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Advanced Maternal Age and Nicotine Consumption during Pregnancy: Additive Effects on Newborn Parameters

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Abstract

Background Nicotine consumption during pregnancy and advanced maternal age are well known independent risk factors for poor pregnancy outcome and therefore serious public health problems.

Objectives Considering the ongoing trend of delaying childbirth in our society, this study investigates potential additive effects of nicotine consumption during pregnancy and advanced maternal age on foetal growth.

Sample and Methods In a medical record-based study, we analysed the impact of maternal age and smoking behaviour before and during pregnancy on newborn size among 4142 singleton births that took place in Vienna, Austria between 1990 and 1995.

Results Birth weight (H=82.176, p<0.001), birth length (H=91.525, p<0.001) and head circumference (H=42.097, p<0.001) differed significantly according to maternal smoking behaviour. For birth weight, the adjusted mean differences between smokers and non-smokers increased from 101.8g for the < 18-year-old mothers to 254.8g for >35 year olds, with the respective values for birth length being 0.6 cm to 0.7cm, for head circumference from 0.3 cm to 0.6 cm.

Conclusion Increasing maternal age amplified the negative effects of smoking during pregnancy on newborn parameters. Our findings identify older smoking mothers as a high-risk group which should be of special interest for public health systems.

Take home message Nicotine consumption during pregnancy and advanced maternal age have an additive negative effect on foetal growth. Smoking pregnant women older than 35 years are a high-risk group which is of special importance for public health programmes.

Introduction

For more than four decades, most high-income countries have been confronted with a remarkable demographic change in childbearing patterns. Starting in the early 1960s the trend has been to delay first child-birth (Wilkie 1981; Huang et al. 2008). This trend was caused by the introduction of effective contraceptives, marked changes in female role models, such as the women's liberation movement, prolonged phases of education and newly defined career goals. Consequently, pregnancy at advanced maternal age has become increasingly common, primarily in developed but also in some developing countries (Huang et al. 2008). In most high-income countries, the proportion of women who gave first birth at the age of 35 years or older increased significantly. In the United States, this proportion increased nearly eight times between 1970 and 2006 (Kenny et al. 2013). Similar trends are reported for Sweden (Jacobsson et al. 2004), the United Kingdom (Fitzpatrick et al. 2017), Poland (Radoń-Pokracka et al. 2019), Japan (Ogawa et al. 2017), China (Shan et al. 2018) and many other developed countries. Between 1970 and 2000, the mean maternal age at first birth increased from 24.4 to 28.5 years in Sweden, from 21.4 to 24.9 years in the United States and from 25.6 to 28.0 years in Japan (Jacobsson et al. 2004). In Austria, the average maternal age at first birth increased from 23.8 years in 1984 to 29.9 in 2019 (Statistik Austria 2019). Currently, delaying reproduction and giving birth at an advanced age is a worldwide trend. But what does "advanced maternal age" actually mean? Traditionally, women 35 years old and older were considered as elderly gravidas (Dulitzki 1998). Today, however, advanced maternal age is defined as 40 years and, the term "very advanced maternal age" is applied to women who are at least 45 years old (Kahveci et al. 2018).

This trend of postponing motherhood, however, also poses certain risks. It is a well-established fact that delaying child-birth beyond the age of 35 or 40 years is not only associated with reduced fertility, but also with several adverse obstetric out-comes. These include increased rates of abortion, stillbirths, preterm births, low birth weight, intrauterine growth restriction unexplained foetal death and even increased rates of Caesarean section (Jolly et al. 2000; Hoffman et al. 2007; Aliyu et al. 2008). Moreover, complications during pregnancy are more frequent in older than in younger women, which results in higher costs for the health system (Tromp et al. 2011). Consequently, there is a clear effect of maternal age on foetal development and birth outcomes (Cleary-Goldman et al. 2005; Briggs et al. 2007; Salem Yaniv et al. 2011). This calls for identifying additive effects of advanced maternal age and other stress factors that have a negative impact on pregnancy, intrauterine development and birth outcome.

A well-documented stress factor during pregnancy is nicotine consumption. The negative effects of smoking during pregnancy on foetal development are undeniable. Many studies have shown negative influences on foetal growth and development (Voigt et al. 2009; Prabhu et al. 2010; Ekblad et al. 2015) . More specifically, birth-weight and birth length are drastically affected by nicotine consumption during pregnancy. This activity is associated with smaller and lighter babies (Kirchengast and Hartmann 2003).

Kharkova and Odland (2019) showed that smoking during pregnancy has a negative effect on the head circumferences of newborns. If, however, the women stopped smoking in the first trimester of pregnancy, the head circumference was similar to that of children of non-smokers. Mook-

Kanamori et al. (2010) reported that smoking throughout pregnancy is associated with a shorter crown to rump length in the first trimester. Furthermore, Jaddoe et al. (2007b) showed that smoking during pregnancy leads to a reduced growth of foetal femur length, head circumference and abdominal circumference. Maternal smoking in late pregnancy increases the risk for low birthweight and preterm birth, moreover, passive smoking also negatively impacts birth weight (Jaddoe et al. 2008). Importantly, smoking during pregnancy not only influences newborn parameters, such as birth length and weight, it is also associated with negative and adverse events during birth, such as an increased Caesarean section rate (Kirchengast and Hartmann 2003). The long-term consequences of nicotine consumption during pregnancy are indisputable as well, with negative effects observable well into adolescence (Knopik et al. 2012; Toledo-Rodriguez et al. 2010).

