Advanced Maternal Age as an Obstetric Risk Factor: Current Experience in a Hospital from Northwestern Spain

A Idade Materna Avançada como Fator de Risco Obstétrico: Experiência Atual num Hospital do Noroeste de Espanha

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ABSTRACT

Introduction: Studies updating the evidence in advanced maternal age as an independent factor of obstetric risk are needed. The aim of this study was to determine the prevalence of ≥ 35-years-old pregnant women who give birth in a Spanish hospital in Northwestern Spain, and to describe the incidence of maternal and perinatal morbidity and mortality.

Material and Methods: Retrospective follow-up observational study including women ≥ 20 years-old who gave birth over one year (n = 1378). Data were collected from medical records, including socio-demographic characteristics, comorbidities, gestational conditions, variables related with the delivery and perinatal outcomes. Multivariable logistic regression analysis was performed to determine the association of advanced maternal age with obstetric and perinatal outcomes.

Results: Forty-two percent of pregnant women were ≥ 35 years old. In the multivariable analysis, advanced maternal age was associated with the likelihood of gestational diabetes (OR = 1.84; 95% CI = 1.10 - 3.07), hypothyroidism (OR = 2.11; 95% CI = 1.17 - 3.80), lower probability of an eutocic delivery (OR = 0.74; 95% CI = 0.56 - 0.98), and a hospital admission > four days (OR = 2.91; 95% CI = 1.95 - 4.35). An association with the rate of C-sections was not found (OR = 1.24; 95% CI = 0.89 - 1.72).

Conclusion: A high prevalence of pregnant women of advanced maternal age was confirmed. There was a higher rate of comorbidities and longer hospital admissions in older women but not a higher rate of higher C-sections and other complications.

Keywords: Cesarean Section; Delivery, Obstetric; Labor, Obstetric/complications; Maternal Age; Pregnancy

RESUMO

Introdução: São necessários estudos que atualizem as evidências sobre a idade materna avançada como fator independente de risco obstétrico. O objetivo deste estudo foi determinar a prevalência de mulheres grávidas com idade igual ou superior a 35 anos admitidas para o parto num hospital espanhol do Noroeste da Espanha, e descrever a incidência de morbilidade e mortalidade materna e perinatal.

Material e Métodos: Estudo observacional retrospetivo que inclui mulheres com idade igual ou superior a 20 anos admitidas para o parto ao longo de um ano (n = 1378). Os dados foram recolhidos em prontuários médicos, incluindo características sociodemográficas, comorbilidades, patologia gestacional, variáveis relacionadas com o parto e resultados perinatais. Foi realizada uma análise de regressão logística multivariada para determinar a relação da idade materna avançada com os resultados obstétricos e perinatais.

Resultados: Quarenta e dois por cento das mulheres grávidas tinham idade igual ou superior a 35 anos. Na análise multivariada, a idade materna avançada estava associada com maior probabilidade de diabetes gestacional (OR = 1,84; 95% CI = 1,10 - 3,07), hipotiroidismo (OR = 2,11; 95% CI = 1,17 - 3,80), menor probabilidade de parto eutócico (OR = 0,74; 95% CI = 0,56 - 0,98), e hospitalização superior a quatro dias (OR = 2,91; 95% CI = 1,95 - 4,35). Não foi encontrada uma associação com a taxa de cesarianas (OR = 1,24; 95% CI = 0,89 - 1,72).

Conclusão: A elevada prevalência de mulheres grávidas com idade materna avançada foi confirmada. As mulheres mais velhas apresentaram maior número de comorbilidades e maior tempo de hospitalização, mas não apresentaram uma maior ocorrência de cesarianas e outras complicações.

Palavras-chave: Cesariana; Gravidez; Idade Materna; Parto Obstétrico/complicações

INTRODUCTION

Advanced maternal age has been a constant in delivery rooms in developed countries for the last couple of decades.[1–3] Some authors,[4–10] including those of a recent meta-analysis,[7] have observed that advanced age entails an increased risk of obstetric and perinatal morbidity and mortality. However, other known factors that can contribute to an abnormal pregnancy also have to be taken into account, such as assisted reproduction techniques[4,5] or previous conditions,[10,11] Improved control and monitoring of pregnancy, delivery, and postpartum, especially in women of advanced age, could contribute to improved results. Therefore, it is necessary to carry out new studies that update the available evidence in advanced maternal age as an independent factor of obstetric risk.

