Can advanced maternal age can negatively impact on the prognosis of the birth? Observational study at the Issaka Gazoby maternity center in Niamey, Niger

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Background: Childbirth at an advanced age is increasing rapidly in the world. This is due to sociological changes and to the development of medically assisted procreation. There are still gaps in knowledge about the risks associated with pregnancy among older women. The objective of our study is to investigate the perinatal risk factors of pregnancy of women over the age of 35, who gave birth at Issaka GAZOBY maternity center in Niamey

Methods: It was a prospective case-control study that spread over 4 months (from January 1 to April 30, 2014). For each parturient whose age is greater than 35 years, we assigned him two witnesses whose age is between 20 and 34 years. Data from 100 women aged over 35 years and 200 women aged 20-34 years and their newborns were analyzed. Through univariate and

multivariate analyses we sought an association between maternal characteristics and perinatal prognosis.

Results: The mean age of the case patients was 38.79 years. The mean age of the controls was 26.93 years. The mean parity of the cases was 6.83 children and that of the controls was 2.33 children. In the case patients, 50% of pregnancies were completed without complications compared to 51.5% of controls. The main complications were anemia, threat of preterm delivery and pre-eclampsia. Seventy-three percent of older women underwent caesarean section. Obstructed labor, retro-placental hematoma, stationary dilation cervix and pre-eclampsia were the main reasons for caesarean section. The proportion of low birth weight was 27% among the case patients and 28% among the controls. Nine percent of the newborns in the cases had macrosomia as opposed to 4% in the control group. There was no significant relationship between maternal age and prematurity (OR = 0.24, 95% CI: 0.02 and 1.96, P = 0.13). Statistical analysis found no significant relationship between maternal age and low birth weight (OR = 2.37, 95% CI: 0.88 and 6.35, P = 0.07). The risk of having a low Apgar score was higher in the case patients (OR = 0.53, 95% CI: 0.32 and 0.88, P = 0.02). Older women were 2.87 times more likely to have a stillbirth child than controls (OR = 2.87, 95% CI: 1.41 and 5.83, P = 0.002).

Conclusion: Neonatal mortality is higher in women over 35 years of age

Key words: advanced maternal age, perinatal prognosis, Niger

Introduction

The average age at childbirth has changed considerably over the last four decades, particularly in the industrialized countries where it has been rising. It has increased from 23.7 years in 1969 to 29.4 years in 2009 in the United States [Statistics Canada 2012]. In Canada, the proportion of women giving birth after 35 years has doubled. It rose from 9.2% in 1991 to 18.3% in 2009

[Statistics Canada 2012]. This is due to recent sociological and economic changes and the development of medically assisted procreation in the last fourty years. In our context, low adherence to family planning, particularly in traditional environments, combined with the desire to have a larger family, means that women are constantly procreating from puberty to menopause. Several studies have shown an association of advanced maternal age with complications such as in utero fetal death, prematurity, low birth weight or macrosomia, pre-eclampsia and gestational diabetes [Joseph et al., 2005 and Berkowitz et al., 1990]. Other studies report that advanced maternal age does not affect neonatal prognosis [Cleary-Goldman et al., 2005]. In Niger, to our knowledge, no studies have been reported in the medical literature on perinatal prognosis of pregnancies in women aged over 35 years. Our aim was to investigate the obstetric and neonatal risk of pregnancy in a population of women aged over 35 years compared to a population of women aged 20 to 34 years.

Patients and methods

Study design and site

This was a case-control study that was carried out over a period of 4 months (January 1 to April 30, 2014) at Issaka Gazobi Maternity (IGM) center in Niamey which is a obstetric and neonatal tertiary referral center, covering the region of Niamey and the surrounding areas. It contains 142 hospital beds of obstetric and 31 infant care beds. It counts 7,500 deliveries and 3,800 neonatal admissions on the average per year.

Study population

The cases were parturients aged 35 years or over and their newborns aged 0 to 7 days. We assigned two witnesses (one case for two witnesses). Parturients aged 20 and 34 who had given birth on the same day and under the same conditions as the case and their newborns. Mothers

were the secondary target of the study. We excluded newborns referred from another center, abortions and those who refused to participate in the study.