A wealth of scientific evidence demonstrates that advanced maternal age as well as nicotine consumption during pregnancy impact foetal development. At the same time, however, little is known about the additive effects of these two factors on child development. Some evidence suggests that increasing age of smokers aggravates the negative effects on the foetal development and newborn parameters (Cnattingius et al. 1985; Cnattingius 1990; Cnattingius 1997). Furthermore, Lamminpää et al. (2013) showed that smoking and maternal age over 35 years are additive risks on adverse birth outcomes such as preterm birth, small size for gestational age, low birth weight and foetal death.

The present study investigates the interaction of maternal age and nicotine consumption on newborn size as well as several vital parameters. Our hypothesis is that increasing maternal age amplifies the negative effects of smoking during pregnancy on the newborn parameters.

Sample and Methods

This medical record- based study analysed a data set of 4142 singleton births at the University Clinic for Gynaecology and Obstetrics in Vienna between 1990 and 1995. This clinic is one of the largest birth clinics in Austria with about 2500 births every year. Prenatal check-ups are also performed there. In the present study, only births, that fulfilled the following very strict inclusion criteria such as singleton term birth (39th and 40th gestational week) of healthy nulliparous mothers of Austrian or Central European origin. Healthy was defined as no registered maternal diseases before and during pregnancy, no hypertension (BP < 150/90 mmHg), no protein or glucose in the urine, no pregnancy related immunization, the absence of HIV infections and gestational diabetes, and no alcohol abuse, or praeclampisa. All prenatal check-ups of the Austrian mother-child passport had to be completed. Additional strict exclusion criteria were any type of medically assisted reproduction such as IVF and congenital maldeformations of the foetus.

Gestational age was calculated in terms of the number of weeks from the beginning of the last menstrual bleeding to the date of delivery (= duration of amenorrhoea) and by two consecutive ultrasound examinations performed before the 12th week of gestation.

The mean age of mothers was 25.2 (± 5.6) years, with the youngest mother being 13 years old and the oldest 46 years old. The mothers were divided into three age groups, whereby the women between the age of 18 and 35 were put into one group associated with the “ideal age for pregnancy”. Mothers younger than 18 years were defined as young mothers, whereas a maternal age above 35 years was defined as advanced maternal age.

Maternal somatometric parameters

The following maternal somatometric parameters were determined according to the recommendations of Knußmann (1988) at the first prenatal visit: Body height and pre-pregnancy weight. Height was measured to the nearest 0.5cm using a standard anthropometer. Pre-pregnancy weight was obtained by interview using the retrospective method. Additionally, body weight was measured to the nearest 0.1 kg on a balance beam scale. According to Gueri et al. (1982), gestational weight gain is extremely low during the first 13 weeks of gestation. Consequently, pre-pregnancy weight was calculated as the mean value of the reported weight and the weight determined at the 8^{th} week of gestation. Finally, maternal weight was measured before delivery (= at the end of pregnancy). The weight gain during pregnancy was calculated by subtracting pre-pregnancy weight from the body weight before delivery. Maternal pre-pregnancy weight status was determined by means of the body mass index (BMI) kg/m^2. To classify maternal weight status, the cut-offs published by the WHO (2000) were used: underweight = BMI $<$ 18.50 kg/m^2; normal weight = BMI 18.50 kg/m^2 to 24.99 kg/m^2; overweight = BMI 25.00 kg/m^2 to 29.99 kg/m^2; obese = BMI $>$ 30.00 kg/m^2.

Nicotine consumption

Nicotine consumption was documented during prenatal check-ups at the University Clinic and subsequently categorised as follows: non-smokers, 1–5 cigarettes daily, 6–10 cigarettes daily, 11–20 cigarettes daily and more than 20 cigarettes daily. Changes in smoking behaviour during pregnancy were also documented and divided into 4 subgroups: non-smokers before and during pregnancy (0), non-smokers only during pregnancy (1), smokers before and during pregnancy (2), and smokers only during pregnancy (3).

Newborn parameters

Newborn measurements were taken immediately after birth, including birth length (cm), birth weight (g), and head circumference (cm). Birth weight is measured with a newborn scale, birth length with an infantmeter from head to heel and the head circumference with a measuring tape.
To evaluate the newborn vital functions, the one- and five-minute APGAR scores were used. The APGAR score was introduced in 1952 as a simple and repeatable method to assess the health status of newborns immediately after birth. Five simple criteria – skin color/complexion, pulse rate, reflex irritability, muscle tone and breathing – are evaluated on a scale from zero to ten. The APGAR scoring system remains as relevant for predicting neonatal survival today as it was 60 years ago (Casey et al. 2001).

Statistical analysis

For statistical analyses SPSS for Windows (version 26.00) was used. After computing descriptive statistics including the Kolmogoroff Smirnov test, group differences in maternal and newborn parameters between the four smoking categories were tested by the Kruskal-Wallis *H*-test with Bonferroni corrections. Pearson χ^2 tests were used to test differences between age categories and maternal smoking behavior. Multiple regression models were calculated including birth weight, birth length and head circumference as dependent variables, independent variables were maternal age, nicotine consumption during pregnancy, BMI, maternal body height and weight gain during pregnancy. For calculating adjusted mean differences for newborn parameters between smokers and non-smokers in each age category linear regression models were used $p<0.05$ was considered as statistically significant.