Already in 1958, the International Federation of Gynaecology and Obstetrics (FIGO), defined 'advanced maternal age' (AMA), 35 years of age and over.[4,8,11–14] Nowadays, there is no consensus on where to establish this age limit[4]: 35, 38, 40, or even 45 years of age.[5,9,15] The optimal reproductive age is considered to be between 18 and 34 years of age, after

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finishing the pubertal development, growth, and maturation.

\In Spain, the average age of first-time mothers is 30.79 years of age, and the global average is 31.3 years.[2] Spain is the only country in Europe after Italy on this list.[3] This average has been increasing since the 1980s, when mothers had their first child at the age of 25.[2] This was due to the social changes that occurred during this time, especially more women entering the workforce and receiving a higher level of education.[2,3] In America, there is also a trend towards a higher maternal age. In Brazil, 30-year-old (or older) women deliveries comprise up to 31.3% of the total. In the USA in 2016, the average age of first-time mothers was 26.6 years.[1]

Despite the advanced age at which Spanish women have their first child, few studies have analysed the obstetric and perinatal results,[16–19] as well as comorbidities of women older than the optimal pregnancy age during pregnancy. In addition, it is interesting to analyse if, despite the improved quality of healthcare available to pregnant women in recent years and the early detection of conditions, there is still a high incidence of maternal and neonatal morbidity and mortality.

The objectives of this study are to determine the prevalence of pregnant women aged 35 and overwho gave birth in a hospital in the Northwestern Spain (Lugo, Galicia), and to describe the incidence of maternal and perinatal morbidity and mortality in these pregnant women as well as in newborns, in comparison with younger women.

MATERIAL AND METHODS

Retrospective follow-up observational study of all the deliveries at the Lucus Augusti University Hospital (also known as HULA) (Lugo, Northwest of Spain) over one year. This hospital was inaugurated in 2011 and is the hospital of reference for a province of approximately 355 000 inhabitants.

From an initial sample of 1420 pregnant women who gave birth over the period of the study, 11 were excluded for being uncontrolled pregnancies, and 31 as women were younger than 20 years old. Therefore, the sample of the study includes 1378 pregnant women. This sample size allows to estimate the incidence rate of obstetric and perinatal outcomes with a relative precision of ± 2.7% and a 95% confidence level.

The analysed data was taken from the patients' medical records, after receiving consent to access it, thus preserving data confidentiality according to current legislation. The study was performed after obtaining approval from the ethics committee (Committee of Research Ethics of Santiago-Lugo), code 2015/258).

The following variables were collected from each pregnant woman:

· **Characteristics of pregnant women**: maternal age at the time of birth and place of residence (urban/rural areas). Comorbidities before pregnancy (thyroid disease, arterial hypertension, diabetes, obstetric or gynaecological surgeries, autoimmune diseases, cancer, and heart disease), and obstetric history (full-term pregnancies, labour, abortions, C-sections, and pregnancies by assisted reproduction).

· **Related with pregnancy**: pregnancy complications (gestational diabetes, hypertension, gestational age < 37 weeks, intrauterine growth restriction) and weight gain during pregnancy. Threatened premature delivery was defined by the presence of regular uterine contractions associated with cervical changes that occurred after 20 weeks and before 37 weeks of gestation. The body mass index (BMI) was calculated at the beginning of the pregnancy and the weight gain during the pregnancy was classified according to the recommendations of the WHO[20]:

§ BMI < 18.5: should aim to gain 13 - 18 kg, underweight women
§ BMI 18.5 - 24.9: should aim to gain 11.5 - 16 kg
§ BMI 25 - 29.9: should aim to gain 7 - 11 kg
§ BMI ≥ 30: should aim to gain 5 - 9 kg

· **Related with the delivery**: gestational age at the time of delivery, type of onset (spontaneous, induced, programmed C-section) type of delivery (eutocic, instrumental, or C-section) and total number of admission days. An admission is considered prolonged if it lasts for more than four days.

· **Newborn measurements**: weight (small for gestational age, large for gestational age or normal weight) and Apgar at minute 1 and 5 after birth, gestational age (< 37 weeks/ ≥ 37 weeks) and destination of the newborn after birth.