Ethical consideration

The study was approved by the Institutional Review Board of the University of Niamey and the Committee of Ethics, Issaka GAZOBY Maternity. Participation was voluntary and written informed consent was obtained from participants.

Operational definitions of variables

For the purposes of this study we defined primipara as a woman who has given birth for the first time. Pauciparous is the one who has given birth 2 to 3 times. Multipara is the one who has experienced 4 to 6 deliveries. Grand multipara is the woman who has had 7 or more deliveries. According to the World Health Organization (WHO), a woman of advanced maternal age is the one on whose age is over or equal to 35 years. Perinatal risk is the probability of morbidity and mortality for the pregnant woman and the f~~o~~etus starting from the 22nd week of amenorrhea, then the mother and the newborn after delivery. The housewife is defined as any woman whose main activity is housework.

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Parameters studied

For each mother, we collected socio-demographic datas (age, occupation~~,~~ and residence), obstetrical and medical history, pregnancy monitoring, pregnancy complications and mode of delivery. For each newborn we collected gestational age at birth, sex, birth weight, Apgar score at birth, necessity of resuscitation or not at birth, the existence of congenital malformations, neonatal complications and the mode of discharge from maternity center.

Statistical Analysis

The data were entered into the Epi Info software version 3.5.2 and then exported and analyzed using the STATA 12 software. We used Yates' Chi2 test for qualitative variables and Fisher's exact test when the conditions to use Chi^2 are not met; the odds ratio (OR) and her confidence interval for perinatal risk assessment. P <0.05 was considered statistically significant.

Results

Our sample consisted of 100 cases and 200 controls. The mean age of cases was 38.79 years with extremes of 35 to 47 years. The mean age of the controls was 26.93 years. The mean parity of the case patients was 6.83 children and that of the controls was 2.33 children. The maximum parity was 14 children for the cases and 10 for the controls. Most of the cases and the controls had a low level of education. Table 1 summarizes the socio-demographic characteristics of the patients. Housewives accounted for 72% of cases and 61.5% of controls. Sixty-one percent of the case patients and 76% of the controls lived in urban areas. The mean number of antenatal visits was 3.08 ± 1.53 and 3.29 ± 1.58 for cases and controls respectively. Three percent of the case patients and 6.5% of the controls did not receive any prenatal care. Of the cases, 40% had received more than 4 prenatal consultations while 47% of the controls had more than 4. From case patients, 50% of pregnancies were completed without complications compared to 51.5% of controls. The main complications during pregnancy (Table 2) were: ~~anaemia~~anemia, 9% for the cases and 16% for the controls; the threat of preterm delivery, 6% for cases and 10.5% for controls; and preeclampsia with 3% for cases and 5.5% for controls. Twenty-six percent of the cases had a vaginal delivery and 73% had a caesarean sections. In the controls, 24.5% had delivered by vaginal delivery versus 75.5% by caesarean sections. The main indications for caesarean sections were: Obstructed labor (6% versus 26%); Retro-placental hematoma (10% versus 11% control); Stationary dilation (4% versus 9% control); premature rupture of membranes (25% versus 15% controls) and pre-eclampsia-/-eclampsia (7% versus 8% control). The mean gestational age was 38.08 weeks and 37.25 weeks respectively for the cases and

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controls. For the cases, 83% of births were at term compared with 17% of premature births. For the controls, 84% of births were at term; 4% were post term and 12% premature. The mean birth weight was 2950 ± 735g and 2885 ± 733g, respectively, for the cases and controls. Table 3 summarizes the characteristics of the newborns. The proportion of low birth weight was 27% in the cases and 28% in the controls. Nine percent of the cases (newborn) were macrosomic as opposed to 4% of the controls. The rest of the newborns weighed between 2500g and 4000g. Table 4 summarizes the neonatal prognosis. For 35% of the cases (newborns), the Apgar score was less than 7 at the 5 minutes compared to 26.5% of the controls. We found 6 cases of congenital malformations in the cases (3 cases of trisomy 21, 2 cases of spina bifida and 1 case of ichthyosis) compared to 4 cases of congenital malformations in the controls (one case of spina bifida, two cases of trisomy 21 and one case of anorectal malformation). We had 20 deaths in cases (newborns) including 14 stillborn and 6 cases of neonatal deaths. Among the witnesses, there were 16 deaths, including 5 stillborn and 11 cases of neonatal death.

