



ORIGINAL ARTICLE

Maternal factors associated with smoking during gestation and consequences in newborns: Results of an 18-year study

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ABSTRACT

Background: Tobacco use is one of the most important causes of obstetric and perinatal pathologies. Its frequency during pregnancy is high and could be related to various socioeconomic and cultural characteristics of the mothers.

Aim: The aim of this study is to determine the trend and prevalence of smoking in pregnant mothers in our area over the years and the socio-cultural or obstetric factors associated with smoking as well as the repercussions on the newborns related to its consumption.

Methods: Retrospective study of 18,959 mothers of healthy newborns in the maternity ward of the regional hospital during the years 2002–2019. The variable under study was maternal smoking during pregnancy compared with various maternal, obstetric, and perinatal factors.

Results: A mean percentage of 20.4% of the mothers smoked, with significantly decreasing percentages over the years. There was a significant association between smoking and mothers' age, origin, level of education, the occurrence of previous abortions, parity, type of breastfeeding at discharge, type of delivery, low birth weight, and need for neonatal resuscitation.

Conclusions: This defines a profile of pregnant smokers on whom it is important to act: young, Spanish, with a low level of education, multiparous, and with previous miscarriages. Its repercussions are also evident with a lower birth weight in newborns. Knowledge of these factors will make it possible to design more effective intervention strategies to reduce smoking during pregnancy.

Relevance for Patients: Any effort that reduces smoking habits can improve the health status of mothers and newborns and the first step is to know who are risk pregnant.

1. Introduction

The prevalence of smoking in Spanish women is 21.3%, and in the age range between 16 and 44 years, the period that includes the reproductive stage; it reaches 35.2%, rising to 42.7% if only those under 24 years of age are considered [1]. In Europe, the prevalence of smoking among women reached 26.16% in 2009. In Aragon, smoking has already exceeded 20% among women for more than 10 years. At present, 1 in 3 women in Spain smokes at the beginning of their pregnancy, a higher figure than in many European countries and even in the United States; of these, 25–50% stop smoking during pregnancy, and the majority restart smoking after giving birth. Low health risk perception and tobacco addiction may be the main factors maintaining this prevalence. Obstetric problems that have been associated with smoking include miscarriage, premature delivery, ectopic pregnancy, placenta previa or placental abruption, and premature rupture of membranes. There are many reported

effects on the fetus and newborn: prematurity, low birth weight and sudden infant death, among others [1-3].

Previous studies have shown that some characteristics of pregnant women influence smoking behavior; these include education levels, maternal parity, partner relationships, and smoking among partners or parents. In addition, Ooka *et al.* [2] found that certain regional characteristics, including regional socioeconomic status (SES) and ethnicity, are associated with maternal smoking behavior.

Although our study is retrospective and we only analyzed data collected during pregnancy and delivery, it is well known that there may be other implications of smoking during pregnancy. Monasso *et al.* [4] have even postulated alterations in DNA methylation that they demonstrated in a study carried out in Rotterdam and published in 2020, in which they analyzed the maternal smoking-related cytosine-phosphate-guanine sites; correlating by linear regression that there is a direct relationship between alterations in methylation in children exposed to tobacco during pregnancy, this being greater if it occurs in the third trimester. Another point studied by Chahal *et al.* [5] is immune development. In a study published in 2016, they measure the levels of interleukin (IL)-1 α , IL-1 receptor antagonist, IL-6, IL-8, C-reactive protein, tumor necrosis factor alpha, and immunoglobulins. In children of smoking mothers, they object to an increase in IL8 and elevated levels of IgG3 related to the possibility of developing atopic dermatitis and respiratory problems in the future.

Anderson *et al.* [6] take the database of the Centers for Disease Control and Prevention Birth Cohort Linked Birth/Infant Death Data Set during the years 2007–2011, the variables under study being death in children under 1 year of age and smoking mothers during the year. They conclude that there is a double risk of sudden death in children of smoking mothers (odds ratio [OR] 2.44; 95% confidence interval [CI]), decreasing the risk if the number of cigarettes is lower or if they do not smoke. These data support the need for intervention that would lead to a substantial reduction in sudden death.

Furthermore, Cabral *et al.* [7] evaluated 4295 children recruited between 2005 and 2006 and collected data during pregnancy that included smoking. At 4 years of age, they re-evaluated the children and found an increase in the z-score of systolic pressure in children of smoking mothers, although they did not find an alteration in diastolic pressure.

Another variable studied on numerous occasions is the risk of infant overweight associated with smoking during pregnancy. Chattrapiban *et al.* [8] analyzed 3241 children born to obese, smoking or smoking and obese mothers, obtaining results that indicate that those who are children of obese and smoking mothers do not present differences with respect to smokers or obese mothers, so it is likely that both are nullified factors, both being risk of low birth weight and obesity during childhood.

These data are also reflected by Smart *et al.* [9] who obtain an increased risk (OR 0.72) of childhood obesity if the mother has smoked during pregnancy.

Regarding mental health, an increased risk of developing mental disorders related to smoking has been observed.

One of the most studies is the increased risk of developing attention deficit hyperactivity disorder [10,11]. Although in some studies such as that of Gustavson *et al.* [11], it is difficult to rule out that there are other alterations during intrauterine development that may be associated.

In addition to the aforementioned, there are some studies that conclude that the risk of smoking during pregnancy may be related to malformations or alterations in development such as cryptorchidism [12], strabismus [13], or hypodontia [14].

The aim of this study is to find out the trend and prevalence of smoking in pregnant mothers in our environment over the years and the socio-cultural or obstetric factors associated with smoking as well as the repercussions on the healthy newborn related to its consumption. This will allow the design of more specific strategies aimed at a target population at risk in our community.

2. Materials and Methods

2.1. Materials

A retrospective study was conducted on a sample of 18,959 mothers of healthy newborns admitted to the maternity ward of our hospital during the years 2002–2019. The main variable under study was the smoking habit of the mother during pregnancy declared in the obstetric admission history (she was considered a smoker if she had consumed tobacco until the end of gestation, regardless of the amount). Data were obtained from the register of our hospital.

Inclusion criteria were mothers of all newborns admitted to the maternity ward of the center. Exclusion criteria were mothers without smoking information registered or with a newborn admitted to the neonatal unit or transferred to another center due to serious pathology.