Statistical analysis

Advanced maternal age is considered to be 35 years of age and over (according to FIGO), and these pregnant women were compared to women younger than 35.[4,8,11–14] So in order to explore differences in the risk of complications depending on the maternal age (< 40 or ≥ 40 years old), and following other authors, a comparison between three age groups was performed (20 - 34 years old, 35 - 39 years old and ≥ 40 years old).

A descriptive study of all the variables was performed, both globally and according to maternal age (< 35 and ≥ 35 years of age). The quantitative variables are shown as mean ± standard deviation. Qualitative variables are shown as absolute value and percentage, with an estimation of its 95% confidence interval (CI).

The baseline characteristics of pregnant women were compared according to their age, development of pregnancy, delivery, and perinatal results. In order to compare the quantitative variables, the Student's *t*-test or the Mann-Whitney test were used, after checking normality with the Kolgomorov-Smirnov test. In order to compare the percentages, the statistic

chi-square test or Fisher's exact test were used.

The *odds ratio* (OR) values related to advanced maternal age were calculated for the different obstetric and perinatal results obtained, both crude and adjusted, with multivariable logistic regression models. The multivariable analysis was adjusted for each case using a direct approach, including as covariates those variables that were associated ($p < 0.20$) with each obstetric or perinatal outcome in the bivariate analysis, along with other potential confounding factors according to the results reviewed in the literature.

Additionally, we examined the strength and shape of the relationship of maternal age with the log odds of of the different obstetric and perinatal outcomes studied using restricted cubic splines, using the 50th percentile (age = 34 years) as reference point. This approach allows for a flexible association between age and the incidence of the complications studied, without assuming a linear association. Therefore, it could be useful to identify the age at which the risk of a determined adverse outcome starts to increase.

All tests were performed with a bilateral approach. *P* - values < 0.05 were considered statistically significant.

RESULTS

During the period of the study, 1378 women gave birth, of which 581 (42.2%) were between 35 and 50 years old at the moment of the birth (n = 126, 9.1% were ≥ 40 years-old), with a global average age of 37.8 ± 2.5 years (Table 1). We identified 60.9% of women as being first-time mothers (53.0% in the AMA group), with 40 (2.9%) twin pregnancies (26 in the AMA group).

AMA pregnant women had a higher proportion of previous conditions (42.2 % *vs* 20.2%, $p < 0.001$), with a higher prevalence of both obstetric-gynaecological surgical interventions (26.5% *vs* 19. %, $p = 0.001$) and hypothyroidism (10.2% *vs* 6.1%, $p = 0.006$). On the other hand, smoking habits were more frequently observed in younger women (18.1% *vs* 11.4%; $p = 0.001$). The use of assisted reproduction techniques was significantly higher in older women (11.4% *vs* 2.1%, $p < 0.001$). Differences in the prevalence of hypertension, diabetes, overweight, or obesity were not observed (Table 1).

Regarding pregnancy complications and obstetric outcomes, the presence of gestational diabetes was more frequent in AMA pregnant women (7.4% *vs* 4.3%; $p = 0.012$), as well as gestational hypothyroidism, although in this case without statistical significance (5.5% *vs* 3.4%; $p = 0.055$). On the other hand, no difference was observed as regards preeclampsia, premature delivery threat, gestational hypertension, or intrauterine growth restriction. Weight gain during pregnancy was similar in both groups. 40.9% of women had gained weight within the recommended limits, 32.7% did not gain enough weight, and 26.4% had excessive weight gain (Table 2).

Regarding delivery onset, completion, and duration of the hospital admission, labour started spontaneously more frequently in younger women (60.2% *vs* 54.9%, $p = 0.048$), and more scheduled C-sections were performed in older women (9.6% *vs* 5.4%) ($p = 0.003$). An eutocic delivery was more frequent in young women (56.5% *vs* 50.4% $p = 0.027$) and emergency C-sections were more frequent in older women (30.1% *vs* 24.3%) ($p = 0.017$), without any significant differences in the duration of labour. In addition, AMA women stayed longer in the hospital (42.3% *vs* 27.9% $p < 0.001$).

We recorded 1436 births (56.2 % males), of which 92.9 % were full-term births, without differences in maternal age. No significant differences were observed in the newborn weight across the maternal age range, with 82.9% of the newborns being within the normal percentile. Fetal unfavourable results, such as APGAR < 7 at minute 1 and 5 (both in single and twin pregnancies) or fetal death, were infrequent, without differences between both age groups (Table 3).

