Research Article

Late pregnancies outcome: assessment of the obstetrical risks at the university hospital of gynaecology and obstetrics, Befelatanana, Madagascar

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ABSTRACT

Background: Late pregnancies incur more obstetric complications compared to pregnancies which happen at age 20 to 34. The obstetrician meets difficult challenges to bring these late pregnancies to term delivery, while minimizing the harmful impacts of this non-modifiable risk factor. In addition, few studies have addressed the issue in developing countries, particularly in Madagascar. This study aims to specify the frequency of late pregnancies and to determine maternal and foetal outcome of these pregnancies over age 40, at the University Hospital of Gynaecology and Obstetrics of Befelatanana (HUGOB), Madagascar.
Methods: A cross-sectional study was conducted, including women over 40 years old who delivered after 22 weeks in the exposed group, and randomly recruited parturients aged 20 to 34 who gave birth after 22 weeks in the unexposed group.
Results: In Madagascar, and particularly at the HUGOB, frequency of late pregnancies after age 40 is low (1.40%). Our study demonstrates these late pregnancies generate more obstetric complications, including pregnancy-induced hypertension and preeclampsia, caesarean section, postpartum haemorrhage, prematurity, foetal distress and foetal death *in utero*. Some pathology known to complicate these pregnancies such as gestational diabetes and chromosomal defects were probably underestimated in our study because of insufficient means of screening.
Conclusions: Advanced maternal age is a significant risk factor of bad pregnancy outcome. Therefore, monitoring of pregnancy for these women should be far more rigorous in order to identify and manage often predictable complications in this situation.

Keywords: Late pregnancy, Obstetrical complications, Referral hospital, Madagascar

INTRODUCTION

In recent decades, childbearing age has increased steadily in developed countries.[1] The international federation of gynaecology and obstetrics defines in 1958 elderly gravidas as pregnancy among elderly women over 35 years; then, with the increase in childbearing age, the term elderly parturient was addressed to women aged 40. Since the era of egg donation, we now speak of very advanced maternal age.[2] Today, pregnancy after age 35 or 40 years has become a real social phenomenon in most developed countries.[3] Few studies have addressed this problem in developing countries, especially in Madagascar.

In addition, late pregnancies incur more obstetric maternal and foetal risks. The first pitfall of foetal risk is the high rate of spontaneous abortion (54% at age 42 against 8% at 22).[4] Increased levels of chromosomal aberrations is well known (3% at 45 against 0.1% at 30),[5]

as well as increased risk of congenital malformations (5% after 40 against 3.5% at 20),[6] and the risk of foetal death *in utero* (RR= 1 to 2 compared to young patients).[7] In mothers, several conditions can be found, such as Gestational Diabetes (GD) and Hypertension (HTA). The risk of GD in women over age 40 is increased; it is estimated to be three times higher compared to mothers <40.[8,9] HTA during pregnancy and preeclampsia are increased in women over 40, with primiparity as a major risk factor.[8] In addition, the risk of occurrence of an abruptio placentae increases with age and parity, and the risk of occurrence of placenta previa in older parturients is 2.6 times larger;[10] advanced maternal age is a risk factor for placenta accreta.[11] The risk of bleeding in the third trimester of pregnancy in older pregnant is higher compared to younger patients.[12,13] Concerning the pathologies of delivery, the rate of outmoded terms is identical regardless of the age of the patient but the need of triggers would be higher after 40 (OR = 1.2 to 1.75).[9,14] The risk of foetal presentation abnormalities including non-cephalic presentations is increased (7.6% versus 5%).[8,15] The risk of planned and emergency Caesarean Sections (CS) is higher in the 40 years age group (40% versus 19%).[15] The use of instrumental extractions is important in the elderly especially in nulliparous parturients[8] (25% versus 17%).[10] Postpartum haemorrhage are more common after 40 (OR = 1.55), especially during a first delivery, but not all the authors share this view.[9] Maternal prognosis is related to the frequency of obstetric haemorrhage, stroke, amniotic embolism, infection and cardiomyopathies that are higher in older patients. In addition, maternal mortality is also higher for this population[10]. Foetal prognosis is related to prematurity (RR = 4),[8] birth weight (higher risk of foetal macrosomia or intrauterine growth retardation[9]), APGAR score (risk of APGAR score <7 at birth increases with the transfer to intensive care,[16,17] and neonatal mortality (twice, mostly in multiparous[16]).