The study has been approved by the Hospital's Ethics and Research Committee under Code 9/2019.

Table 1 shows the independent variables under study related to maternal, obstetric or neonatal factors.

The consumption of alcohol and other drugs was not recorded in an accessible file, so these items were not analyzed.

2.2. Methods

All data were managed with Excel (Microsoft) datasheet. Statistical analysis of the data was carried out using R software (version 4.0.2). First, a descriptive analysis of the study variables was done to determine the personal or obstetric characteristics of the mothers. Categorical variables were described by absolute frequencies and percentages. Quantitative variables were summarized by their mean, standard deviation and quartiles.

Next, to study the association of maternal, or obstetric characteristics with smoking during gestation, a bivariate analysis was performed. The association between categorical variables was assessed using Fisher's exact test (with Monte Carlo simulation of the *P*-value in the case of variables with more than two categories) and OR calculation.

In addition, a multiple logistic regression analysis was performed to assess maternal factors that may be related to gestational smoking. The response variable was smoking during

pregnancy (no, yes) and the following were considered as possible explanatory variables: age (<26 years, 26–34 years, 35 years or more), origin (native, foreign), level of education (no education or primary, medium, high), paid work (no, yes), parity (primiparous, multiparous), and previous abortions (no, yes). The model was constructed following a backward stepwise variable selection procedure based on the *P*-value criterion and considering a significance level of 0.05. This procedure begins fitting a model that contains all explanatory variables under consideration and then starts removing the least significant variables (with the highest *p*-value in the model), one after the other until the stopping rule is reached (all remaining variables in the model have a *P*-value smaller than 0.05). Furthermore, the forward and bidirectional selection procedure, and other criteria to add or subtract each variable in the model, such as Akaike Information Criterion and Bayesian Information Criterion [15], were also considered. All procedures and criteria led to the same model. Participants with missing data in the variables of the final regression model (6% of the total) were excluded from the analysis. Associations between the loss of data in the response variable (smoking during pregnancy) and the explanatory variables were studied. We did not find any relationship between the missingness of data in smoking and the maternal factors considered. The goodness of fit of the model was assessed using the Hosmer-Lemeshow test and by exploring the residuals (verifying that there were no observations with large residuals). The predictive ability of the model was assessed by calculating the area under the receiver operating characteristic curve (Area under curve [AUC]), sensitivity (Se), and specificity (Sp).

In all analyses, a statistically significant relationship between the variables was considered at a significance level of 0.05.

3. Results

3.1. Trend and prevalence of smoking in gestation

The average percentage of mothers smoking during the period 2002–2019 in our county is 20.4%. Figure 1 shows the annual evolution of the percentage of maternal smoking in each of the years of the study period. With some year on year variations, over time there has been a significant decrease ($P < 0.001$) in the number of mothers smoking, although over the last 9 years there has been a stabilization (Figure 1).

3.2. Analysis of the study variables

Tables 2-4 describe the personal and obstetric characteristics of the mothers and neonates.

Tables 5-7 show the relationship of gestational smoking to maternal, obstetric and neonatal factors.

A statistically significant association was observed between smoking during pregnancy and mothers' age, origin, educational level, previous abortion, parity, type of newborn feeding at discharge, type of delivery, neonatal low birth weight, and the need for neonatal resuscitation.

Given the precedents in the literature relating the influence of gestational age and smoking [1], in Figure 2, we show a box plot with the distribution of gestational age of mothers according to smoking during gestation. As can be seen, the distribution of gestational age is similar in the smoking and non-smoking mothers in our study.

Table 1. Independent variables under study

Maternal factors	
Parity (primiparous vs. multiparous)	
Maternal origin or provenance (native: from any part of Spain vs. foreign: immigrant)	
Maternal education (no education or primary, middle, high)	
Maternal employment status (paid work yes vs. no)	
Maternal age (categorized in quartiles: under 26 years, 26–34 years, 35 years and over)	
Previous abortions (yes vs. no)	
Feeding (breast: includes exclusive and mixed breastfeeding vs. bottle: formula-fed only)	
Obstetric factors	
Completion of labor (spontaneous delivery vs. cesarean section)	
Type of delivery (euthocic vs. dystocic)	
Presentation (cephalic vs. other)	
Multiple births (yes: twins or more vs. no: single new-born)	
Neonatal factors	
Gender (female vs. male)	
Gestational age (preterm: <37 weeks vs. term: ≥37 weeks)	
Low birth weight (<2500 g vs. ≥2500 g)	
Apgar at 1 min of life (≤5 vs. >5)	
Neonatal resuscitation (Yes: involving deep resuscitation vs. NO neonatal resuscitation or only shallow resuscitation including use of ambu with oxygen or brief positive pressure)	
Hearing screening result with otoacoustic-emission (normal/pass vs. impaired/fail)	

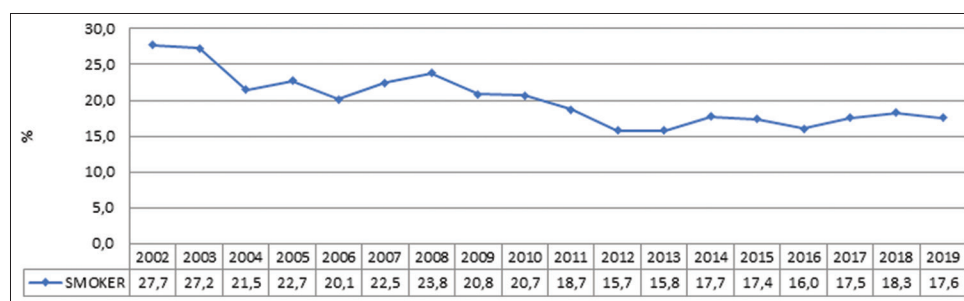


Figure 1. Percentage of mothers who smoke by year

Table 2. Maternal factors

	n=18959		
	n	%	Missing
Tobacco during pregnancy			
No	15031	79.64%	85 (0.45%)
Yes	3843	20.36%	
Age (years) “Quantitative”			
Mean/sd.			9 (0.05%)
30.17 (5.73)			
Median (1 st , 3 rd Q.)			
31 (26, 34)			
Age (years) “Categorical”			
<26	3980	21%	9 (0.05%)
26–34	10554	55.69%	
≥35	4416	23.3%	
Origin			
Native	12660	67.16%	109 (0.57%)
Foreign	6190	32.84%	
Studies			
Primary education	9770	53.98%	861 (4.54%)
Middle	4845	26.77%	
High	3483	19.25%	
Paid profession			
No	8119	44.11%	551 (2.91%)
Yes	10289	55.89%	
Previous abortion			
No	13000	68.76%	54 (0.28%)
Yes	5905	31.24%	
Parity			
Primiparity	6823	36.01%	14 (0.07%)
Multiparity	12122	63.99%	
Lactancy			
Bottle feeding	5630	29.74%	30 (0.16%)
Breastfeeding	13299	70.26%	

