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Original Research – Quantitative

The impact of delayed maternity on foetal growth in Spain: An assessment by population attributable fraction

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ABSTRACT

Background: Delayed childbearing is considered a risk factor for maternal–foetal health. As in other higher-income countries, in Spain age at maternity has steadily increased during the last two decades.
Aim: To quantify the impact of the delay in the age at maternity on small for gestational age (SGA) categories of <3rd, 3rd–5th and 5th–10th percentiles.
Methods: 2,672,350 singleton live births born to Spanish mothers in 2007–2015 were analysed. Adjusted relative risk was calculated to estimate the adjusted partial population attributable fractions (PAF_p) for mothers aged 35–39 and ≥40 years for each category of SGA considering the interaction between age at maternity and parity.
Findings: Primipara 35–39 years old mothers have the highest PAF_p in the three categories of SGA, with the maximum value for SGA <3rd percentile (2.57%, 95% CI 2.25, 2.88). PAF_p for both primipara and multipara ≥40 years old mothers were less than 1%. PAF_p for primipara older mothers increased significantly in 2007–2015 for the three categories of SGA, more clearly among those aged 35–39 years. The contribution of multipara mothers of both age groups did not increase significantly during the period.
Conclusion: Delayed maternity is a significant adjusted risk factor for SGA, contributing to the increase of its prevalence. However, results also suggest a limited clinical impact of delayed maternity on foetal growth. Positive changes in maternal profile associated with the shift in maternal age might contribute to explain the limited impact of mothers aged 35 years and older on negative birth outcome in Spain.

Statement of significance

Problem

Delayed childbearing is a trend across higher-income countries, being increasingly considered a major public health concern as an independent risk factor for maternal–foetal health.

What is already known

Delayed childbearing is an independent obstetric, labour, and birth outcome risk factor, becoming more evident with increasing age over 40 years old. Some studies, however, find that this impact may be significantly reduced or eliminated after adjustment for potential confounders.

What this paper adds

Delayed maternity associated with primiparity is a significant adjusted risk factor for SGA, contributing to the increase of its prevalence. However, results suggest a limited clinical impact, perhaps as a consequence of the high socioeconomic status profile of older mothers.

1. Introduction

The past decades have seen a remarkable trend in higher-income countries towards delaying childbirth to later reproductive years, a tendency driven by the free access to highly effective contraception, expanding opportunities for higher education and professional employment among women, and the subsequent option of assisted reproductive techniques (ART). Older mothers

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(considered as women aged 35 years and older) may be psychologically and socially better prepared for childbearing when compared to younger mothers due to greater education, higher-income, and better prenatal care. Due to biological limits on fertility, older mothers are more heavily involved in their "valuable pregnancies".[1] However, the trend to delayed childbearing is being increasingly regarded as a major public health concern in higher-income countries, considering that it is an independent risk factor for maternal health and birth outcome. It has been suggested that delayed childbearing may be reversing the general improvement achieved during the previous decades in the health of mothers and neonates.[2] Moreover, the growing predominance of primipara mothers with an ever-increasing age at first maternity, and their growing rates of multiple pregnancies (twins, triplets) as a result of the rise in ART, have been proposed as the main explanations for the increasing rates of low birthweight (LBW) and preterm births described in almost all higher-income countries over the past two decades.[3]

Some biological mechanisms have been proposed to explain the potential negative effect of delayed maternity on maternal and foetal health and type of delivery. Uteroplacental perfusion decreases as women grow older independently of parity, affecting foetal growth and even determining a higher risk of perinatal mortality.[4] In a growing population of older primipara mothers, primiparity contributes negatively to birth outcome mainly due to a lesser vascular uteroplacental capacity.[5] Additionally, the life course increasing prevalence of chronic medical diseases (diabetes and hypertension) and obesity among older mothers contributes to poorer birth outcome and increased maternal health problems (pregnancy-induced hypertension, preeclampsia, and diabetes mellitus) compared with healthy younger women.[6] Finally, delayed childbirth has been associated with rising rates of intrapartum complications and, consequently, of Caesarean section (CS) and operative vaginal deliveries as a consequence of impaired myometrial function.[7]

The recent reviews by Carolan et al.[8,9] confirm that delayed maternity is significantly associated with an increased prevalence and risk of obstetric complications (placenta praevia and placental abruption), adverse labour (breech presentation, and operative vaginal or CS delivery), and negative birth outcome (stillbirths, preterm birth, and newborns with LBW or small for gestational age). However, these associations are significantly reduced or disappeared after adjustment for potential confounders (parity, maternal health profile, and socioeconomic and lifestyle factors), and are more evident with increasing age from ≥40 years old. Subsequent analyses in higher-income countries seem to confirm that delayed age at maternity is an independent obstetric, labour, and birth outcome risk factor,[10,11] although methodological disparities—specifically on the age groups compared and selection of confounders—make it difficult to draw strong conclusions.