This study aims to (i) specify the frequency of late pregnancies and to (ii) determine maternal and foetal outcome of these pregnancies over age 40, at the University Hospital of Gynaecology and Obstetrics Befelatanana (HUGOB), Madagascar.

METHODS

Type, site and study period

This is a cross-sectional study conducted at the University Hospital of Gynaecology and Obstetrics Befelatanana (HUGOB) of Antananarivo from 01 June 2011 to 31 May 2012.

Eligibility criteria

The study included patients within the "Pregnancies at risk" ward and the "Obstetrics" ward of the HUGOB. In the "exposed" group, we selected women over 40 years old who delivered after 22 weeks. In the "unexposed"

group, we included randomly recruited parturients aged 20 to 34 who gave birth after 22 weeks. We considered an exposed patient for two unexposed patients.

Exclusion criteria

We excluded women with multiple pregnancies, or whose delivery did not occur at the HUGOB, or with an incomplete folder as file was reviewed.

Setting

The HUGOB is a university hospital located downtown in Antananarivo, the capital of Madagascar. With 196 beds for women, 32 cradles and incubators distributed in 5 wards (Gynaecology, Pregnancies at risk, Obstetrics, Intensive care, and Neonatology), and a whole floor for the Delivery ward, this hospital accepts referrals from a large geographical area. About 6,600 deliveries, 500 preterm births, 2,200 caesarean sections (1,200 emergencies and 1,000 planned), and 1,900 admissions in neonatology take place annually at this institution. Eclampsia and post-partum haemorrhage yield among the first causes of maternal mortality and morbidity respectively (unpublished data). There is also a ward for Family Planning at the HUGOB.

Variables

We collected information on patients (age, parity, occupation, marital status, medical history, prenatal care attendance), and pregnancy outcomes (diseases encountered during pregnancy, delivery complications, maternal postpartum complications, and foetal prognosis for which low birth weight is defined as <2500 g).

Statistical analysis

Statistical analysis was performed using Epi Info 3.5.3 software. P <0.05 was used as the criterion of statistical significance. The strength of associations between pregnancy outcomes (pathologies during pregnancy, delivery complications) and exposition was estimated by the OR. Mantel-Haenszel stratified analysis has been done to examine the effects of confounders on pregnancy outcome. The most significant confounder was parity.[8,9,16]
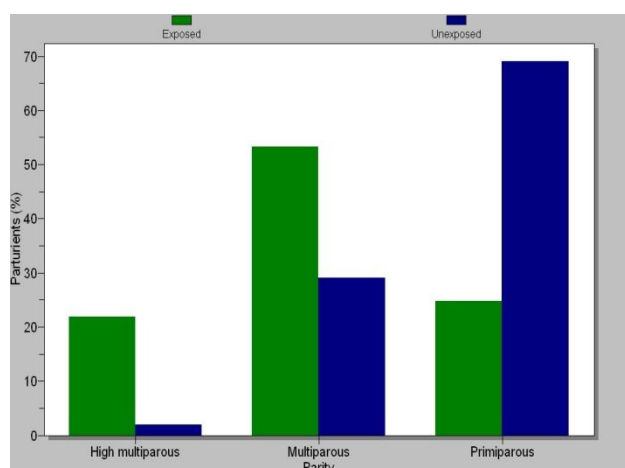
RESULTS

Descriptive results

Figure 1 shows pregnancy rate after age 40 on the total live births from 01 June 2011 to 31 May 2012.

Over this study period, pregnancies after age 40 represented 1.40% of live births. In total, 105 exposed and 211 unexposed women were enrolled. For exposed and unexposed respectively, extreme ages ranged from 40 to 49 and from 20 to 34. Primiparous over 40 accounted for only 24.40% of this age group (Figure 2).
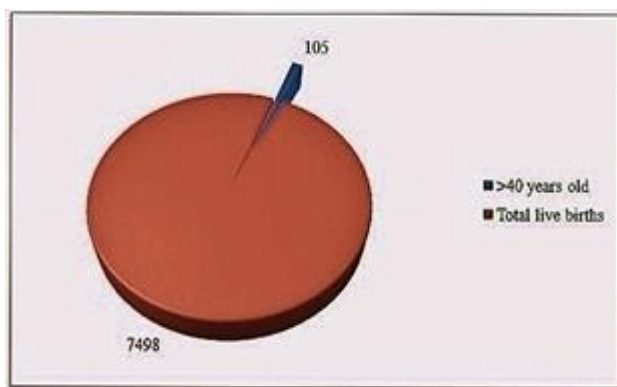
Figure 1: Pregnancy rate after age 40 on the total live births from June 1st 2011 to May 31st 2012.