Table 3. Obstetric factors

	n=18959		
	n	%	Missing
Completion of childbirth			
Vaginal	13697	72.49	63 (0.33%)
Cesarean section	5199	27.51	
Type of delivery			
Eutocic	11369	60.11	46 (0.24%)
Dystocic	7544	39.89	
Presentation			
Cephalic	17807	94.28	72 (0.38%)
Other	1080	5.72	
Multiple births			
No	18442	97.42	28 (0.15%)
Yes	489	2.58	

Table 4. Neonatal factors

	n = 18959		
	n	%	Missing
Gender			
Female	9391	(49.6)	26 (0.14%)
Male	9542	(50.4)	
Gestational age			
<37 weeks	550	(3.08)	1086 (5.73%)
≥37 weeks	17323	(96.92)	
Weight<2500 g			
No	18257	(96.3)	
Yes	702	(3.7)	
Apgar 1 min			
≤5	177	(0.93)	
>5	18782	(99.07)	
Neonatal resuscitation			
No	16100	(87.74)	610 (3.22%)
Yes	2249	(12.26)	
Hearing screening			
Normal (Pass)	16841	(92.80)	813 (4.28%)
Altered (Fail)	1305	(7.20)	

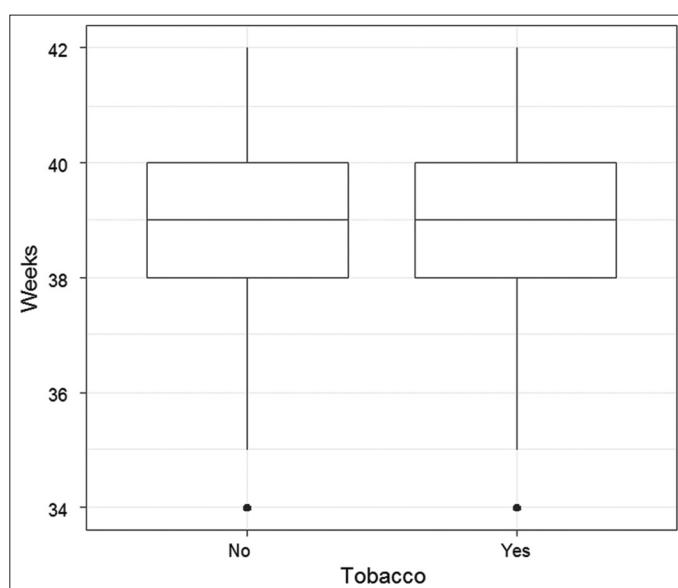


Figure 2. Box plot of the distribution of gestational age according to maternal smoking during gestation

We, therefore, did not observe an association between the incidence of late preterm birth (>34 weeks) and smoking, in the maternity ward, verifying the results shown in Table 7.

3.3. Maternal factors

- Paid profession: In our series, 55.9% of mothers were employed.

Table 5. Comparison of maternal factors according to gestational smoking

Smoking	Smoking during gestation		P-value/OR (IC 95%)
	No 15,031 (79.64%)	Yes 3843 (20.36%)	
Maternal factors	n/(%)	n/(%)	
Age (categorical)			<0.001*
<26 years	2975 (19.8)	984 (25.63)	-
26–34 years.	8438 (56.16)	2065 (53.79)	0.74 (0.679–0.807)
≥35 years.	3613 (24.04)	790 (20.58)	0.661 (0.595–0.735)
Origin			<0.001*
Native	9469 (63.34)	3131 (82.05)	-
Foreign	5480 (36.66)	685 (17.95)	0.378 (0.346–0.413)
Studies			<0.001*
No or Primary	7126 (49.8)	2602 (69.98)	-
Middle	3986 (27.86)	842 (22.65)	0.579 (0.53–0.631)
High	3196 (22.34)	274 (7.37)	0.235 (0.206–0.267)
Paid profession	n/(%)	n/(%)	0.052
No	6395 (43.75)	1696 (45.52)	-
Yes	8223 (56.25)	2030 (54.48)	0.931 (0.866–1.001)
Previous abortion			<0.001*
No	10507 (70.1)	2433 (63.48)	-
Yes	4481 (29.9)	1400 (36.52)	1.349 (1.252–1.453)
Parity			<0.001*
Primiparity	5506 (36.65)	1287 (33.53)	-
Multiparity	9516 (63.35)	2551 (66.47)	1.147 (1.064–1.236)
Lactancy			<0.001*
Bottle feeding	3909 (26.04)	1692 (44.12)	-
Breast feeding	11100 (73.96)	2143 (55.88)	0.446 (0.414–0.48)

Table 6. Comparison of maternal obstetric factors according to gestational smoking

Smoking	Smoking during gestation		P-value/OR (IC 95%)
	No 15,031 (79.64%)	Yes 3843 (20.36%)	
Obstetric factors	n/(%)	n/(%)	
Completion of childbirth			0.952
Vaginal	10852 (72.45)	2780 (72.51)	-
Cesarean section	4126 (27.55)	1054 (27.49)	0.997 (0.921–1.079)
Type of delivery			0.040*
Eutocic	8955 (59.72)	2359 (61.54)	-
Dystocic	6040 (40.28)	1474 (38.46)	0.926 (0.861–0.996)
Presentation			0.507
Cephalic	14119 (94.23)	3609 (94.53)	-
Other	865 (5.77)	209 (5.47)	0.946 (0.808–1.103)
Multiple births			0.007*
No	14595 (97.25)	3764 (98.02)	-
Yes	412 (2.75)	76 (1.98)	0.717 (0.555–0.912)

A percentage of 54.5% of mothers who smoke do paid work versus 56.2% of mothers who do not smoke. The relationship is not statistically significant.