Results

Sample description

Table 1 summarises maternal and newborn characteristics. Most mothers were classified as normal weight, 15.5% of the mothers were overweight, only 4.4% corresponded to the definition of obesity. The proportions of smokers and non-smokers before pregnancy were 36.1% and 63.9% respectively, changing to 28.6% and 71.4% of smokers and non-smokers during pregnancy.

Smoking behaviour during pregnancy

The analysis of the maternal smoking behaviour shows that most of the women reduced or stopped smoking with pregnancy (Figure 1).

The highest age category (>40 years) encompassed the most women who smoked more than twenty cigarettes a day during pregnancy. As evident in Table 2, smoking behaviour differed significantly between the maternal age groups ($\chi^2=25.411$, $df=6$, $p<0.001$). More younger women (<18 years) continued smoking (31.1%) or even started smoking during pregnancy (7.8%), than women of 18 to 35 years of age (23.7% and 4.8% respectively) and the oldest mothers (17.2% and 4.7% respectively). In the oldest age category (>35 years) the proportion of non-smokers (70.7%) was higher than expected but fewer women stopped smoking than expected (7.4%).

Smoking behaviour during pregnancy and maternal as well as newborn parameters

Birth weight ($H=82.176$, $p<0.001$), birth length ($H=91.525$, $p<0.001$) and head circumference ($H=42.097$, $p<0.001$) differed significantly between the smoking categories (Table 3). The post-hoc tests show that the offspring of absolute non-smokers and of the smokers who quit during pregnancy were significantly heavier than smokers before and during pregnancy. The latter group had significantly shorter offsprings than the absolute non-smokers and the non-smokers only during pregnancy. Additionally, the offspring of the absolute non-smokers are significantly larger than those of the smokers only during pregnancy. The head circumferences of the newborns of the absolute non-smokers are significantly larger than those of the smokers before and during pregnancy. The APGAR 1 and APGAR 5 scores did not differ significantly between the groups.

To analyse the independent effect of nicotine consumption and age on the newborn parameters (birth weight, birth length, head circumference) we performed a multiple regression model (Table 4). The effect was corrected for the following parameters: the height of the mother, her weight gain during pregnancy and her pre-pregnancy BMI. The results show that smoking behaviour and maternal age had an independent effect on all three parameters: birth weight ($R^2=0.148$, $p<0.001$), birth