Approximately 41.90% of exposed and 45% unexposed patients were housewives. The vast majority of parturients were married in both groups. Concerning the antenatal care attendance, about a quarter of patients were examined at the HUGOB (25.71% of exposed and 29.52% of unexposed patients). As for medical history, a higher rate of HTA was observed in the exposed group with 9.52% against 0.95% in the other group. No case of obesity or chronic diabetes was recorded in the two groups.

Figure 2: Distribution of parity among exposed and unexposed women from June 1st 2011 to May 31st 2012.

Primiparous: 1 child; Multiparous: 2-4 children; High multiparous >4 children

Analytical results

Pathologies during pregnancy

We found more pregnancy-induced HTA among exposed primiparas (OR = 0.10 [0.03-0.31], P = 0.0001), and more occurrence of preeclampsia in the same group. We had no cases of either gestational or chronic diabetes in both populations (Table 1).

Table 1: Pathologies during pregnancy among exposed and unexposed women at the HUGOB from 01 June 2011 to 31 May 2012.

Pathologies	Exposed n_1 (%)* n_2 (%)**	Unexpos-ed n_1 (%)* n_2 (%)**	OR¥ [95% CI]	P value
Pregnancy-induced hyperten-sion	15 (19.00) 2 (7.70)	1 (1.50) 3 (2.10)	0.10 [0.03-0.31]	0.0001
Preeclam-psia	3 (3.80) 1 (3.80)	0 (0.00) 2 (1.40)	0.13 [0.01-1.21]	0.02
Superimp-osed preeclam-psia	3 (3.80) 1 (3.80)	1 (1.50) 1 (0.70)	0.31 [0.05-1.97]	0.07
Chronic diabetes	0 (0.00) 0 (0.00)	0 (0.00) 0 (0.00)	-	-
Gestational diabetes	0 (0.00) 0 (0.00)	0 (0.00) 0 (0.00)	-	-
Abruptio placentae	1 (1.30) 0 (0.00)	0 (0.00) 0 (0.00)	0.00 [0.00-47.40]	0.55
Preterm birth	6 (7.60) 2 (7.70)	1 (1.50) 12 (8.30)	0.52 [0.17-1.55]	0.16

*n_1: among multiparas
**n_2: among primiparas
¥ ORs are parity-adjusted. We considered only two strata for the analysis: primiparous, and multiparous women (composed by "multiparous" and "high multiparous" women as defined in Figure 2).
95% CI: 95% Confidence Interval

Maternal prognosis

The only maternal complications encountered after childbirth were postpartum haemorrhage, which were higher in the exposed group (2.85% versus 0.95%, OR = 3.07 [0.41-26.72], P value = 0.34).

Foetal prognosis

In our study, new-born with Apgar score <7 rate was higher among exposed women (12.40% versus 6.20%, OR = 0.46 [0.20-1.04], P value = 0.06). In addition, there were more exposed patients' new-borns admitted to neonatal intensive care (20% versus 14.28%, OR = 0.66 [0.36-1.23], P value = 0.19). Low birth weight rate was 23% in exposed, 16% in unexposed (Figure 3). OR = 1.54 [0.08-2.88], P value = 0.14). This was the main indication for admission to neonatal intensive care. There were fewer foetal macrosomia among women over 40 (Figure 3). Foetal death *in utero* rate was higher among them (4.76% versus 1.42%, OR = 0.29 [0.04-1.52], P value = 0.08). We did not observe any cases of congenital malformations or chromosomal abnormalities during the study period.

Delivery complications

Table 2: Delivery complications among exposed and unexposed women at the HUGOB from 01 June 2011 to 31 May 2012.

