
Neonatal weight (gr)	3280.52 (±609.79)	3324.14 (±558.11)	0.599
SGA	4.39% (28/638)	8% (4/50)	0.243
LGA	8.15% (52/638)	14% (7/50)	0.155
IUGR	3.45% (22/638)	4% (2/50)	0.838
Neonatal length (cm)	49.58 (±2.91)	49.6 (±3.52)	0.961
Cranial circumference (cm)	34.27 (±1.98)	34.4 (±2.28)	0.694
APGAR at 1° minute	8.06 (±1.19)	8.06 (±1.2)	0.993
APGAR at 5° minute	8.94 (±0.62)	9.04 (±0.45)	0.153
Male gender	52.66% (336/638)	62% (31/50)	0.203
NICU hospitalization	3.76% (24/638)	4% (2/50)	0.932
Oxygen therapy	7.84% (50/638)	6% (3/50)	0.639
Intra-ventricular haemorrhage	0.94% (6/638)	2% (1/50)	0.472
RDS	2.51% (16/638)	2% (1/50)	0.824
ROP	0.78% (5/638)	0% (0/50)	0.530
Necrotizing enterocolitis	0.47% (3/638)	0% (0/50)	0.627
Neonatal hypoglicemia	1.1% (7/638)	0% (0/50)	0.457
Neonatal syndrome of maternal diabetes	0.63% (4/638)	0% (0/50)	0.574
Acute sufferance during labour	0.63% (4/638)	2% (1/50)	0.271
Scalp trauma	0.16% (1/638)	0% (0/50)	0.779
Clavicula fracture	0.63% (4/638)	4% (2/50)	<0.05
Perinatal death	0.31% (2/638)	4% (2/50)	<0.05
Perinatal death at term	0% (0/584)	2.17% (1/46)	0.073
Any neonatal malformation	7.37% (47/638)	8% (4/50)	0.869

CI95% 1.2 - 40.59, p<0.05), adjusted for BMI, weight gain during pregnancy, tobacco smoke during pregnancy, operative delivery, cesarean section, glucose metabolism disorders in pregnancy, chronic hypertension, PRHDs, parity, medical induction of labour, neonatal weight, and medically assisted reproduction techniques.

Overall risk of perinatal death is statistically higher in advanced aged women group (p<0.05), and higher but without statistical significance in older women at term of pregnancy (p0.073) (table 3). By multivariate analysis, investigating perinatal death as dependent variable in relation to advanced maternal age, BMI, weight gain during pregnancy, tobacco smoke during pregnancy, medically assisted reproduction techniques, chronic hypertension, PRHDs, type 1 diabetes mellitus, IGT and GDM, IUGR, ante-partum hemorrhage, abruptio placentae, PROM, operative delivery and cesarean section, pre-term delivery, post-term delivery and labour induction, women older age is an independent risk factor for perinatal death, as well as chronic hypertension, medical-assisted reproduction techniques, higher weight gain during pregnancy, and pre-term delivery (figure 2).

There seems to be no statistical difference concerning foetal malformations in both groups (table 3).

Considering only nulliparous women (table 4), those over 40 have a mean age of 41.06 years, about 10 years older than the younger group, and have a significantly higher BMI. Analysing the differences among maternal and neonatal outcomes in nullipara, women aged 40 and older have a higher prevalence of cesarean sections (p<0.05), a shorter first delivery stage (p<0.05), a higher prevalence of LGA babies (p<0.05) and, even if without the statistical significance, of GDM and other neonatal complications, such as IVH, acute suffering during labour, and perinatal death (table 4).

DISCUSSION

In this study, the mean age of women is 31.87 years (±5.33) that it is not statistically different from the total amount of women who delivered in our clinic during 2005 that is 31.89 years (±5.18) . Also the incidence of women over 40 years of age is not statistically different from the

Figure 2.Perinatal death and its prevalence in the two different aged groups of women.

Table 4.Analysis of the subgroup of primiparous women. Mean ±sd, t-test; median (interquartile range), Wilcoxon test, Chi-square test and Fisher exact test where appropriate.