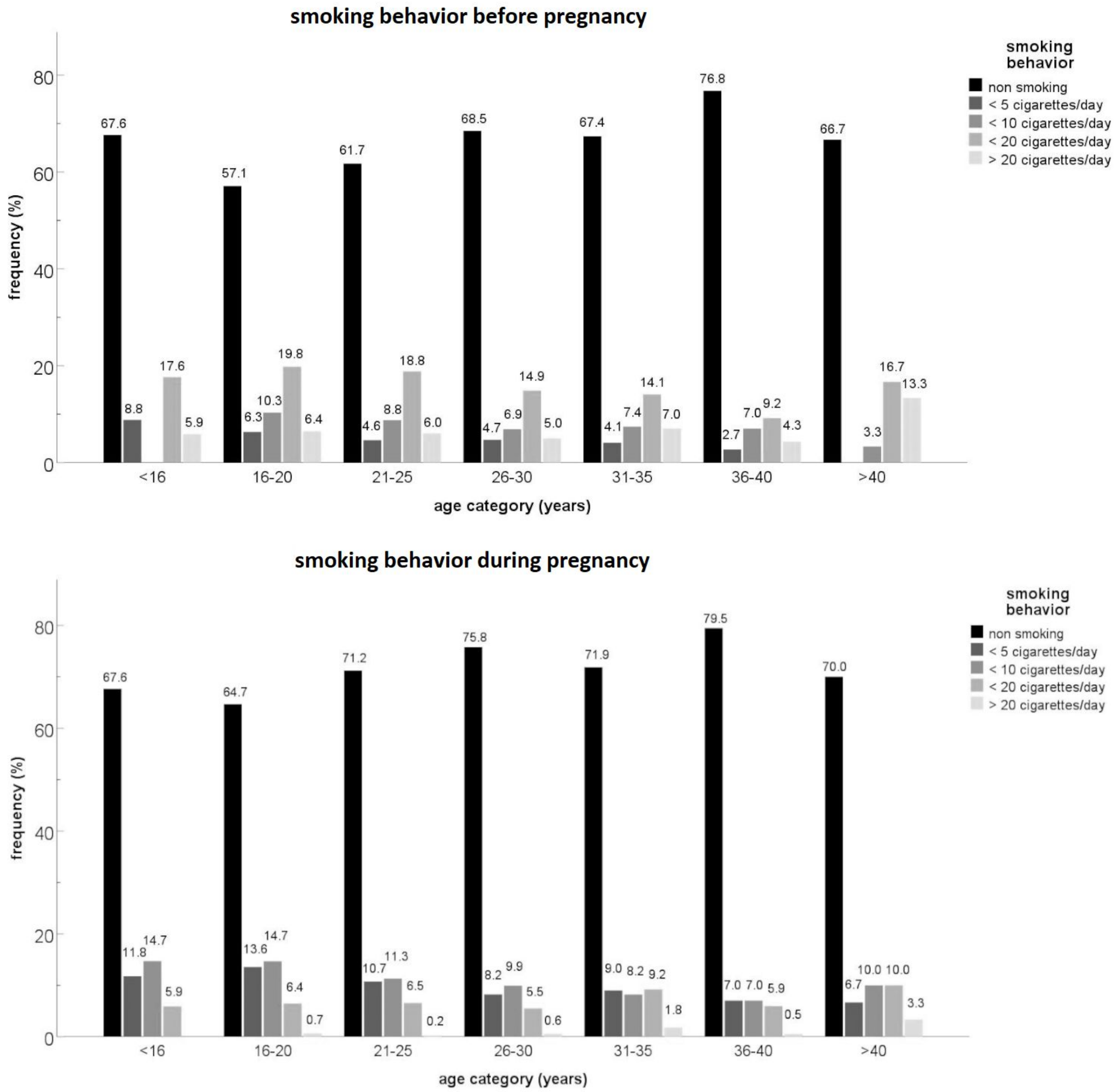

Figure 1 Comparison between the amount of daily smoked cigarettes before and during pregnancy

length (R^2=0.114, p<0.001) and head circumference (R^2=0.079, p<0.001). Smoking during pregnancy had a negative effect on those parameters, while the maternal age had a positive effect. With increasing maternal age, the newborns became bigger and heavier. Newborns of smokers were in general smaller and lighter, independent of the maternal age.

Smoking behaviour and maternal age

Kruskal-Wallis H-tests and Dunn-Bonferroni post-hoc tests were performed to test differences in maternal (Table 5) and newborn parameters (Table 6) between age categories in each smoking behaviour category.

Maternal stature (H=13.353, p<0.05), pre-pregnancy BMI (H=31.658, p<0.05), birth weight (H=13.160, p<0.05) and head circumference (H=18.689, p<0.05) differed significantly between the maternal age

groups among the non-smoking before and during pregnancy category. Those under 18 years and the 18–35-year-olds differed significantly in stature, BMI, birth weight and head circumference, in the sense that the values of these parameters of the <18-year-olds are smaller. Additionally, the <18 years have a significantly lower BMI, birth weight and head circumference than the >35-year-olds. Concerning head circumference, the >35- and 18–35-year olds differed significantly. The older women tend to have children with larger head circumferences. Moreover, in category non-smoking only during pregnancy, the <18-year-olds had a significantly lower BMI than the 18–35-year-olds.
Finally, a linear model was performed to compare the newborn parameters from the offspring of smoking and non-smoking mothers during pregnancy for each age category (Table 7). With increasing maternal age, the mean differences of the parameters birth weight, birth length and head circumference increased, between smoking and non-smoking mothers. Note that the means are adjusted by the maternal parameters, body height, pre-pregnancy BMI and gestational weight gain.

Discussion

This study was designed to assess the effects of smoking during pregnancy on the foetal development with special focus on the interaction with maternal age. This involved analysing 4142 singleton births from primiparous women from Vienna and compared newborn size as well as vital parameters between mothers of different age groups and smoking behaviour.
Certain limitations of this study deserve mention. The socio-economic status of women was not incorporated, although this status is often very meaningful in the context of birth and pregnancy because it is an indicator of maternal and children's parameters (Lu et al. 2001; Phung et al. 2003; Cnattingius 2004). Even with an adequate health care system, socio-economic status also has a clear influence on birth mode and birth complications (Kim et al. 2018). Moreover, smoking behaviour was only surveyed and not controlled in any manner, raising some uncertainty whether the information provided by the women is fully reliable since smoking is socially undesirable during pregnancy, some underestimates about smoking behaviour and the number of cigarettes smoked per day are possible. Finally, we have no information about possible consumption of other substances, such as alcohol, that could influence on foetal development (Jaddoe et al. 2007a). Note also the relatively small representation of young (< 18 years old) and old mothers (> 35 years) in the sample, especially when they are divided into the smoking subgroups. The data for this study were collected from the early to mid-1990s and smoking behaviour in Austria has changed in the meantime (Griebler et al. 2017). Importantly, however, a change in smoking prevalence among women has no influence on the effect of smoking during pregnancy on the foetal parameters. That effect remains negative.
The analysis of the newborn parameters showed that newborns of mothers who smoke before and during pregnancy were significantly lighter, shorter and had a smaller head circumference than newborns of non-smokers. This trend is consistent with previous studies (Kirchengast and Hartmann 2003; Kharkova and Odland 2019). This impaired foetal development by tobacco consumption were explained by negative morphological and molecular changes in the placenta (Zdravkovic et al. 2005). Breton et al. (2009) also showed that epigenetic modifications that occur in

children of mothers who smoked throughout pregnancy can affect and impair foetal development. We could not find any significant differences in newborn size between the children of non-smokers and those children whose mothers stopped smoking during pregnancy. This indicates that smoking before pregnancy did not have a significant effect on foetal development and growth. Thus, quitting smoking at the beginning of pregnancy, seems to prevent foetal growth restriction. In the present study, some women started smoking with pregnancy. The newborns of these mothers showed a similar newborn size to those of mothers who smoked before and during pregnancy. Nafstad et al. (1996) reported a small but still considerable percentage (7%) of women who started smoking with pregnancy, but those authors provided no information about the effects on newborn size and vital parameters. To our knowledge, no previous study has investigated this issue and this could be an interesting topic for future studies. APGAR 1 and APGAR 5 did not differ significantly between smokers and non-smokers. We therefore omitted these two parameters in our further analysis.