Statistical analysis did not find a significant relationship between maternal age and prematurity. The proportion of preterm delivery was the same in both cases and controls; (OR = 0.24,-95% CI: 0.02 and 1.96, P = 0.13). Similarly, there was no statistically significant association between the age of the mother and post term delivery. Statistical analysis found no significant relationship between maternal age and low birth weight (OR = 2.37, 95% CI: 0.88 and 6.35, P = 0.07) but the risk of having a low Apgar score at birth was higher (OR = 0.53, 95% CI: 0.32 and 0.88, P = 0.02). At 5%, we found no statistically significant association between maternal age and congenital malformations (OR = 3.12, 95% CI: 0.86 and 11.34, P = 0.07). Statistical analysis showed that cases were 2.87 times more likely to have a deceased child than controls (OR = 2.87, 95% CI: 1.41 and 5.83, P = 0.002).

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Discussion

The impact of advanced maternal age on pregnancy outcomes remains controversial, with sometimes contradictory results in the literature. Perinatal outcomes are a source of ongoing debate, with some studies describing comparable results in different age groups [Bianco et al., 1996] and others reporting an increase in perinatal risk [Delbaere et al., 2007, Berkowitz et al., 1990]. The mean parity of the cases was 6.83 children and that of the controls was 2.33 children. The maximum parity was 14 for the cases and 10 for the controls. For cultural reasons and low adherence to family planning and contraception methods, women marry very early in our ~~countries~~ country and continue to give birth until an advanced age, which results in a high rate of grand multiparas and high average parity, which is of 7 children per woman in Niger. The aims of antenatal care are to prevent, detect early and manage complications that may affect the health of the mother and the unborn child, but also to accompany the woman and her family during pregnancy [Ngassam et al., 2013] Regular monitoring of pregnancies deemed at risk is an absolute necessity in order to early diagnose problems and solve them [Khoshnood et al., 2008]. Repetitive pregnancies can negatively affect the health of the mother and the uterus. Some authors report that the negative perinatal prognosis of elderly women's pregnancies is due to several morbidity factors such as poor intra-uterine environment and deficient placentation due to vascular alteration of the elderly woman [Crawford et al., 1997]. Several case-control studies [Lisonkoya et al., 2013. Xiaoli et al., 2014. Khalil et al., 2013] reported a predominance of low birth weight and macrosomia from elderly women contrary to our study where cases and controls had the same risk. In series reported by Timofeev et al. and Carolan et al., 2013 premature delivery is more common in women under 20 and over 35 years of age. Advanced maternal age is not significantly associated with preterm delivery in our study. Newborns from elderly mothers are more likely to have a low Apgar score at the first 5 minutes. Several similar results have been reported in the literature [Lamminpaa et al., 2012; Ngassam et al., 2013].

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Congenital malformations are higher in elderly women than in younger women, although we did not find a statistically significant relationship between advanced age and congenital malformations. However, for Roman et al., 2004, the risk of the occurrence of chromosomal abnormalities is multiplied by 7 in elderly women. The results of Vincent et al., 2012 corroborate those of Roman with 6.3% of newborns having malformation in the cases as opposed to 0.84% in the controls. Neonatal mortality was 2.87 times higher in elderly women than in controls. The main causes of death were asphyxia, neonatal infections and birth defects. Several authors [Jahromi et al., 2008; Koo et al., 2012 and Roman et al., 2004] reported a higher risk of neonatal mortality in older women. Our study has several limitations. First of all is the sample size and duration of the study, which did not allow us to draw exhaustive conclusions. The second difficulty is the determination of gestational age which is approximate in some women. The third difficulty is the very short follow-up time for apparently healthy newborns that are released after only 6 hours of surveillance. Finally, we did not meet all the requirements from a comparability point of view. Not-with-standing, this work may allow us to contribute to the knowledge of the relationships between maternal age and perinatal risk.