The multivariable analysis, after being adjusted for different variables, showed that AMA women had a significantly higher risk of developing gestational diabetes (OR = 1.84; 95% CI = 1.10 - 3.07), gestational hypothyroidism (OR = 2.11; 95% CI = 1.17 - 3.80), a longer hospital admission (OR = 2.91; 95% CI = 1.95 - 4.35). A decrease in the rate of eutocic deliveries was also observed (OR = 0.74; 95% CI = 0.56 - 0.98) (Table 4). On the other hand, AMA was not associated with weight gain during the pregnancy, threatened premature delivery, or with the admission of the newborn to the NICU. Intrauterine growth restriction, Small for gestational age, a lower probability of having a spontaneous labour, or a higher rate of C-sections were not associated with AMA either. The analysis based on cubic regression splines is shown in Fig. 1. The results suggested that age around 35 years can be a good cut-off point from which both the risk of gestational diabetes and gestational hypothyroidism increases, as well as the probability of a prolonged hospital admission. On the other hand, the chances of having a eutocic delivery do not seem to start to decline until a slightly older age.

DISCUSSION

The objective of this study was to describe the characteristics of pregnant women aged 35 and over, and the problems associated with these women in a hospital in Northwestern Spain. These data may be usefulto adapt current guidelines and provide healthcare centres with the necessary resources in order to treat those pregnancies formerly considered high-risk.

It is worth highlighting that in this study there was a high prevalence of AMA pregnant women (42.4 %) and the higher risk these women had of developing diabetes and hypothyroidism during pregnancy, the decrease in the rate of eutocic deliveries, and the probability of having a longer hospital admission. However, despite having a higher number of previous

conditions, no differences were observed in terms of other another pregnancy complications, threatened preterm labour, orperinatal outcomes.

As stated, this study stands out due to the high percentage of AMA women. AMA has become common in Spain in recent years due to several factors: the economic crisis of the last decade, a higher percentage of women educated at university level, job positions with more responsibilities, etc. This makes maternity something more likely to be postponed to a period of greater economic and professional stability. Despite these factors being common throughout Spain, the percentage of AMA in this hospital in Northwestern Spain is even higher compared to other Spanish regions by almost eight points.[16] If we compare this data internationally, we observe a lower prevalence of AMA in other studies: 8.5%,[15] 14%,[21] 15%,[9] 21%[8] and 35.8%.[4] These may be influenced by the current uncertainty of the job market (lack of stability), the high housing prices, and a lack of rental market, which delays emancipation. This high prevalence rate shows the importance of studying the obstetric and perinatal outcomesin this age group, which is increasingly growing.

During pregnancy, advanced maternal age entails risks, one of them being the increased proportion of previous conditions, as shown in this study (42.0 % *vs* 30.2 %). The prevalence of previous co-morbidities was higher than that shown in other studies (between 8% and 39 % in older pregnant women, and between 1% and 25% in women younger than 35 years old).[4,5,9,22,23] Similarly, there is also a higher prevalence of conditions as maternal age increases.[5,22,23]

Our findings also support a greater need for the use of reproduction techniques in the case of AMA (11.4% *vs* 2.1%, $p < 0.001$), as shown in Ankarcroma *et al*[15] and Macías Villa *et al*[4] and even higher than other studies: 4.3% *vs* 0.2%.[9] These assisted reproduction treatmentsare associated with an increase in the number of twin pregnancies, which are more frequent in AMA, in addition to spontaneous pregnancies, as the study by Rydahl *et all*[9] shows.

Even though 5.6% of patients were diagnosed with gestational diabetes, that percentage increased to 7.4% in women of advanced maternal age. This finding showed the increasing trend of diabetes related to maternal age, which is similar to the study by Ben-David et *al*. Shan *et al* also observed an increased risk of 2.78 times in women older than 35.[24]

Thyroid disease is frequent in the Northern Spain, especially in Galicia. Before the inclusion of the intake of iodized salt in the general population, there was a deficit of this element and, as a consequence, a high number of patients with thyroid disease. This is the reason why thyroid disease is assessed during pregnancy in this region. The results show that AMA women suffer from gestational hypothyroidism twice as much as young women. Since this is not a frequent condition, other hospitals are less likely to include these checks in routine care and they are only performed if there are symptoms. Therefore, we do not have other data with which to compare.