Multiple regression models showed that the number of smoked cigarettes per day had a significant, independent effect on newborn parameters. A higher value had a significant negative impact on birthweight, head circumference and birth length. Such a dose dependent effect of nicotine consumption during pregnancy has also been shown by Jaddoe et al. (2008). The model is controlled for the maternal parameters maternal age, body height, BMI and weight gain during pregnancy because they also clearly influence child development.

Our study highlights that the negative effects of smoking during pregnancy on the newborn size are amplified with increasing maternal age. Comparison of newborn parameters between maternal age categories within each smoking group showed significant differences only in the non-smoking group for birth weight and head circumference, i.e. these parameters increase with maternal age. However, the trend that the offspring of older mothers weigh more and have larger head circumferences seems to vanish if the mothers smoke during pregnancy. We found no differences for any newborn parameter between mothers who smoked before and during pregnancy and those who started smoking with pregnancy. Instead the values of the 18–35- and over 35-year-olds are similarly low as the values of the adolescent mothers under 18 years of age. This seems surprising because adolescent mothers tend to have smaller and lighter children because their bodies are not fully developed yet and competition for nutrients leads to smaller offspring compared to adult women (Kirchweger et al. 2018).

We then compared the newborn parameters of the smoking group and those of the non-smoking group within each age category. As expected, the negative effects of nicotine consumption increased during pregnancy. For birthweight the effect was most evident: the mean difference increased from 101.8 g for the <18-year-olds to 245.8 g for the oldest mothers (>35 years of age). A similar pattern emerged for head circumference: a 0.3 cm mean difference for the youngest and 18–35-year old mothers versus 0.7 cm for the older women. The effect is somewhat weaker for birth length: a slight increase from 0.6 cm in the youngest group to 0.7 cm in the middle and oldest age group. These results are in line with the findings of Phung et al. (2003) and Zheng et al. (2016). The advantage of our study, however, is that we controlled for confounding factors such as maternal stature, pre-pregnancy BMI and weight gain during pregnancy, which have been shown to significantly influence birth weight (Pölzlberger et al. 2017). This makes our results more accurate than those of previous studies.

Cnattingius (1997) reported a higher risk of small gestational age newborns (SGA) for older mothers. He argued that this effect is not due to differences in smoking habits between younger and older mothers, but rather to a different biological response to tobacco consumption in older women. Possible explanations are on the one hand, that older women may have smoked for a longer time than younger women and therefore the toxic tobacco substances caused more damage to their organisms. On the other hand, increased maternal age is an independent risk factor for adverse birth outcomes and restricted foetal growth (Cleary-Goldman et al. 2005; Salem Yaniv et al. 2011) as is smoking during pregnancy, as our study has shown. Accordingly, the effects of advanced maternal age and nicotine consumption on the developing foetus are apparently additive.

Other possibilities besides direct biological differences between younger and older mothers, should also be addressed. The actual number of smoked cigarettes may differ between age groups. Jaddoe et al. (2008) reported that the effect on the developing foetus gets worse with a higher dose of smoked cigarettes per day. Even though the older mothers in our sample had the highest percentages of non-smokers during pregnancy, this age category also had more heavy smokers (>20 cigarettes per day). If older mothers are more likely to be heavy smokers during pregnancy, this could lead to the observed increased negative effects on the newborn parameters. Our study did not control for the number of cigarettes smoked per day when comparing newborn parameters between age groups, because the sample sizes were too small for the youngest and oldest mothers. Future studies should include the smoking dose in their analysis.

Zheng et al. (2016) argued that the amplified effects of smoking on foetal development might not be directly caused by age but rather by indirect factors linked to advanced maternal age. Such possible age-related factors could be socio-economic status and educational level. Some authors drew a correlation between smoking during pregnancy and the socio-economic status of the women (Lu et al. 2001; Phung et al. 2003; Cnattingius 2004; Jaddoe et al. 2008; Tsakiridis et al. 2018; Wolff et al. 2019). More highly educated women are more likely to stop smoking during pregnancy (Phung et al. 2003; Jaddoe et al. 2008) and the mean differences in birth weight between smokers' and non-smokers' offspring decrease with educational level (Phung et al. 2003). Furthermore, low socio-economic status is associated with a higher risk for adverse birth outcomes (Kim and Saada 2013). The question arises if socio-economic status of smoking mothers differs between age groups. If yes, that could influence this interaction of maternal age and the negative effects of nicotine consumption on newborn parameters.

Conclusion

The present study once again highlighted the negative effects of nicotine consumption during pregnancy on the foetal development. Furthermore, our results indicate that the effects of tobacco consumption during pregnancy are modified through the mother's age. With increasing age, the well-known negative effect of smoking during pregnancy increases, and this is accompanied by stronger consequences for newborn size, especially for birth weight. Our results show the importance of focusing on this high-risk group of older smoking mothers during prenatal care.

Especially against the background of increasing maternal age in our society these findings are of special interest for public health systems and smoking prevention programmes.