- Education: In our series, 45% of mothers had completed secondary or higher education.

A percentage of 70% of mothers who smoke have no education or have primary education versus 50% of mothers who do not smoke who

have no education or have primary education. A high education was registered in 7.4% of mothers who smoke versus 22.3% of mothers who do not smoke. The odds in favor of smoking are multiplied by 1.7 (=1/0.579) for mothers with no or primary education compared to mothers with medium education. The odds in favor of smoking are 4 (=1/0.235) times higher in mothers with no education or primary education compared to mothers with high education.

- Origin: In our series, 32.8% of mothers have an immigrant background.

A percentage of 82% of smoking mothers are native vs. 63% of native mothers in the non-smoking group. The odds in favor of smoking are 2.5 (=1/0.378) times higher in native mothers compared to foreign mothers.

- Multiparity: In our series, 64% of women are multiparous.

There is a higher percentage of multiparous mothers in the smoking group. The odds in favor of smoking are multiplied by 1.15 in multiparous mothers compared to primiparous mothers. However, this relationship is no longer significant in the regression model when all other maternal factors are considered. This may be related to the number of previous abortions among other reasons.

- Previous abortions: In our series, 31.2% of women had previous abortions.

There is a significantly higher incidence of miscarriage among mothers who smoke ($p < 0.0001$ and OR 1.35).

- Age: 55.69% were aged between 26 and 34.

Smoking mothers are significantly younger ($P < 0.0001$ with progressively higher ORs the younger they are). The odds in favor of smoking increase by 35% (multiplied by 1.35 = 1/0.74) in mothers aged <26 years compared to mothers aged 26–34 years. The odds in favor of smoking increase by approximately 50% (multiplied by 1.51 = 1/0.66) in mothers aged <26 years compared to mothers aged 35 years and older.

- Breastfeeding (BF): In our series, 70.3% of mothers chose to breastfeed.

Smoking mothers choose not to breastfeed significantly more often than non-smoking mothers ($P < 0.0001$) and the odds in favor of BF are approximately twice (1/0.446) higher in non-smoking mothers compared to smoking mothers.

In view of all these results, it was decided to analyse the interrelationship between these factors. Table 8 shows the results of the multiple logistic regression model fitted to assess the factors that may explain or influence smoking during gestation. The explanatory variables considered in the model were all those related

Table 7. Comparison of neonatal factors according to gestational smoking

Smoking	Smoking during gestation		P-value/OR (IC 95%)
	No 15031 (79.64%)	Yes 3843 (20.36%)	
Neonatal factors	n/(%)	n/(%)	
Gender			0.600
Female	7433 (49.52%)	1919 (50%)	-
Male	7577 (50.48%)	1919 (50%)	0.981 (0.914–1.053)
Gestational age			0.115
<37 weeks	425 (2.98%)	124 (3.5%)	-
≥37 weeks	13,830 (97.02%)	3422 (96.5%)	0.847 (0.693–1.043)
Weight<2500 grams			< 0.001*
No	14,575 (96.97%)	3598 (93.62%)	-
Yes	456 (3.03%)	245 (6.38%)	2.177 (1.854–2.551)
Apgar 1 min			0.398
≤5	145 (0.96%)	31 (0.81%)	-
>5	14,886 (99.04%)	3812 (99.19%)	1.193 (0.82–1.793)
Neonatal resuscitation			0.001*
No	12,696 (87.34%)	3335 (89.36%)	-
Yes	1841 (12.66%)	397 (10.64%)	0.821 (0.731–0.920)
Hearing screening			0.153
Normal (Pass)	13,368 (93.0%)	3403 (92.30%)	-
Altered (Fail)	1012 (7.0%)	285 (7.70%)	1.107 (0.964–1.267)

* $P < 0.05$

Table 8. Results of the multiple logistic regression model to analyse maternal factors that may be related to smoking during pregnancy

Variables	Estimated coefficients (IC 95%)	Standard error	P-value	Odds ratio (IC 95%)
(Intercept)	-0.594 (-0.682–-0.507)	0.045	<0.001*	0.552 (0.506–0.602)
Age: 26–34	-0.261 (-0.357–-0.165)	0.049	<0.001*	0.770 (0.700–0.848)
Age: ≥35	-0.404 (-0.522–-0.287)	0.060	<0.001*	0.668 (0.594–0.750)
Origin: Foreign	-1.208 (-1.305–-1.112)	0.049	<0.001*	0.299 (0.271–0.329)
Studies: Middle	-0.532 (-0.622–-0.442)	0.046	<0.001*	0.588 (0.537–0.643)
Studies: High	-1.505 (-1.643–-1.371)	0.069	<0.001*	0.222 (0.193–0.254)
Previous abortion: Yes	0.389 (0.309–0.469)	0.041	<0.001*	1.476 (1.362–1.599)

$P < 0.05$, Area Under Curve: 0.696, Sensibility: 0.661, Specificity: 0.652

to maternal characteristics. Variables related to birth or neonatal characteristics were not considered as explanatory variables for gestational smoking, as they would be its consequence rather than its cause.

Based on the results obtained, we can conclude that:

The likelihood of smoking during pregnancy is significantly lower in mothers aged 26 years or older compared to those under 26 years.

The likelihood of smoking during pregnancy is significantly lower in foreign mothers compared to native mothers.

The likelihood of smoking during pregnancy is significantly lower in mothers with intermediate and higher education compared to those with no or primary education.

The likelihood of smoking during pregnancy is significantly higher in mothers who have had previous abortions compared to those who have not had abortions.

Specifically, of all the characteristics of the mothers, the only ones that are not significantly associated with smoking during pregnancy, in the presence of the others, are employment status and parity. Based on the results of the model constructed, the profile of pregnant smokers could be established (with no or primary education, native women, with previous abortions and under 26 years of age).

3.4. Obstetric factors

- Type of delivery: In our series, 72.49% of mothers had a spontaneous delivery.

There is no significant difference ($P = 0.952$) comparing spontaneous versus other types of birth.

- Presentation: In our series, 94.3% of neonates had a cephalic presentation.

There are no significant differences ($P = 0.507$) comparing cephalic presentation versus other presentations.