Regarding high blood pressure (HBP) present during pregnancy, the tendency is the same, although the difference is minimal. (2.3% *vs* 1.9%). This may be due to the low number of cases found, since HBP tends to increase as maternal age increases. Other authors have observed greater differences.[8,9,13,25,26] but in general all studies show a tendency of HBP increasing with age.[5,10,21,24]

Regarding threatened premature labour, other studies have found a bigger tendency in AMA, although the differences are not always significant.[6,9,13,27] In this study, the rate of threatened premature labour is slightly higher in the AMA group (5.5 % *vs* 4.4 %), although this association cannot be confirmed (OR = 0.94; 95% IC: 0.52 - 1.70).

Given that the observed conditions are frequent, it is not always possible to wait for women to start labour spontaneously, but it may be necessary to terminate the pregnancy due to medical causes. Sometimes, elective C-sections are necessary. Several studies associate an advanced maternal age with a higher number of C-sections[4,6,8,11,16,21] and instrumental deliveries.[5] In this sample, the probability of an eutocic delivery was significantly lower in the AMA group (OR = 0.75). However, the risk of C-section was not associated with maternal age OR = 1.24 IC (0.89 - 1.72) after adjusting, among other variables, for previous and gestational conditions.

Something similar happens with prematurity: the number increases slightly with age (8.1 % *vs* 6.4 %), but these results are not associated with advanced age OR = 0.96 IC (0.57 - 1.60). In other studies, the percentages of premature births are much higher, and this may be because the age of these patients is also higher: they consider older pregnant women to be between 40 and 45 years old. This may also be due to less monitoring of threatened premature lbour.[5,6,8,10,16,26,28] It is also very important to take into account that prematurity is influenced by other factors like smoking, HBP during pregnancy, and the quality of healthcare and monitoring during pregnancy.

It is especially noteworthy that AMA is associated with longer hospital admissions, even after considering C-sections in the analysis, and despite the absence of significant differences in obstetric events in both groups, such as previous co-morbidities and gestational diseases. We cannot discard that this difference could be explained due to other confounding variables not included in this study. In the hospital where the data was gathered, pregnancies are not finalised depending on the maternal age, it is only finalised if there is an obstetric pathology or a prolonged pregnancy regardless of the age of the pregnant woman, but it is possible that there is a bias that leads to believe that pregnant women with AMA can develop more diseases after labour and therefore end up extending hospital admissions without justification, which will mean more hospital expenses in this age group.

As for neonatal results, we found a slightly higher percentage of AMA newborn admissions to NICU, and this is supported by studies like the one conducted by Schwartz *et al* and the one by Kahveci *et al*.[6,13] However, after performing a

multivariable analysis, a significant association with AMA was not obtained OR = 1.25 IC (0.82 - 1.89).

Low weight at birth is more frequent in AMA children,[5,11,14–16] and this matches the results observed, although the differences are not statistically significant.

The results of this study have to be interpreted of a number of possible limitations.

One of the main limitations is the lack of statistical power to detect differences in the incidence of less frequent obstetric or perinatal events. For the same reason, this study was not designed to analyse the differences in the rates of complications in the subgroups aged 35-39 and ≥ 40, as other studies did.[29] This is a study carried out in a specific geographical area during oneyear, and therefore these results may not be generalisable. The data could also vary between a public hospital (like the one in this study) and a private hospital, especially in terms of C-section rates, since they are only performed under justified circumstances.

In addition, one must also consider that this study is retrospective and based on information from medical records, which can be subject to bias. Only one person was responsible for collecting the data from the medical records, which minimized biases. As opposed to other studies, a multivariable analysis adjusted for previous and gestational conditions was performed, which minimized confounding. The thoroughness of the information collected allowed the adjustment of this analysis for multiple variables, which could explain the differences in the results obtained in other papers that did not perform this adjustment.

It is important to be aware tha women's role in society is changing and that this leads to a higher maternal age. This seems to be a tendency that will carry on over time. A consequence of this fact will be increased healthcare expenses, especially due to long hospital admissions and to less favourable obstetric-perinatal outcomes. Therefore, it is necessary to adapt guidelines to this new reality especially in terms of both the number of consultations of pregnant women and the moment when they take place, and the training of healthcare professionals. It is important to 'normalize' AMA in pregnancies and not to over-diagnose or perform unnecessary tests only due to an advanced maternal age.