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Appendix

Table 1 Sample characteristics

Maternal parameters	Mean (SD)	Range	*N* (%)
Age (years)	25.2 (5.6)	13-46	4142
<18			193 (4.7%)
18-35			3734 (90.1%)
>35			215 (5.2%)
Stature (*cm*)	163.7 (6.4)	120-188	4105
Pre-pregnancy weight (kg)	60.5 (10.9)	43-130	4142
End of pregnancy weight (kg)	73.4 (12.0)	44-143	4142
Gestational weight gain (kg)	13.0 (5.5)	-6-38	4142
Pre-pregnancy body mass index (kg/m^2)	22.55 (3.78)	14.15-52.78	4105
< 18.50 kg/m^2			299 (7.3%)
18.50 – 24.99 kg/m^2			2989 (72.8%)
25.00 – 29.99 kg/m^2			635 (15.5%)
≥ 30.00 kg/m^2			179 (4.4%)
Nicotine consumption before pregnancy			
Smokers			1495 (36.1%)
Non-smokers			2647 (63.9%)
Nicotine consumption during pregnancy			
Smokers			1186 (28.6%)
Non-smokers			2156 (71.4%)
Newborn parameters			
Birth length (cm)	49.9 (1.9)	31-58	4137
Birth weight (g)	3386.3 (430.4)	1800-5180	4142
Head circumference (cm)	34.4 (1.4)	30-40	3815
APGAR 1	8.6 (1.1)	1-10	4107
APGAR 5	9.8 (0.6)	5-10	3878

Table 2 Maternal smoking behaviour during pregnancy per age category

Age categories		Smoking categories			
		0	**1**	**2**	**3**
<18	%	47.7%	13.5%	31.1%	7.8%
	N	92	26	60	15
	Expected *N*	113.9	23.9	45.8	9.5
	Residuals	-21.9	2.1	14.2	5.5
	Standardised residuals	-2.1	0.4	2.1	1.8
18-35	%	58.9%	12.6%	23.7%	4.8%
	N	2200	470	886	178
	Expected *N*	2203.3	461.6	886.2	183.0
	Residuals	-3.3	8.4	-0.2	-5.0
	Standardised residuals	-0.1	0.4	0.0	-0.4
>35	%	70.7%	7.4%	17.2%	4.7%
	N	152	16	37	10
	Expected *N*	126.9	26.6	51.0	10.5
	Residuals	25.1	-10.6	-14.0	-0.5
	Standardised residuals	2.2	-2.1	-2.0	-0.2

Chi^2 test from Pearson: value=25.411; df=6; asymptotically significant < 0.001; number of valid cases=4142
Legend: smoking categories
category 0: non-smokers before and during pregnancy
category 1: non-smokers only during pregnancy
category 2: smokers before and during pregnancy
category 3: smokers only during pregnancy

Table 3 Comparison of maternal and newborn parameters between the four categories for smoking behaviour during pregnancy Kruskal-Wallis H test

		Maternal parameters				Newborn parameters				
Smoking categories		Age [a,b] (years)	Stature [a,b,e] (cm)	BMI [a,b] (kg/m²)	Weight gain [a,b,c] (kg)	Birth length [b,c,d] (cm)	Birth weight [b,d] (g)	Head circumference [b] (cm)	APGAR 1	APGAR 5
0	*N*	2444	2416	2416	2444	2441	2444	2259	2424	2283
	Mean	25.6	163.3	22.66	12.3	50.1	3427.8	34.5	8.7	9.8
	SD	5.6	6.4	3.64	5.3	1.8	420.0	1.4	1.1	0.6
	Median	25	163	22.01	12	50	3400	34	9	10
	Q1/Q3	21/29	160/168	20.20/24.22	9/15.75	49/51	3150/3700	34/35	8/9	10/10
1	*N*	512	508	508	512	510	512	476	508	459
	Mean	24.4	164.9	22.35	14.0	50.0	3413.5	34.4	8.6	9.7
	SD	5.1	6.0	3.74	5.5	1.8	430.9	1.3	1.3	0.6
	Median	24	165	21.45	14	50	3400	34	9	10
	Q1/Q3	21/27	161/169	19.99/23.79	11/17	49/51	3150/3700	33/35	8/9	10/10
2	*N*	983	979	979	983	983	983	898	975	936
	Mean	24.4	164.1	22.42	13.7	49.4	3279.6	34.2	8.6	9.8
	SD	5.5	6.2	4.12	5.4	2.0	440.3	1.4	1.2	0.6
	Median	23	164	21.30	14	50	3300	34	9	10
	Q1/Q3	20/28	160/168	19.61/24.22	10/17	48/51	3000/3550	33/35	8/9	10/10
3	*N*	203	202	202	203	203	203	182	200	200
	Mean	24.7	163.3	22.43	14.4	49.6	3334.4	34.2	8.6	9.8
	SD	5.8	6.7	3.81	6.7	1.8	411.9	1.3	1.1	0.5
	Median	24	163	21.62	14	50	3350	34	9	10
	Q1/Q3	20/29	159/168	19.92/23.94	10/19	48/51	3070/3600	33/35	8/9	10/10
	H	49.347**	33.454**	18.852***	82.883***	91.525***	82.176***	42.097***	2.570	2.010

Significance levels: ***p<0.001, **p<0.01, *p<0.05

Dunn-Bonferroni Post-hoc test:

a= sign. difference between the smoking categories 0 and 1

b= sign. difference between the smoking categories 0 and 2

c= sign. difference between the smoking categories 0 and 3

d= sign. difference between the smoking categories 1 and 2

e= sign. difference between the smoking categories 1 and 3

f= sign. difference between the smoking categories 2 and 3

Legend smoking categories:

category 0: non-smokers before and during pregnancy

category 1: non-smokers only during pregnancy

category 2: smokers before and during pregnancy

category 3: smokers only during pregnancy

Table 4 Associations between the newborn parameters birth weight, birth length and head circumference, and the maternal parameters age, nicotine consumption during pregnancy. Multiple regression analyses.