- Completion: In our series, 27.5% of mothers completed delivery by cesarean section.

There is no significant difference ($P = 0.952$) comparing vaginal and cesarean delivery.

- Multiple births: In our series, 2.6% of mothers had multiple births.

There is a significantly lower incidence of multiple births in mothers who smoke ($P = 0.008$, OR 0.72).

3.5. Neonatal factors

- Birth weight: In our series, 3.7% of neonates weighed <2500 g.

There is a significant relationship between mothers who smoke and a higher incidence of low birth weight (<2500 g) with a $P < 0.0001$ and OR: 2.18.

- Gestational age: In our series, 3% of neonates were <37 weeks gestational age.

There is no significant relationship between mothers who smoke and late preterm (34–37 weeks) infants admitted to the maternity ward with $P = 0.115$.

- Resuscitation: In our series, 12.26% of neonates required non-superficial resuscitation.

There is a significant association between smoking during gestation and reduced need for neonatal resuscitation with $P < 0.001$.

- Apgar at 1 min <5: In our series, 0.9% of newborns had this. There is no significant relationship between smoking mothers and Apgar at a minute <5 with $P = 0.39$.

- Otoemissions at discharge from maternity: 7.2% of neonates had impaired otoemissions screening at discharge.

There is no significant relationship between smoking mothers and the otoemission result at discharge with $P = 0.153$.

- Gender: In our series, 50.4% of neonates were male.

There is no significant relationship between smoking mothers and the gender of the newborn with $P = 0.60$.

Specifically, after studying the association between smoking during gestation and newborn characteristics, a significant association was observed between smoking during gestation, low birth weight of the newborn and reduced need for resuscitation.

4. Discussion

4.1. Trend and prevalence of smoking in gestation

With some unexplained year on year variations that can be related to some different educational campaigns in years 2004–2006, over time there has been a significant decrease ($P < 0.001$) in the number of pregnant smokers from 27% to 17%, although the last 9 years there has been a stabilization (Figure 1).

The high percentage at the beginning of the study is consistent with previous studies [3] where they conclude that, in the study years (1995–2002), 30.31% of mothers smoked during pregnancy, with variations among different ethnic groups. A secular increase in the prevalence of maternal smoking is observed between 1978 and 1991, stabilizing thereafter at 27 and 28%. No secular decline is observed in the analyses by maternal age, number, and region. Only mothers with higher levels of schooling show a decline in smoking in 1993, stabilizing at around 23%.

In other studies [16], in Aragón, one in three women smokes at the beginning of pregnancy; of these, 25–50% stop smoking during pregnancy and most resume smoking after childbirth. In the most recent CALINA study, the prevalence of smoking during pregnancy was 19.6%, and although it is high, it is similar to other Spanish studies and higher than in international studies, such as those carried out in North America, in which 26% of women smokers abstain from smoking during pregnancy and only 10.7% of pregnancies maintain consumption [1].

Other studies [17] show that 28.3% of women of childbearing age in Spain smoke daily, while in Andalusia the figure exceeds 35%. With regards to pregnant women, various European publications place the prevalence of smoking at around 20%. Epidemiological data on gestational consumption at the national level show great variability between autonomous communities, ranging from 19% to 34%.

These data confirm the importance of the problem despite the many institutional campaigns that are carried out, and it may be more useful to focus efforts on risk profiles.

4.2. Factors assessed

4.2.1. Maternal factors

- Maternal work: There is a similar percentage of mothers with a paid profession in the smoking and non-smoking group.

This is inconsistent with other studies such as that of Ooka [2] where the unemployment rate was significantly associated with maternal smoking (OR: 1.41, 95% CI: 1.102–1.805). In this study, the unemployment rate and Financial Strength Index (FSI) were considered as regional factors related to economic status, and the only unemployment rate was significantly associated with maternal smoking. The FSI indicates the wealth of the municipality itself, and the affluence of the municipality does not mean the wealth of local residents, while high unemployment rates are apparently related to worse economic conditions. The unemployment rate is also known to be related to difficulty in quitting smoking.

In our case, we did not differentiate between housewives and unemployed women, so perhaps we cannot relate work and SES so directly and this could explain our results.

- Education: There is a higher percentage of mothers with no education or primary education in the group of smokers than in the group of non-smokers.

These results are consistent with Rygh *et al.* [18] who conclude that higher education was a powerful predictor of smoking cessation. Furthermore, Mateos *et al.* [17], after multivariate analysis, concluded that one of the factors associated with gestational smoking was lower educational level (no education and first grade compared to university women (OR: 1.98; CI: 1.22–3.22).

Factors such as level of addiction, low-risk perception or low educational level have also been associated with continued smoking during pregnancy and BF [16].

- Origin: There is a higher percentage of native mothers in the group of smokers than in the group of non-smokers.

The prevalence of smoking during pregnancy is higher among mothers of Spanish origin (21.9%) than among immigrant mothers (8.7%). Furthermore, in the CALINA study [19], when subdivided by nationality, the prevalence increases to 23% in the Spanish group. Other studies also conclude that foreign mothers smoke less than Spanish mothers [1].

Given the growing immigrant population in Spain, previous studies [19] analyzed smoking among different ethnic groups in Spain. The results showed that the proportion of women who smoked during pregnancy in these groups was 27.61% (7600/27530) in white, 18.69% (20/107) in black, 20.00% (2/10) in eastern, 20.99% (110/524) in gypsy, and 17.92% (50/279) in the rest of the groups. The differences between all of them were statistically significant ($P < 0.00001$).

These results could be related to other modifying factors such as economic status and also to the type of BF (immigrant mothers breastfeed more often).

- Multiparity: There is a higher percentage of multiparous women in the smoking group than in the non-smoking group. Although, the relationship is not significant in the regression

analysis. This is in line with the results of Ooka *et al.* [2] where mothers with 4 or more children smoked more prevalently.

This may also be related to the number of miscarriages among other reasons. Another option is that they may be more careful with the first pregnancy than with subsequent pregnancies. For example, Rygh *et al.* [18] conclude that, in their study, a strong predictor of smoking cessation, both with respect to snus (snuff) use and smoking, was true for women who gave birth to their first baby compared to those with previous parity and this is consistent with the results of a previous US study on smoking during pregnancy.