	< 40 years old	**40 years old**	**p**
Mothers©characteristics			
Age (years)	30.02 (±5.05)	41.06 (±1.81)	<0.05
BMI (Kg/m²)	21.89 (±3.68)	23.49 (±4.97)	0.222
Weight gain (Kg)	13.42 (±5.55)	14.81 (±5.5)	0.337
Medical-assisted reproduction	0.6% (2/331)	0% (0/16)	0.755
Tobacco smoke during pregnancy	5.74% (19/331)	6.25% (1/16)	0.932
Tobacco smoke the year before pregnancy	27.19% (90/331)	37.5% (6/16)	0.368
Pregnancy and delivery characteristics			
PRHDs	4.23% (14/331)	6.25% (1/16)	0.698
Gestational diabetes	1.81% (6/331)	6.25% (1/16)	0.218
Medical induction of labour	8.76% (29/331)	0% (0/16)	0.216
Spontaneous delivery	50.15% (166/331)	31.25% (5/16)	0.140
Vacuum assisted extraction	15.11% (50/331)	6.25% (1/16)	0.329
Caesarean section without labour	14.8% (49/331)	50% (8/16)	<0.05
Caesarean section during labour	12.08% (40/331)	18.75% (3/16)	0.429
I delivery stage (minutes)	360 (220-510.75)	180 (120-240)	<0.05
II delivery stage (minutes)	45.5 (25-70.5)	52.5 (30.75-63)	0.770
Abruptio placentae	0.6% (2/331)	0% (0/16)	0.755
Ante-partum haemorrhage	1.81% (6/331)	0% (0/16)	0.587
Post-partum haemorrhage	1.21% (4/331)	0% (0/16)	0.658
Neonate characteristics and outcomes			
Gestational age at birth (weeks)	38.78 (±2.41)	38.62 (±1.15)	0.630
LGA	6.65% (22/331)	25% (4/16)	<0.05
SGA	3.93% (13/331)	12.5% (2/16)	0.100
APGAR at 1° minute	7.91 (±1.21)	7.69 (±1.49)	0.567
NICU hospitalization	4.23% (14/331)	6.25% (1/16)	0.698
Oxygen therapy	7.85% (26/331)	6.25% (1/16)	0.815
Intra-ventricular haemorrhage	0.91% (3/331)	6.25% (1/16)	0.051
Acute sufferance during labour	0.6% (2/331)	6.25% (1/16)	<0.05
Perinatal death at term	0.3% (1/331)	6.25% (1/16)	<0.05

total amount of women who delivered in our clinic during 2005 (7% vs 6%). It is also important to notice that age at first pregnancy in our clinic is 30.6 years (±5.22) and in this study is 30.53 years (±5.46), which is not significantly different if compared with the mean age at first delivery in the past 10 years, but is higher than the mean age at first delivery in the most european countries.

Advanced maternal age is known to be a risk factor for pregnancy complications and worse pregnancy outcomes (Astolfi et al., 2005), even if no clear cut-off exists to determine whether a mother could be defined old or not. Anyway, such definition loses in importance with the progressive increment of maternal age at the first delivery (Billeri and Kohler, 2004). In our clinic the mean age of women at delivery is 31.89 years old (±5.18), and for this reason we decided to consider advanced aged mothers all women wo delivered after their 40th year of age.

In our population, both gravidity and parity in women aged 40 and over are significantly greater than in younger. They have shorter duration of labour stages and greater prevalence of pregnancy complications, such as gestational hypertension and gestational diabetes, in particular related to higher BMI and weight gain during pregnancy. We see in our study a lower incidence of IVF in the older group of women, because in italy age limit for IVF techniques is 40 years old.

Table 2 shows women over than 40 to have shorter first and second stage of labour ($p<0.05$), which may be due to the higher prevalence of multipara among older women (82% vs 55.8%). Anyway in table 4, first labour stage results shorter among older women also in the nullipara subgroup ($p<0.05$), while the second labour stage is longer (p0.770), which represents a probable bias, as the majority of nullipara aged over than 40 have delivered by caesarean section, and only a minority had an uncomplicated pregnancy and a physiologic delivery. Advanced aged women seem to undergo more frequently cesarean section, influenced by higher BMI, increased risk of pre-eclampsia, IUGR, and LGA.

Our study confirms a significant higher incidence of GDM and gestational hypertension among older women (Franz and Husslein, 2010; Tabcharoen et al., 2009; Jahromi and Husseini, 2008; Delbaere et al. 2007), and demonstrates a trend to have other obstetrical and neonatal complications among older mothers, including IGT, placenta previa, IUGR, LGA, and acute sufference during labour. Also in the nullipara subgroup, older mothers seem to have a higher prevalence of IVH, acute suffering during labour, perinatal death, and LGA, associated to a not significant increment in the prevalence of GDM.

According to the literature, cesarean section rate increases with age (corrected OR 2.2, CI95% 1.14 - 4.24, $p<0.05$) (Franz and Husslein, 2010; Jahromi and Husseini, 2008; Tomic et al., 2008). In spite of the higher prevalence of cesarean section, and due to a probable decrease in maternal tissues elasticity, newborn of older women have a higher prevalence of clavicle fracture, independently by neonatal weight and GDM (corrected OR 6.99, CI95% 1.2 - 40.59, $p<0.05$).

Perinatal death seems to have a higher prevalence among newborne of older women (Franz and Husslein, 2010; Huang et al., 2008; Montan, 2007), and is also associated with low weight gain during pregnancy, medical-assisted reproduction techniques, chronic hypertension and pre-term delivery. On the other hand, no statistical significance was noticed about foetal malformations in the different age groups.

Despite the evident increase of complications prevalence by advanced aged pregnancies, in our setting exsist a persistent trend to delay the first pregnancy, over than a general increment of age at any pregnancy. Therefore, in our opinion, it is very important to educate women to recognise the risks due to their age, in order to prevent both maternal and neonatal complications. To invert the tendencies and obtain a lowering of childbearing age, it is important to modify social and cultural backgrounds, which obviously request a lot of fatigue and time.