Spain is currently one of the European countries with the highest mean age at first maternity.[12] Between 1996 and 2015 age at first maternity among Spanish national mothers increased from 29.23 to 32.21 years old, and mean age at maternity (all parities considered) increased from 30.03 to 33.30 years old (compiled by the authors from the Spanish Birth Statistical Bulletin), a trend strengthened during the current economic crisis beginning in 2007.[13] Simultaneously, throughout the decade prior to the economic crisis, Spain registered the greatest increase in LBW among the European countries in spite of the reduction in the prevalence of preterm births.[3] In this context, the aim of this study is to quantify the possible impact of delaying maternity on foetal growth (small for gestational age—SGA) in Spain during the period 2007–2015 by the assessment of adjusted partial population attributable fraction (PAF_p) for primipara and multipara mothers with advanced (35–39 years old) and high (≥40 years old) age at maternity considering previous evidences on the interaction between age at maternity and parity on birth outcome.[11]

2. Methods

Data analysed came from the Spanish birth certificate (Spanish Birth Statistical Bulletin, *Boletín Estadístico de Partos*), the compulsory civil registration of all births. Since 1996 the Spanish birth certificate includes the nationality of parents, and in the revised version of 2007 includes new variables of interest, including marital status, level of education of both parents, and type of delivery. Validation studies have concluded that data provided by the Spanish birth certificate are highly reliable when compared with hospital birth statistics.[14] The three main groups of immigrant mothers in Spain (Latin-American, North African, and Eastern European women) have very different lifestyles, cultural practices, nutritional behaviour and genetic heritage, showing different trends in reproductive profile and birth outcome compared with Spanish mothers.[15] As in other high income countries,[3] delayed maternity is associated in Spain with an increased access to ART and the consequent increase in multiple pregnancies, so that 70% of twin pregnancies are estimated to be due to fertility treatment.[16] Due to these reasons, analysis was restricted to Spanish women that delivered singleton live births (final sample n = 2,672,350, 64.9% of all births registered in the analysed period: Fig. 1).

SGA <3rd, 3rd–5th and 5th–10th percentiles were considered the dependent variables. Values of the three SGA categories have been established according to national birthweight charts by parity and type of delivery for the 2010–2014 period.[17] Age at maternity was considered the independent variable and categorised in six age groups: <20 years old, 20–24 years old, 25–29 years old, 30–34 years old, 35–39 years old, and ≥40 years old. Potential confounding variables included in the analysis were maternal education (primary education, secondary education, or university education), maternal occupation (professionals, administrative employees, service sector workers, primary sector workers, qualified workers, unskilled workers, students, or housewives), marital status (married, with stable partner, or with non-stable partner), residence of the mother (rural or urban residence), parity (primipara or multipara mothers), sex of the newborn, type of delivery (vaginal or CS delivery), and year of birth. Following descriptive analysis, adjusted PAF_p by parity and maternal age group on the three categories of SGA were calculated.

Firstly, interactions between pairs of potential confounders on birth outcome were checked by bivariate Poisson regressions. Interaction between age at maternity and parity on the three categories of SGA was confirmed. No other interactions between potential confounders on birth outcome were detected.

Secondly, to avoid unnecessary adjustment when performing multivariable analysis, bivariate Poisson regressions on each category of SGA have been carried out between age at maternity and the aforementioned maternal–foetal variables in order to identify the confounders of the effect of age at maternity on birth outcomes. Because the conventional change-in-estimate (CIE) criterion of 10% between unadjusted and adjusted relative risk (RR) has been questioned,[18] models established by this criterion were compared with those based on the z-score test, considering significant a change between unadjusted and adjusted regression coefficients [Ln(RR)] with a p-value <0.05. Goodness-of-fit of adjusted models was checked by the likelihood ratio test and accuracy was checked by analysing Area Under ROC Curve (AUC). Both for primipara and for multipara mothers CIE criterion based on p-value <0.05 yield models with the highest Log-Likelihood and accuracy. Maternal occupation, maternal education, marital status, gestational age, type of birth, parity and the interaction term

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