- Previous abortions: There is a higher percentage of mothers with previous abortions in the smoking group than in the non-smoking group.

Women smokers are up to 33% more likely to have a miscarriage and suffer significantly elevated risks of various obstetric complications. For smokers, the rate of intrauterine fetal death increases by 23% and the overall risk of giving birth to a child with a congenital malformation increases by 13%. Babies born to smokers are more likely to be small for gestational age (SGA) and suffer from intrauterine growth restriction, as well as to be born before term, which means a higher likelihood of stillbirth [20].

- Age: Smoking mothers are significantly younger ($P < 0.0001$) and ORs are progressively higher the younger they are.

In the study by Mateos *et al.* [17] after multiple regression, one of the factors associated with gestational smoking in the model was being younger (OR: 0.956; CI: 0.92–0.99), and also Ooka [2] showed that the characteristics of individual pregnant women that were significantly associated with smoking were the birth of the third child or more, age at birth of 24 years or less, and birth weight of the new-born of <2500 g. Furthermore, in the study by Frías [3] mothers under 25 years of age were the most likely to smoke in all years of the study.

On the other hand, Marino *et al.* [21] report that adolescent mothers have a greater risk of drug abuse, growing up in the family of unstructured families, risk of social exclusion and greater risk of smoking with the consequences that this entails. This points to a well-defined group of pregnant women to target, probably related to the low-risk perception and psychology associated with young mothers.

- BF: There is a higher percentage of mothers choosing BF in the non-smoking group compared to the smoking group.

As expected from other studies, smoking was shown to be unfavorable for both initiation and maintenance of BF [22]. Given the known detrimental effects of smoking on health, it is likely that some mothers who smoke may choose bottle-feeding rather than initiate BF, not adequately weighing the benefit-risk ratio of opting for BF despite not quitting smoking [10].

Furthermore, the Malama study [24] concludes that the Relative Risk (RR) for BF was being a smoking mother with a figure of 1.89. In addition, maternal smoking was found to decrease the duration of BF, as has been shown in previous work. In addition, a dose-dependent effect on the duration of BF was observed for relatively small exposures to tobacco. Although the

pathophysiological mechanism is not clearly established, it has been suggested that nicotine decreases prolactin production.

Other studies also conclude this difference, such as that of Cuadron [16] and also that of Oves [19] who observed in both the group of mothers of Spanish origin and immigrant mothers, that maintenance of BF at 4 months of age was more frequent in those mothers who did not smoke ($P = 0.001$).

Another national study by Rius [22] also concludes that being a smoking mother, despite quitting smoking during pregnancy, is associated with an increased risk of early cessation of BF (OR 1.70; 95% CI 1.15–2.49). This risk does not change even if smoking continues during pregnancy (OR 1.71; 95% CI 1.26–2.32).

Biosca *et al.* [25] in the Calina cooperative group also confirm that smoking during gestation is one of the maternal factors significantly associated with a lower likelihood of BF (RR 0.53; 95% CI 0.37–0.77).

This is also supported by other European studies, such as that of Simpson *et al.* [26] in Great Britain where smoking clearly demonstrated a negative effect on the decision to initiate BF.

And articles such as Ramiro *et al.* [27] and Lechosa [28] agree with ours in that maternal smoking habits are considered a high impact factor on BF: non-smoking versus smoking (RR = 1.76 [95% CI 1.59–1.95]). In the group of women who smoked, the probability of formula feeding was increased 2.32-fold ([95% CI 1.50–3.58] $P < 0.001$). When stratified by smoking into light, moderate and severe, they found a statistically significant dose-response pattern.

The explanation for this is complex and Chimoriya *et al.* [29] comment that since women who smoke are less likely to breastfeed, rather than a physiological effect, the negative association between smoking and BF duration could be attributed to psychosocial factors. These social and behavioral factors among women who smoke include lower motivation to breastfeed, a belief that smoking is a barrier to BF, and a reduced ability to seek help with BF difficulties. In addition, due to a clustering of unhealthy lifestyle practices among women from lower socio-economic groups, they may be less inclined to breastfeed. Therefore, it is vital to educate all pregnant mothers about the harmful effect of smoking on BF practices and therefore in the health status of newborn and it is very important to reinforce and explain the benefits of BF in pregnant mothers to change smoking habits.

4.2.2. Obstetric factors

There are studies that support the idea that smoking leads to obstetric problems such as one from Shobeiri *et al.* [30] who, in two different meta-analyses, found that women who smoked during pregnancy were more likely to experience placental abruption (OR: 1.80, [95% CI: 1.75, 1.85] and RR ratio RR: 1.65; [95% CI: 1.51–1.80]) and placenta previa (OR 1.42; [95% CI: 1.30–1.54] and RR 1.27; [95% CI: 1.18–1.35]) compared to women who did not smoke during pregnancy. Both situations lead to frequent preterm births and thus to an increase in perinatal death and low birth weight.

In our study, we found that:

- The presentation had no significant differences ($P < 0.507$)

comparing cephalic presentation versus other presentations.

- The completion of childbirth had no significant difference ($P < 0.952$) comparing vaginal and cesarean delivery.
- In the type of delivery: There are significantly more eutocic deliveries in mothers who smoke, although at low risk ($P < 0.04$, OR 1.08). We have no explanation for this item and more studies are needed.
- In Multiple births: there is a significantly lower incidence of multiple births in mothers who smoke ($P < 0.007$, OR 1.28), perhaps due to lower fertility or more miscarriages, and this may also condition the higher probability of eutocic delivery mentioned above, given that many multiple births end in cesarean section.
- C.-Neonatal factors:
- Birth weight: There is a highly significant association between mothers who smoke and a higher incidence of low birth weight (<2500 g) with a $P < 0.0001$ and OR: 2.18.

This would be consistent with the CALINA study [19] where they conclude that no smoking is one of the most important environmental factors in preventing low birth weight. Both in our study and in the CALINA group, smoking is significantly more common among mothers in the SGA group of newborns. Smoking during pregnancy is associated with a considerable reduction in birth weight in different geographic areas, with the range of weight reduction ranging from 77.7 to 232.7 g. In the CALINA study [19], the difference was 140 g more in infants not exposed to smoking. It is known that for every 10 cigarettes smoked daily by a pregnant woman; the infant will weigh approximately 100 g less at birth than would have been expected.