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Conclusion

Birth from women of advanced age is a general phenomenon in the world. Several studies have shown that advanced maternal age is an obstetrical and neonatal risk factor. In our study, neonatal mortality among women over 35 years of age was 2.87 times higher than among women aged 20 to 34 years. However, the advanced age of parturient women did not prove to be a risk factor for caesarean delivery, low birth weight, prematurity, macrosomia or congenital malformation. Further studies are needed to confirm or refute our findings.

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Table 1: Socio-demographic characteristics

	Cases N (%)	*Control N (%)*	*P*
Level of education			
Illiterate	39 (39%)	82 (41%)	0.09
Primary	27 (27%)	27 (13.5%)	0.03
Secondary	23(23%)	54 (27%)	0.65
Superior	11 (11%)	37 (18.5%)	0.20
Professional activities			
Student	0	21 (10.5%)	0.850
Official	22 (22%)	41 (20.5%)	1.17
Tradeswoman	6 (6%)	17 (7.5%)	0.59
Housewife	72 (72%)	123 (61.5%)	0.002
Residence			
Urban	61 (61%)	152 (76%)	0.03
Rural	39 (39%)	48 (24%)	0.750

Table 2: pathologies during pregnancy

Pathology	*Cases n (%)*	*Control n (%)*	*OR*	*CI (95%)*	*P*
Hepatitis B	1 (1%)	3 (1.5%)	1	0.1; 9.72	0
HIV	2 (2%)	5 (2.5%)	1.2	0.23; 6.28	0.09
Diabetes	0	1 (0.5%)	0	0	1
Syphilis	1 (1%)	1 (0.5%)	3.02	0.19; 48.74	0.5
Hypertension	5 (5%)	0	0	0	1
Heart disease	1 (1%)	0	0	0	1
Malaria	19 (19%)	22 (11%)	1.9	0.97; 3.7	0.31
Urinary tract infection	1 (1%)	1 (0.5%)	3.02	0.19; 48.7	0.5
Anemia	9 (9%)	32 (16%)	0.52	0.24; 1.14	0.32
Obstetric complications					
Retro-placental hematoma	2 (2%)	0	0	0	1
Eclampsia	3 (3%)	11 (5.5%)	0.53	0.14; 1.94	0.31
Preterm delivery	6 (6%)	21 (10.5%)	0.54	0.21; 1.38	0.3
No complications	50 (50%)	103 (51.5%)	0.94	0.58; 1.52	0.03

Table 3: newborns characteristics

Parameter	*Case n (%)*	*Control n (%)*	*P*
Gestational Age			
Normal term (37-42 w)	83 (83%)	168 (84%)	0.04
Post term (>42 w)	0	8 (4%)	0.31
Premature (33 w-36 w +6 days)	13 (13%)	20 (10%)	0.15
Medium premature (28 w to 32 w + 6 days)	4 (4%)	2 (1%)	0.61
Very premature (< 28 w)	0	2 (1%)	1
Birth weight			
<2500g	27 (27%)	56 (28%)	0.89
2500-4000g	64 (64%)	138 (68%)	0.09
> 4000g	9 (9%)	8 (4%)	0.13
APGAR score			
APGAR score < 7 at 5 min	35 (35%)	53 (26.5%)	0.02
APGAR score > 7 at 5 min	65 (65%)	147 (73.5%)	0.2

Table 4: neonatal prognosis

Outcome	*Cases n (%)*	*Control n (%)*	*OR*	*CI (95%)*	*P*
Delivery in term	83 (83%)	168 (84%)	0.94	0.53; 1.66	0.94
Preterm	17 (17%)	24 (12%)	1.5	0.76; 2.94	0.31
Post-term	0	8 (4%)	0.24	0.02; 1.96	0.28
Low birth weight	27 (27%)	57 (28.5%)	0.92	0.54; 1.58	0.89
Macrosomia	9 (9%)	8 (4%)	2.37	0.88; 6.35	0.13
Congenital malformation	6 (6%)	4 (2%)	3.12	0.86;11.34	0.07
death	20 (20%)	16 (8%)	2.87	1.41; 5.83	0.002