	Exposed n_1 (%)* n_2 (%)**	Unexposed n_1 (%)* n_2 (%)**	OR¥ [95% CI]	P value
Vaginal delivery	54 (68.90) 12 (46.20)	54 (83.10) 107 (73.80)	2.67 [1.48-4.81]	0.001
Caesarean section				
Planned	3 (3.80) 4 (15.40)	0 (0.00) 1 (0.70)	0.03 [0.00-0.34]	<10⁻³
Emergenc-y	22 (27.80) 10 (38.50)	11 (16.90) 36 (24.80)	0.53 [0.29-0.96]	0.02
Emergency caesarean section indication				
Stagnation of dilation	6 (7.60) 0 (0.00)	4 (6.20) 6 (4.10)	1.16 [0.35-3.80]	0.95
Abnormal foetal heart rate	3 (3.80) 0 (0.00)	1 (1.50) 10 (6.90)	0.56 [0.08-3.77]	0.35
	2 (2.50) 3 (11.50)	1 (1.50) 10 (6.90)	0.58 [0.17-1.91]	0.21
HTA	6 (7.60) 3 (11.50)	1 (1.60) 5 (3.40)	0.23 [0.07-0.82]	0.007
Instrumental extractions				
Forceps	0 (0.00) 1 (3.80)	1 (1.50) 3 (2.10)	1.19 [0.15-9.74]	0.69
Spatula	0 (0.00) 0 (0.00)	0 (0.00) 1 (0.70)	-	-
Vacuum	2 (2.50) 0 (0.00)	0 (0.00) 1 (0.70)	0.17 [0.01-5.03]	0.11

*n_1: among multiparas
**n_2: among primiparas
¥ ORs are parity-adjusted. We considered only two strata for the analysis: primiparous, and multiparous women (composed by "multiparous" and "high multiparous" women as defined in Figure 2).
95% CI: 95% Confidence Interval
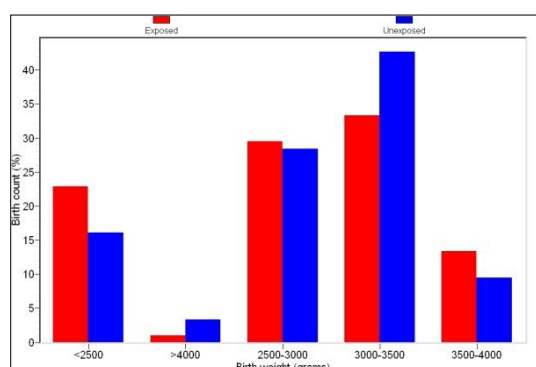
Figure 3: Birth weight of exposed and unexposed women at the HUGOB from 01 June 2011 to 31 May 2012.

DISCUSSION

Study limitations

The setting is a referral hospital. The research question demands a community-based approach to determining frequencies and making comparisons. The use of only referral hospital patients might result in selection bias.

There were no obese women in the sample. Obesity was, however, not defined. Only overweight history has been collected, as data on present weight was not available.

Epidemiology

Frequency

In recent years, the number of late pregnancy has been increasing in developed countries. As an illustration, in Australia, pregnant women over 35 years old deliveries accounted for 25% of all deliveries in 2006.[18] In developing countries, very few studies discuss the problem. The frequency of women who gave birth after age 40 accounted for 1.40% of all deliveries in our centre. This figure is well below the values found in the literature.

Parity

Late pregnancy management is completely different depending on whether the pregnant woman' parity, namely the much more common management with a planned caesarean section. The cause of this late primiparity is often a matter of education: it is more likely observed in developed countries and in women who have a high level of study.[19] Moreover, the availability of technical resources for the implementation of a medically assisted procreation allows women in developed countries to become pregnant for the first time at an older age. This phenomenon is not observed in our study where multiparas predominated among exposed patients. As a referral hospital, the HUGOB is likely to receive women from different backgrounds, cultures and beliefs on family planning. In addition, the majority of our exposed patients are housewives, with a low level of study, which would not facilitate education about contraception. Only a quarter of patients attended antenatal care at the HUGOB, only a quarter would have been in touch with the hospital family planning counselors and ward.

Pathologies during pregnancy

Pregnancy-induced hypertension and preeclampsia

In our study, exposed primiparas were more likely to be affected by the problem of pregnancy-induced HTA and preeclampsia. The statistical difference was highly significant. Our study also demonstrates more history of HTA in the exposed group. Luke Brown found an increase in HTA in primiparas as well as in multiparas

respectively with a 2.6 and 2.3 OR compared to the unexposed group aged 30 to 34.[20] But more studies demonstrated increased HTA and preeclampsia rate after 40, regardless of parity.[8] This would mean that as risk factors for preeclampsia, maternal age goes beyond the notion of primiparity.