One of the main results of the present study is that the risk of having a newborn with a low birth weight <2500 g if the mother smoked during pregnancy is more than double that if she did not smoke, which implies associated morbidity. The number of newborns with low birth weight for their gestational age in the group of mothers who smoke coincides with that described in the literature [1].

Also Biosca [25] concludes something similar since mothers of SGAs newborns smoked more during gestation (32.3 vs. 18.5%; $P = 0.003$) RR = 1.92; (95% CI: 1.31–3.02). Rygh *et al.* [18] also demonstrate the same with their results showing that the mean birth weight of children born to mothers who had been daily or occasional smokers during the third trimester ($n = 506$) was 3278 g (CI; 3229–3328, $P < 0.001$), with a statistically significant reduction of 246 g in birth weight.

This low birth weight already occurs in utero as Mund *et al.* [23] comment in their article since intrauterine growth retardation of the fetus is the most important smoking-induced pathology. Two studies from 1999 and 2006 associated maternal smoking with a dose-dependent increased risk of not only adverse birth outcomes, such as SGA and intrauterine growth restriction but also preterm birth with an adjusted OR 1.42; (95% CI: 1.27–1.59) for both male and female babies. These findings are supported by numerous studies, which concluded that children born to mothers who had smoked during pregnancy had significantly lower birth weights compared to children of non-smokers such as a Brazilian

study cited in that article on newborns exposed to tobacco smoke during pregnancy that showed an average decrease in birth weight of 223.4 g (95% CI 156.7–290.0).

Not only maternal smoking plays a role, but also passive smoking. Another study by Alonso [31] found that the OR for low birth weight in the group of mothers who smoked was 1.42 (95% CI: 1.01–1.985) and in the group of those whose partner smoked it was 1.37 (95% CI: 1.014–1.863). And Ribot *et al.* [32] demonstrated that it can be observed that women exposed to tobacco have children with significantly lower birth weights than non-smokers. Specifically, about 114–129 g less (95% CI 0.3–243.4) in the active smoking group and about 160–178 g less (95% CI 0.5–338.2) in the passive smoking group.

- Gestational age: There is no significant relationship between mothers who smoke and late preterm (>34 weeks) infants admitted to the maternity ward with $P = 0.91$.

This may be because we only analyzed late preterm births (range 34–37 weeks), which are common in the hospital maternity ward, and therefore may not be in agreement with some publications such as Ribot *et al.* [32] who conclude that active and passive smokers have a higher risk of preterm birth than non-smokers (OR: 6.5, [95% CI: 1.4–30.8] and OR: 6.2 [95% CI 1.0–38.9]), respectively. In addition, the offspring of passive smokers had significantly lower gestational age (38.1 weeks) compared to non-smokers and quitters (39.1 and 39.4 weeks, respectively), and also lower birth weight (2,927.5 g) than non-smokers and quitters (3,251.1 and 3,276.7 g, respectively). This may also underlie a recent review by Gould *et al.* [33] that concludes that tobacco exposure during pregnancy has been consistently reported to result in low birth weight and preterm newborns. In fact, tobacco smoking during pregnancy may increase the odds of low birth weight by 200% (OR = 2.00, 95% CI: 1.77–2.26) often associated with lower gestational age.

Our results may indicate that beyond a certain gestational point (34 weeks) the influence of smoking on gestational length is less intense, although not negligible in other areas such as newborn weight.

- Resuscitation: There is a significant association between reduced need for neonatal resuscitation and maternal smoking during gestation.

We have not found any literature on the subject and this is an item to be corroborated in subsequent studies as it is not to be expected. The only thing that could justify this result is the fact that smoking mothers have fewer multiple births (which are more likely to be resuscitated) and more eutocic births (which are less likely to be resuscitated) since we found no differences in the other obstetric factors.

- Apgar at 1 min <5: There is no significant relationship between smoking mothers and Apgar at 1 min <5 with $P = 0.39$.

These studies are consistent with Rygh *et al.* [18] where smoking during pregnancy was associated with a reduction in mean birth weight, but with no significant effect on Apgar scores. There were no statistically or clinically significant differences in Apgar scores in infants born to mothers who had used snus (snuff) or smoked cigarettes during pregnancy compared to non-smokers.

- Oto-emissions at maternity discharge: There is no significant relationship between smoking mothers and oto-emissions outcome at maternity discharge with $P = 0.494$.

The relationship between smoking and otoemissions is based on the pathophysiological effects of smoking that have been shown to cause vascular injury and changes in some blood characteristics, leading to hypoxia-induced injury of various tissues, including the auditory organ. The effect appears to be related to cochlear damage [34] because nicotine administration induced damage to outer hair cells (OHC) that were distorted in shape with vacuolated cytoplasm and heterochromatic nuclei. Topography revealed damage to the stereocilia including disorganization, folding and laxity or complete loss and expansion of the surrounding supporting cells. These changes were most pronounced in the basal gyrus of the cochlea. Therefore, nicotine has been shown to be harmful to the cells of the cochlea, particularly the OHC of the basal gyrus, and this is very important because normal otoacoustic emissions depend on the activity of the OHC.

Some other studies [35–38] confirm this effect and have suggested that smoking and/or tobacco use may result in a reduced response to otoacoustic emissions (TEOAE).

Korres [37] also concluded that, in utero, exposure to smoking appears to have an impact on OHC. These effects appear to be equally true for all exposed newborns, regardless of the degree of exposure. According to the results of this study, smoking during pregnancy appears to influence the fetal cochlea, although the effects detected on OHC were small. Adverse effects of smoking on OHC were measured as significantly lower mean TEOAE responses in some frequencies in exposed compared to unexposed infants. Frequency analysis revealed significantly lower TEOAE amplitudes at 4000 Hz. This adverse effect of smoking appears to be equally true for infants with low and high exposure and not as dose-related as would be expected, since, when comparing subgroups with low, moderate and high exposure to each other, Korres found no significant differences, neither in mean TEOAE responses across frequencies nor at the mean amplitudes of the frequencies tested.

In addition, Vinay [39] found that TEOAE amplitudes were significantly reduced in smokers compared to non-smokers. The results found a significant effect of age on the amplitude of efferent suppression in smokers; however, no significant effect was found in the non-smoking group.