In spite of the limits of the retrospective organisation of our study and of the moderate number of patients, if compared to greater numbers in the literature (Jahromi and Husseini, 2008), our study accurately reviews the global pregnancy course and many neonatal outcomes, in order to detect every possible maternal or neonatal complication, which may be influenced by maternal age.

In conclusion, advanced aged women seem to have higher risk of pregnancy complications, such as gestational hypertension and diabetes, higher risk of neonatal clavicle fracture and perinatal death, and undergo more frequently to cesarean section.

REFERENCES

Astolfi P, Ulizzi L, Zonta L A (2002). Trends in childbearing and stillbirth risk: heterogeneity among italian regions. Hum. Biol. 74(2):185-196.

Astolfi P, Pasquale AD, Zonta L (2005). Late childbearing and its impact on adverse pregnancy outcome: stillbirth, preterm delivery and low birth weight. *Rev.* Epidemiol. Sante Publique, 53 Spec No 2, 2S97–2105.

Battin M, Bevan C, Knight D (2007). Neonatal intensive care utilisation by infants born to mothers older than 40 years of age: a 10-year review. N Z Med. J. 120(1267):U2859.

Berkowitz GS, Skovron ML, Lapinski RH, Berkowitz RL (1990). Delayed childbearing and the outcome of pregnancy. N. Engl. J. Med. 322(10):659–664.

Billeri F, Kohler H (2004). Patterns of low and lowest-low fertility in europe. Pop. Stud. *58*, 161-176.

Breart G (1997). Delayed childbearing. Eur. J. Obstet. Gynecol. Reprod. Biol. 75(1):1-73.

Delbaere I, Verstraelen H, Goetgeluk, S, Martens G, Backer GD, Temmerman M (2007). Pregnancy outcome in primiparae of advanced maternal age. Eur. J. Obstet. Gynecol. Reprod. Biol. 135(1):41-46.

Delpisheh, A, Brabin L, Attia E, Brabin B (2008). Pregnancy late in life: a hospital -based study of birth outcomes. J. Women's Health (Larchmt), 17(6):965-970.

Expert Committee on the Diagnosis and Classification of Diabetes

Mellitus (2003). Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care, 26 Suppl 1, S5–20.
Franz MB, Husslein PW (2010). Obstetrical management of the older gravida. Women's Health (Lond Engl), 6(3), 463-468.
Huang L, Sauve R, Birkett N, Fergusson D, Walraven C (2008). Maternal age and risk of stillbirth: a systematic review. CMAJ. 178(2), 165–172.
Jahromi BN, Husseini Z (2008). Pregnancy outcome at maternal age 40 and older. Taiwan J. Obstet. Gynecol. 47(3):318-321.
Kirchengast S (2007). Maternal age and pregnancy outcome–an anthropological approach. Anthropol. Anz. 65(2):181-191.
Lowe SA, Brown MA, Dekker GA., Gatt, S, McLintock CK, McMahon LP (2009). Guidelines for the management of hypertensive disorders of pregnancy 2008. Aust. N. Z. J. Obstet. Gynaecol. 49(3):242-246.
Montan S (2007). Increased risk in the elderly parturient. Curr. Opin. Obstet. Gynecol. 19(2), 110–112.
Nabukera S, Wingate M, Alexander G, Salihu H (2006). First-time births among women 30 years and older in the united states: patterns and risk of adverse outcomes. J. Reprod. Med. 51:676-82.
Oddsberg J, Jia C, Nilsson E, Ye W, Lagergren J (2008). Influence of maternal parity, age, and ethnicity on risk of esophageal atresia in the infant in a population-based study. J. Pediatr. Surg. 43(9):1660-1665.
Richardus JH, Graafmans WC, Verloove-Vanhorick SP, Mackenbach JP (1998). The perinatal mortality rate as an indicator of quality of care in international comparisons. Med. Care 36(1):54-66.
Sabbadini L (2001). Gravidanza e parto. Roma Istat, *12*.
Suzuki S, Miyake H (2008). Obstetric outcomes in nulliparous women aged 35 and over with singleton pregnancies conceived by in vitro fertilization. Arch. Gynecol. Obstet. 277(3):225-227.
Tabcharoen C, Pinjaroen S, Suwanrath C, Krisanapan O (2009). Pregnancy outcome after age 40 and risk of low birth weight. J. Obstet. Gynaecol. 29(5):378-383.
Tebeu PM, Kouam L, Nghonguia MF, Obama MT, Major AL, Ludicke F (2007). [historical cohort study of delivery in women of forty years of age and older]. Rev. Med. Liege, 62(7-8):509-514.
Tomic V, Grizelj B, Zadro M (2008). Perinatal outcome in primiparous women aged 35 and older: a case-control study. Med. Arh. 62(1):18-19.
Topalovska, D, Batashki I, Milchev N, Terzhumanov R, Uchikova E (2006). pregnancy outcomes in women of advanced maternal age. Akush Ginekol (Sofiia), 45(1):7-11.
Yoon PW, Freeman SB. Sherman SL., Taft LF, Gu Y, Pettay D (1996, Mar). Advanced maternal age and the risk of down syndrome characterized by the meiotic stage of chromosomal error: a population-based study. Am. J. Hum. Genet. 58(3):628-633.