CONCLUSION

This study brings to light the high prevalence of AMA pregnant women in Spain and partly confirms its impact on obstetric and perinatal outcomes. Although older women tended to have worse outcomes, the differences in many cases were not as substantial as shown in previous studies. We can conclude that it is important to continue studying older pregnant women in order to prevent or identify, at an early stage, potential problems during pregnancy.

AUTHORS CONTRIBUTION:

LPM: Conception and design of the work, data acquisition and analysis, draftof the paper, critical review and approval of the final version.

SBL, NLC, RNA: Conception and design of the work, data acquisition, critical review and approval of the final version.

TSP, SPD: Conception and design of the work, data analysis, critical review and approval of the final version.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Table 1 – Maternal demographic, medical background data and obstetric characteristics on the study population

	Total (n = 1378)	**20 - 34 age** (n = 797)	**35 - 39 age** (n = 455)	**≥ 40 age** (n = 126)		
	n (%)	**n (%)**	**n (%)**	**n (%)**	***p*§**	***p*‖**
Maternal age at delivery, Mean ± SD	33.2 ± 5.2	29.7 ± 3.7	36.7 ± 1.4	41.7 ± 2.0	< 0.001	< 0.001
Parity, Mean ± SD	1.4 ± 0.5	1.3 ± 0.5	1.5 ± 0.5	1.5 ± 0.5	< 0.001	< 0.001
nulliparous	839 (60.9)	531 (66.6)	239 (52.5)	69 (54.8)		
multiparous	539 (39.1)	266 (33.4)	216 47.5)	57 (54.2)		
Previous CS	122 (8.9)	57 (7.2)	48 (10.5)	17 (13.5)	0.020	0.014
Nº abortions, Mean ± SD	0.4 ± 0.7	0.3 ± 0.7	0.4 ± 0.8	0.6 ± 0.9	---	0.001
0	1005 (72.9)	605 (75.9)	318 (69.9)	82 (65.1)		
1	272 (19.7)	148 (18.6)	100 (2.0)	24 (19.0)		
≥ 2	101(16.4)	44 (5.5)	37 (8.1)	20 (15.9)		
	n (%)	**n (%)**	**n (%)**	**n (%)**	***p*§**	***p*‖**
Region					< 0.001	< 0.001
urban	938 (68.1)	493 (61.9)	351 (77.1)	94 (74.6)		
rural	440 (31.9)	304 (38.1)	104 (22.9)	32 (25,4)		
Chronic illness[a]	485 (35.2)	241 (30.2)	183 (40,2)	61 (48,4)	< 0.001	< 0.001
Previous gynaecological surgery	306 (22.2)	152 (19.1)	118 (25.9)	36 (28.6)	0.004	0.001
Assisted reproduction	83 (6.0)	17 (2.1)	34 (7.5)	32 (25.4)	< 0.001	< 0.001
Hypothyroidism	108 (7.8)	49 (6.1)	39 (8.6)	20 (15.9)	0.001	0.006
Chronic hypertension	14 (1.0)	9 (1.1)	3 (0.7)	2 (1.6)	---	0.623
Pre-gestational diabetes	8 (0.6)	4 (0.5)	1 (0.2)	3 (2.4)	---	0.653
Smoking	210 (15.2)	144 (18.1)	57 (12.5)	9 (7.1)	0.001	0.001
BMI (kg/m²)					0.308	0.235
underweight (< 18.5 kg/m²)	18 (1.5)	7 (1.0)	10 (2.5)	1 (0.9)		
normal (18.5 – 24.9 kg/m²)	680 (55.6)	398 (56.1)	226 (55.9)	56 (51.9)		
overweight (25 – 29.9 kg/m²)	358 (29.3)	202 (28.5)	124 (30.7)	32 (29.6)		
obese (≥ 30 kg/m²)	166 (13.6)	103 (14.5)	44 (10.9)	19 (17.6)		

CS: caesarean section; BMI: body mass index
a: diabetes, hypertension, hypothyroidism, cancer and autoimmune diseases
§: *p*-value for the comparison of three age groups: 20 - 34 *vs* 35 - 39 *vs* ≥ 40 years old
‖: *p*-value for the comparison of two age groups: 20 - 34 *vs* ≥ 35 years old