	Birth weight (R^2=0.148)			
Independent variables	*B*	*SE of B*		*p*
Maternal age	5.253	1.134	0.068	≤ 0.001
Maternal stature	12.082	0.985	0.179	≤ 0.001
Weight gain during pregnancy	17.053	1.158	0.217	≤ 0.001
Maternal BMI	24.564	1.681	0.216	≤ 0.001
Nicotine consumption during pregnancy	-11.640	1.039	-0.162	≤ 0.001
	Birth length (R^2=0.114)			
	B	*SE of B*		*p*
Maternal age	0.020	0.005	0.059	≤ 0.001
Maternal stature	0.055	0.004	0.187	≤ 0.001
Weight gain during pregnancy	0.056	0.005	0.163	≤ 0.001
Maternal BMI	0.078	0.007	0.157	≤ 0.001
Nicotine consumption during pregnancy	-0.054	0.005	-0.171	≤ 0.001
	Head circumference (R^2=0.079)			
	B	*SE of B*		*p*
Maternal age	0.019	0.004	0.075	≤ 0.001
Maternal stature	0.033	0.003	0.150	≤ 0.001
Weight gain during pregnancy	0.029	0.004	0.114	≤ 0.001
Maternal BMI	0.059	0.006	0.161	≤ 0.001
Nicotine consumption during pregnancy	-0.029	0.004	-0.124	≤ 0.001

Table 5 Maternal somatic parameters per smoking category and per age category. Kruskal-Wallis *H*-test

		Smoking categories											
		0			1			2			3		
		Age categories (years)			Age categories (years)			Age categories (years)			Age categories (years)		
		<18	18-35	>35	<18	18-35	>35	<18	18-35	>35	<18	18-35	>35
Stature (cm)	*N*	92	2172	152	26	467	15	60	882	37	15	177	10
	Mean	161.3	163.4	162.5	165.7	164.8	165.9	162.9	164.1	166.0	162.6	163.4	164
	SD	5.9	6.4	6.7	5.5	6.1	4.2	6.1	6.2	7.2	6.0	6.8	6.9
	Median	160.5	164	163	166	165	166	162.5	164	165	162	163	163
	Q1/Q3	157.3/165	160/168	158/167	162/170	161/169	164/169	158.5/166.5	160/168	161/172	160/165	159/168	160/169.3
Kruskal-Wallis *H* test	*H*		13.353*[a]			1.337			5.914			0.252	
BMI (kg/m²)	*N*	92	2172	152	26	467	15	60	882	37	15	177	10
	Mean	21.61	22.60	24.22	20.88	22.40	23.13	21.47	22.44	23.55	21.75	22.45	23.24
	SD	2.47	3.61	4.37	3.37	3.71	4.64	3.22	4.13	4.92	1.51	4.0	2.20
	Median	21.41	21.94	23.10	20.67	21.48	21.09	20.64	21.31	22.19	21.48	21.38	23.67
	Q1/Q3	19.71/ 22.95	20.20/ 24.21	21.23/ 26.03	18.40/ 21.89	20.05/ 23.88	20.55/ 24.80	19.33/ 22.79	19.61/ 24.22	20.54/ 25.28	20.57/ 22.58	19.72/ 24.01	22.03/ 24.86
Kruskal-Wallis *H* test	*H*		31.658*[a,b]			6.160*[a]			5.958			2.496	
Weight gain (kg)	*N*	92	2200	152	26	470	16	60	886	37	15	178	10
	Mean	12.3	12.4	11.5	11.8	14.1	14.1	13.4	13.7	13.2	16.2	14.1	15.6
	SD	5.3	5.3	5.6	6.0	5.5	6.1	5.4	5.4	5.1	8.4	6.5	8.2
	Median	12.0	12	12	12	14	13.5	13	14	14	15	14	12.5
	Q1/Q3	9.0/16.0	9/16	8/15	8.8/15.3	11/17.3	10.5/18.8	10/16.8	10/17	9.5/17.5	9/22	10/18.3	11.8/21.8
Kruskal-Wallis *H* test	*H*		4.210			3.153			0.654			0.241	

Significance levels: ***p≤0.001. **p≤0.01. *p≤0.05;
Dunn-Bonferroni Post-hoc test: [a]= sign. difference between <18 and 18–35; [b]= sign. difference between <18 and >35; [c]= sign. difference between 18–35 and >35
Legend smoking categories: category 0: non-smokers before and during pregnancy; category 1 : non-smokers only during pregnancy; category 2: smokers before and during pregnancy category 3: smokers only during pregnancy

Table 6 Newborn parameters per smoking category and per age category. Kruskal-Wallis *H*-test