Gestational and chronic diabetes

We have no cases of GD or chronic diabetes among our exposed patients. The explanation is probably that the implementation of screening for GD was not systematic despite the presence of risk factors. Nevertheless, recent studies showed a similar increased rate of GD in multiparas and primiparas.[8,9] We thus concluded that if our patients were screened for diabetes, the age but not parity could be at stake, considering the risk is three times greater in late pregnancy.

Abruptio placentae

In our study only one exposed multiparas presented abruptio placentae. Ananth showed that abruptio placentae increases with age and especially with parity,[10] which joins our results. Bianco concluded that there is no correlation between age and the occurrence of that third trimester accident of pregnancy.[11] We also found no association, although the statistical difference was not significant. The analysis with a greater sample could be helpful at the HUGOB in establishing an association.

Premature delivery

Most studies agree that the number of preterm labour is higher among elderly primiparas.[8,16] In our study, risk of preterm delivery is increased in the exposed, though the difference is not significant despite the stratified analysis. A study at La Reunion Island in 2004 found no significant difference in the risk of preterm delivery between both groups.[19]

Delivery complications

Caesarean sections

The CS rate is much higher among women over 40. Though particularly higher in primiparas, it is also increased in multiparas.[8,15] The number of planned CS is significantly increased after 40 in our study. A study in Boston in 1998 on 3 715 patients demonstrated the same trend with 21.1% planned CS after 40 against 3.6% before 25.[21] Our study demonstrated more indications of planned CS among women over 40, confirming that everything is combined for the planned CS rate increase with age.

The number of emergency CS is also high. This is mainly due to the lowering quality of myometrial activity with age. Acute foetal distress is more frequent, also explaining the frequency of CS during labour.[22] The indications for emergency CS vary but the trend is towards an excess risk of stagnant dilation of the cervix.[8,11,19,22] But our study demonstrated that the first indication of an emergency CS was HTA and its complications among exposed patients. This can be explained by the predominance of HTA among these women, associated with poor HTA therapeutic compliance, favouring the occurrence of common complications.

Instrumental extractions

This rate is higher among women over 35 in Prysak's study.[10] Gilbert also showed that the risk was increased among multiparas over 40.[14] However, our study did not show an increase in instrumental deliveries during the expulsion. There were no significant differences between exposed and unexposed women. Yet, a community-based study with a higher number of participants might demonstrate a significant difference among Malagasy women.

Maternal prognosis

In our study, we observed a higher rate of postpartum haemorrhage in the exposed group. Poor myometrial contractility with age as well as increased frequency of uterine fibroids, affecting the quality of uterine contractile muscle,[22] undoubtedly contributes to the large occurrence of post-partum haemorrhage among our patients. But we did not identify maternal deaths during the study period, though the risk of maternal death increases sharply from age 35, being 12 times higher after 45.[14] This can be explained by the short duration of the study and the number of patients collected.

Foetal prognosis

APGAR score

Our study demonstrated a high rate of new-borns with an Apgar score <7 at the fifth minute in exposed patients. Publications diverge completely on this or do not mention it.

Birth weight

Among primiparous aged 35 or more, Berkowitz states there are children with smaller birth weight than among younger mothers, but without any real growth retardation.[14] Our study reported higher low birth weight rate in elderly patients, probably due to the increased incidence of HTA in the exposed group.

Foetal death in utero

A study conducted in La Reunion Island in 2004 reported a high rate of foetal death in women over 40 with an 11.2 OR.[19] In another study focused on more than 94,000 births, Fretts showed that advanced maternal age is a powerful risk factor for foetal death *in utero*.[7] Our study confirms these findings.

Congenital malformations

According to Lisa's study, the incidence of congenital malformations with normal karyotype increases with maternal age from 3.5% at 5 to 20% at age 40 or over.[6] Most encountered abnormalities according to the National Vital Statistics Report are cardiac abnormalities and diaphragmatic hernia.[23]

The absence of congenital malformations in our study may be explained by the frequency of cardiac malformations (as stated in the literature) that are not always obvious during the neonatal examination; moreover, it appears there is no systematic antenatal screening because of lack of technical resources in our country.

CONCLUSION

In Madagascar, and particularly at the HUGOB, frequency of pregnancies after age 40 is really low compared to that observed in developed countries. This study demonstrates these late pregnancies generate more obstetric complications, including pregnancy-induced hypertension and preeclampsia, caesarean section, postpartum haemorrhage, prematurity, foetal distress and foetal death *in utero*. Some pathology known to complicate these pregnancies such as gestational diabetes and chromosomal defects were probably underestimated in our study because of insufficient means of screening. Advanced maternal age is a significant risk factor. Therefore, monitoring of pregnancy for these women should be far more rigorous in order to identify and set an early management of often predictable complications in this situation.