Table 2 – Pregnancy and delivery outcomes for the study population

	Total (n = 1378)		20 - 34 age (n = 797)	35 - 39 age (n = 455)	≥ 40 age (n = 126)		
	n (%)	95% CI	n (%)	n (%)	n (%)	*p*§	*p*‖
Gestational diabetes	77 (5.6)	4.3 – 6.8	34 (4.3)	30 (6.6)	13 (10.4)	0.011	0.012
Gestational hypothyroidism	59 (4.3)	3.2 – 5.4	27 (3.4)	4 (5.3)	8 (6.3)	0.138	0.055
Pre-eclampsia	22 (1.6)	0.9 – 2.3	15 (1.9)	5 (1.1)	2 (1.6)	---	0.322
Gestational hypertension	28 (2.0)	1.3 – 2.8	15 (1.9)	12 (2.6)	1 (0.8)	---	0.644
Premature contractions	67 (4.9)	3.7 – 6.0	35 (4.4)	24 (5.3)	8 (6.3)	0.562	0.341
IUGR	43 (3.1)	2.2 – 4.1	25 (3.1)	15 (3.3)	3 (2.4)	---	0.967
Weight gain in pregnancy (WHO recommendations)						0.184	0.123
low gestational weight	335 (32.7)	29.8 – 35.6	198 (32.4)	101 (31.4)	36 (39.1)		
normal gestational weight	419 (40.9)	37.8 – 43.9	238 (39.0)	145 (45.0)	36 (39.1)		
excessive weight gain	271 (26.4)	23.7 – 29.2	175 (28.6)	76 (23.6)	20 (21.7)		
Delivery characteristics						0.003	0.006
spontaneous onset	799 (58.0)	55.3 – 60.6	480 (602)	261 (57.4)	58 (46.0)		
induction of labour	480 (34.8)	32.3 – 37.4	274 (34.4)	151 (33.2)	55 (43.7)		
caesarean section (elective)	99 (7.2)	5.8 – 8.6	43 (5.4)	43 (9.5)	13 (10.3)		
Mode of delivery						0.007	0.039
natural delivery	743 (53.9)	51.3 – 56.6	450 (65.5)	240 (52.7)	53 (42.1)		
instrumental delivery[a]	266 (19.3)	17.2 – 21.4	153 (19.2)	90 (19.8)	23 (18.3)		
caesarean section (emergency)	369 (26.8)	24.4 – 29.2	194 (24.3)	125 (27.5)	50 (39.7)		
Length of hospitalization (days)						< 0.001	< 0.001
< 2 days	8 (0.6)	0.1 – 1.0	8 (1.0)	0 (0.0)	0 (0.0)	---	
2 - 4 days	901 (65.4)	62.9 – 68.0	566 (71.1)	272 (59.8)	63 (50.0)	< 0.001	
≥ 4 days	468 (34.0)	31.5 – 36.5	222 (27.9)	183 (40.2)	63 (50.0)	< 0.001	

IUGR: intrauterine growth restriction
a: vaginal delivery where either thongs or vacuum extraction was used
§: *p*-value for the comparison of three age groups: 20 - 34 *vs* 35 - 39 *vs* ≥ 40 years old
‖: *p*-value for the comparison of two age groups: 20 - 34 *vs* ≥ 35 years old