In children, there are some studies with similar conclusions to ours, such as Butcher's study [40] on risk factors for permanent childhood hearing loss in a large series of 19,504 children with no hearing risk, who concluded that there is no association between the maternal record of smoking before or during pregnancy and hearing loss, OR: 0.57 (0.23–1.42).

To the best of our knowledge, there are very few studies similar to ours in newborns, but there is one by Seçen [41] in 919 mothers that are also consistent with our results because it showed no differences between smoking and non-smoking mothers in the results of newborn otoacoustic emission tests.

- - Gender: There is no significant relationship between smoking mothers and the sex of the newborn with $P = 0.98$.

We found no studies about this item and it seems that tobacco use did not affect the gender of newborns. More studies are needed.

4.3. Limitations

Our research has limitations, which we must acknowledge:

The sample includes only mothers of healthy new-borns admitted to the maternity ward between 34 and 42 weeks of gestational age and this may interfere with some of the variables studied, since no mothers of infants with severe pathology or very preterm babies were included, but perhaps this is also an advantage given that the group studied is very homogeneous for the study of the factors included and does not present added confounding factors.

The amount of tobacco consumed has not been collected and this could be important in the severity of the factors analyzed.

The collection of smoking history was by a voluntary declaration of the mother and no chemical analysis of nicotine derivatives was done to check the veracity of the declaration which could underestimate the proportion of smokers in the sample, but previous studies [17] show that taking cotinine as the gold standard, the prevalence of smoking was 21.6%, similar to that derived from self-reported smoking (20.3%). This was also reported in another study from Sweden where there was a high agreement between cotinine levels and medical birth register smoking data ($\kappa = 0.82$) and a high correlation between cotinine levels in maternal and umbilical cord serum ($r_s = 0.90$, $P < 0.001$). Of the self-reported nonsmokers, 95% (95% CI: 89–97%) were classified as nonsmokers after cotinine measurements. This indicates that birth register data on pregnancy smoking in Sweden could be considered a valid measure [42].

The data collection was carried out over 18 years with evident socioeconomic and health variations, and for this reason, the sample may appear to be inhomogeneous, but the sample consistency studies are adequate to be representative.

Despite the large number of variables included in the analysis, there may be other influential factors on the studied event that have not been analyzed in our study. For example, there are studies [3] that show that mothers who used drugs also were smokers and drank alcoholic beverages. These results show a close relationship between smoking and the consumption of alcohol and other drugs that could in turn influence the obstetric or neonatal factors studied but do not modify the risk profile of the pregnant mothers.

Only future similar publications with new hypotheses will provide more evidence in this respect.

Another question is that our records did not collect the data about e-cigarette use. A study from Regan [43] concluded that although only 1% of adults used e-cigarettes during pregnancy, among those that use e-cigarettes during pregnancy, e-cigarettes were frequently used daily (44%) and concurrently with combustible cigarettes during pregnancy (64%). The majority of respondents who used e-cigarettes during pregnancy reported previous combustible cigarette smoking during the 3 months before becoming pregnant. Previous studies suggest that pregnant individuals may be vulnerable to messages that present e-cigarettes

as healthy alternatives to cigarette smoking, and it is possible that pregnant individuals engage in e-cigarette use during pregnancy as a means of quitting or curbing combustible cigarette smoking.

One more limitation is that this study refers to our population and may be generalizable for our country and similar ones but not for all world.

5. Conclusions

The number of smoking mothers has decreased over the years studied, reflecting better general information on the toxic effects of tobacco, but approximately 17% of mothers continue to smoke during gestation at a steady rate for the past 9 years, which demonstrates the need to adopt complementary measures to achieve a greater reduction in consumption. These complementary measures should preferably be implemented in the differential profile of pregnant women who smoke: young, Spanish, with a low level of education, multiparous and with previous abortions, which makes it possible to distinguish a group of pregnant women on whom it is important to act in prenatal education and follow-up by obstetricians to promote not smoking during pregnancy, either actively or passively, with comprehensive explanations of its negative effects on the mother and fetus and taking advantage of the fact that at the individual level, motivations for smoking cessation included the fact of being pregnant, risks associated with the infant's health, and desire to breastfeed [44].

This study has shown clear effects on intrauterine growth that are reflected in the risk of having a low birth weight baby more than twice in smoking mothers.

The institutions responsible for health should also increase their preventive actions, with early intervention measures for future mothers who, possibly due to their low perception of risk as showed in Jaber's study [45] where more than 35% of participants agreed that smoking a few cigarettes during pregnancy was safe for them and their baby, and therefore continue to smoke during pregnancy, causing a short- and long-term decline in the health of their future children. To this end, it is interesting to inform mothers and women of childbearing age from the school stage onwards, highlighting the effects that smoking has on pregnancy (e.g., increased chance of miscarriage) and on the new-born (increased chance of not being breastfed and therefore losing in health status, and also having a lower birth weight) and also by strengthening altruistic maternal-fetal attachment that may constitute a promising novel approach for interventions aiming at promoting smoking cessation during pregnancy because it associates with an increased probability of smoking cessation during pregnancy [46].

Knowledge of the results of this study will allow the design of intervention strategies, by and for pregnant women smokers, to reduce smoking following the recommendations of USPSTF that concluded with high certainty that the net benefit of behavioral interventions for tobacco smoking cessation on perinatal outcomes and smoking cessation in pregnant persons is substantial [47]. Effects are already published and, for example, the results show that over a 20-year period, during which Brazil implemented numerous effective tobacco control measures, the country

experienced a dramatic decrease in both maternal smoking prevalence and smoking-attributable adverse maternal and child health (MCH) outcomes. Countries that implement effective tobacco control measures can expect to reduce both maternal smoking and adverse MCH outcomes, thereby improving public health [48].

Our study and those mentioned during its review show that it is necessary to make the population aware, especially pregnant women and those of reproductive age, of the importance of quitting smoking due to the probable implication that it may have in the development of the fetus.

Lumley *et al.* [49] and Chamberlain *et al.* [50] conclude that within health promotion the intervention that obtains the most results is psychological counseling carried out in maternity units.

This convinces us of the importance of initiating these measures in our own environment.

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Conflict of interest

The authors declare no conflict of interest.

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