REFERENCES

1. Belaisch-Allart. Grossesse et al. Accouchement après 40 ans. In: Encyclopédie médico chirurgicale, eds. Gynécologie/Obstétrique. 3rd ed. Paris: Elsevier; 2000: 6.
2. Belaisch-Allart J. Grossesse et al. Accouchement après 40 ans. In: Encyclopédie médico chirurgicale, eds. Gynécologie/Obstétrique. 5th ed. Paris: Elsevier Masson SAS; 2008: 5-016-B-10.
3. Tulsane G, Jamain B. Considérations générales sur la grossesse et al. Accouchement chez la primipare âgée. Rev Praticien. 1974;24:4117-23.
4. Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. Br Med J. 2000;320:1708-12.
5. Vekemans M. Age parental et risques génétiques pour la descendance. Gynecol Obstet Fertil. 2002;30:831-3.
6. Hollier LM, Leveno KJ, Kelly MA, MCIntire DD, Cunningham FG. Maternal age and malformations in singleton births. Obstet Gynecol. 2000;96:701-6.
7. Fretts RC, Schmittdiel J, Mc Lean FH. Increased maternal age and the risk of fetal death. N Eng J Med 1995;333:953-7.
8. Gilbert WM, Nesbitt TS, Danielsen B. Childbearing beyond age 40: pregnancy outcome in 24 032 cases. Obstet Gynecol. 1999;93:9-14.
9. 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;243:3-7.
10. Ananth CV, Wilcox A, Savitz DA, Bowes WA Jr, Luther ER. Effect of maternal age and parity on the risk of uteroplacental bleeding disorders pregnancy. Obstet Gynecol. 1996;88:511-6.
11. Shau WY, Hung TH. Risks for placenta accreta. Obstet Gynecol. 1999;93:545-50.
12. Hansen J. Older maternal age and pregnancy outcome: a review of the literature. Obstet Gynecol Surv. 1986;41:726-42.
13. Kirtz DS, Dorchester W, Freeman RK. Advanced maternal age: the mature gravida. Obstet Gynecol. 1985;152:7-12.
14. Bianco A, Stone J, Lynch L, Lapinski R, Berkowitz G, Berkowitz RL. Pregnancy outcome at age 40 and older. Obstet Gynecol. 1996;87:917-22.
15. La Santé Périnatale. France-Perinat: Réseau National d'Information sur la Naissance. Indicateurs de santé périnatale de 1994 à 2003. Evaluation des pratiques médicales, 2003. Available at: http://audipog.inserm.fr. Accessed 20 September 2012.
16. Tuck R, Yudking P, Turnbul L. Pregnancy outcome in elderly primigravidae with and without a history of infertility. Br J Obstet Gynaecol. 1988;95:230-7.
17. Wong SF, Ho LC. Labour outcome of low-risk multiparas of 40 years and older. A case-control study. J Obstet Gynecol. 1998;38:388-90.
18. Mills TA, Lavender T. Advanced maternal age. Obstet, Gynaecol and Reprod Med. 2011;21(4):107-11.
19. Roman H, Robillard P-Y, Julien C, Kauffmann A, Kauffmann E, Laffitte A et al. Grossesse chez 382 femmes de plus de 40 ans: étude rétrospective dans la population de l'île de la Réunion. J Gynecol Obstet Biol Reprod. 2004;33:615-22.
20. Luke B, Brown M. Elevated risks of pregnancy complications and adverse outcome with increasing maternal age. Hum Reprod. 2007;22:1264-72.
21. Prysak M, Lorentz RP, Kisly A. Pregnancy outcome in nulliparous women 35 years and older. Obstet Gynecol. 1995;85:65-70.
22. Ecker JL, Chen KT, Cohen AP, Riley LE, Lieberman ES. Increased risk of cesarean delivery with

advancing maternal age: indications and associated factors in nulliparous women. Obstet Gynecol. 2001;185: 883-7.

23. US Census Bureau. National Vital Statistics Report. In: Statistical Abstract of the United States: The National Data Book. 125th ed. US: Unabridged Edition; 2002: 5-12.