Table 3 – Neonatal outcomes in women 20 - 34 years and AMA

	Total (n = 1378)		20 - 34 age (n = 797)	35 - 39 age (n = 455)	≥ 40 age (n = 126)		
	n (%)	CI 95%	n (%)	n (%)	n (%)	*p*§	*p*‖
Singleton gestation							
APGAR 1' < 7	23 (1.7)	1.0 – 2.5	12 (1.6)	11 (2.0)	0 (0.0)	0.145	0.532
APGAR 5' < 7	6 (0.5)	0.1 – 0.9	3 (0.4)	3 (0.6)	0 (0.0)	---	0.698
Gestational age at delivery						0.712	0.427
< 37 weeks	81 (6.1)	4.7 – 7.4	44 (5.6)	28 (6.7)	8 (6.7)		
≥ 37 weeks	1255 (93.8)	92.5 – 95.1	738 (94.4)	406 (93.3)	111 (93.3)		
Neonatal birthweight:						0.357	0.466
small for gestational age	92 (6.9)	5.5 – 8.3	51 (6.5)	29 (6.7)	12 (10.1)		
normal birth weight	1132 (84.6)	82.6 – 86.6	670 (85.7)	363 (83.3)	99 (83.2)		
fetal macrosomia	113 (8.5)	6.9 – 10.0	61 (7.8)	44 (10.1)	8 (6.7)		
Intrauterine fetal death	3 (0.2)	0.1 – 0.7	1 (0.1)	2 (0.4)	0 (0.0)	---	0.573
NICU admission	122 (9.1)	7.5 – 10.7	63 (8.2)	46 (10.7)	13(11.1)	0.261	0.102
Multiple gestation							
APGAR 1' < 7	3 (4.2)	0.9 – 11.9	2 (7.4)	1 (2.9)	0	---	0.553
APGAR 5' < 7	1 (1.4)	0.0 – 7.6	0 (0.0)	1 (2.9)	0	---	1.00
Gestational age at delivery						0.813	0.608
< 37 weeks	15 (37.5)	21.3 – 53.8	6 (42.9)	7 (36.8)	2 (28.6)		
≥ 37 weeks	25 (62.5)	46.3 – 78.8	8 (57.1)	12 (63.2)	5 (71.4)		
Neonatal birthwight:						---	0.676
small for gestational age	10 (18.8)	6.1 – 26.1	3 (21.4)	9 (25.0)	0 (0.0)		
normal birth weight	52 (81.3)	73.9 – 93.8	11 (78. 6)	27 (75.0)	14 (100.0)		
Fetal macrosomia	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		
Intrauterine fetal death	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	-	-
NICU admission	31 (40.8)	29.1 – 52.5	14 (50.0)	12 (35.3)	5 (35.7)	0.459	0.212

NICU: neonatal intensive care unit
§: *p*-value for the comparison of three age groups: 20 - 34 *vs* 35 - 39 *vs* ≥ 40 years old
‖: *p*-value for the comparison of two age groups: 20 - 34 *vs* ≥ 35 years old

Table 4 – Crude and adjusted odds ratios (OR) and 95% confidence intervals (CI) for advanced maternal age and risk of the most frequent obstetric, perinatal and fetal outcomes

	OR crude	95% CI	OR adjusted	95% CI
Gestational diabetes (n = 77)	1.80	1.13 – 2.86	1.84†	1.10 – 3.07
Gestational hypothyroidism (n = 59)	1.66	0.99 – 2.81	2.11†	1.17 – 3.80
Gestational hypertension (n = 28)	1.19	0.56 – 2.53	1.40†	0.6 – 3.28
Weight gain (n = 271 above recommended range)	0.75	0.56 – 1.00	0.81‡	0.58 – 1.12
Premature contractions (n = 67)	1.27	0.78 – 2.06	0.96‡	0.53 – 1.74
Intrauterine growth restriction (IUGR) (n = 43)	0.99	0.53 – 1.83	1.19‡	0.59 – 2.40
Spontaneous onset (n = 799)	0.80	0.65 – 0.99	0.77§	0.59 – 1.01
Natural delivery (n = 743)	0.78	0.63 – 0.97	0.74§	0.56 – 0.98
Caesarean section (n = 369)	1.34	1.05 – 1.70	1.24§	0.89 – 1.72
Prolonged hospital admission (≥ 4 days) (n = 468)	1.90	1.52 – 2.38	2.91‖	1.95 – 4.35
Preterm birth (n = 98)	1.29	0.85 – 1.94	0.96‡	0.57 – 1.60
NICU admission (n = 153)	1.36	0.94 – 1.98	1.25‡	0.82 – 1.89

†: adjusted for: BMI, smoking habit, parity, assisted reproduction and chronic illness. Gemelarity was included in the model when sample size requirements were met.
‡: adjusted for: BMI, smoking habit, parity, assisted reproduction, chronic illness, gestational diabetes, gestational hypertension and gestational hypothyroidism. Gemelarity was included in the model when sample size requirements were met.
§: adjusted for: BMI, smoking habit, parity, assisted reproduction, chronic illness, gestational diabetes, gestational hypertension, gestational hypothyroidism, gemelarity and weight gain during pregnancy.
‖: adjusted for: BMI, smoking habit, parity, assisted reproduction, chronic illness, gestational diabetes, gestational hypertension, gestational hypothyroidism, gemelarity, weight gain during pregnancy and C-section delivery.