		Smoking category											
		0			1			2			3		
		Age categories (years)			Age categories (years)			Age categories (years)			Age categories (years)		
		<18	18-35	>35	<18	18-35	>35	<18	18-35	>35	<18	18-35	>35
Birth length (cm)	*N*	92	2198	151	26	468	16	60	886	37	15	178	10
	Mean	50	50.1	50.3	49.6	50	50.1	49.3	49.4	50	50.1	49.5	49.3
	SD	1.5	1.8	1.8	1.5	1.8	1.7	1.8	2	2.1	1.9	1.8	2.7
	Median	50	50	50	49.5	50	50	49	50	50	50	50	50
	Q1/Q3	49/51	49/51	49/51	49/51	49/51	49.3/51	48/51	48/51	48/51	49/51	48/51	48.5/50.3
Kruskal-Wallis *H* test	*H*		3.159			1.960			2.389			1.048	
Birth weight (g)	*N*	92	2200	152	26	470	16	60	886	37	15	178	10
	Mean	3310.2	3428.2	3492.5	3302.7	3417.9	3465.6	3216.3	3282.7	3307.6	3362.7	3340.5	3184
	SD	370.4	420.9	423.4	363	430.9	525.9	418.1	439.9	488.5	496.7	398.8	520.2
	Median	3275	3400	3500	3300	3400	3500	3300	3300	3300	3350	3350	3350
	Q1/Q3	3012.5/ 3547.5	3150/ 3700	3200/ 3800	3150/ 3525	3137.5/ 3700	3162.5/ 3762.5	2900/ 3550	3000/ 3550	2990/ 3570	3100/ 3600	3050/ 3650	3025/ 3500
Kruskal-Wallis H test	*H*		13.160*[a,b]			2.049			0.710			0.380	
Head circumference (cm)	*N*	80	2043	136	23	440	13	59	802	37	15	158	9
	Mean	34	34.5	34.8	34.1	34.4	34.5	33.9	34.2	34.3	33.9	34.3	34.4
	SD	1.2	1.4	1.3	1.2	1.3	1.3	1.5	1.4	1.4	1.4	1.3	1.2
	Median	34	34	35	34	34	35	34	34	34	34	34	35
	Q1/Q3	33/35	34/35	34/35	33/35	33/35	34/35	33/35	33/35	33/35	33/35	33/35	33/35
Kruskal-Wallis *H* test	*H*		18.689*[a,b,c]			1.241			3.097			1.381	
Apgar 1	*N*	92	2180	152	26	466	16	60	879	36	14	176	10
	Mean	8.5	8.7	8.6	8.65	8.6	8.7	8.7	8.6	8.8	8.6	8.6	8.8
	SD	1.1	1.1	1.3	1.2	1.3	1.3	0.8	1.2	1.2	0.7	1.2	0.9
	Median	9	9	9	9	9	9	9	9	9	8.5	9	9
	Q1/Q3	8/9	8/9	8/9	8/9	8/9	8.3/9.8	8/9	8/9	9/9	8/9	8/9	8/9.3
Kruskal-Wallis *H* test	*H*		3.960			0.875			1.549			1.015	
Apgar 5	*N*	88	2055	140	24	419	16	58	842	36	14	176	10
	Mean	9.7	9.8	9.7	9.67	9.7	9.9	9.8	9.8	9.9	9.8	9.7	9.9
	SD	0.6	0.6	0.7	0.7	0.7	0.3	0.5	0.6	0.3	0.4	0.6	0.3
	Median	10	10	10	10	10	10	10	10	10	10	10	10
	Q1/Q3	9.3/10	10/10	10/10	9.3/10	10/10	10/10	10/10	10/10	10/10	9.8/10	10/10	10/10
Kruskal-Wallis *H* test	*H*		3.145			0.985			1.894			0.752	

Significance levels: ***p≤0.001; **Dunn-Bonferroni Post-hoc test**: [a]= sign. difference between <18 and 18–35 ; [b]= sign. difference between <18 and >35; [c]= sign. difference between 18–35 and >35
Legend: smoking categories: category 0: non-smokers before and during pregnancy, category 1: non-smokers only during pregnancy category 2: smokers before and during pregnancy category 3: smokers only during pregnancy

Table 7 Mean values for birth weight, birth length and head circumference for smokers and non-smokers during pregnancy and their adjusted mean differences (95% CI)

	Birth weight (g)					
	Non-smokers		smokers			
Age categories	Mean (SD)	*N*	Mean (SD)	*N*	Adjusted mean difference (95% CI)[a]	*p*-value
<18 years	3308.6 (367.2)	118	3245.6 (435.4)	75	101.8 (-9.0 – 212.6)	0.072 [b,c,d]
18-35 years	3426.4 (422.6)	2670	3292.4 (433.6)	1064	154.9 (126.4 – 183.5)	<0,000 [b,c,d]
>35 years	3490.0 (432.4)	168	3281.3 (492.3)	47	254.8 (115.8 – 393.8)	<0,000 [b,c,d]

	Birth length (cm)					
	Non-smokers		Smokers			
	Mean (SD)	*N*	Mean (SD)	*N*	Adjusted mean difference (95% CI)[a]	*p*-value
<18 years	49.9 (1.5)	118	49.5 (1.8)	75	0.6 (0.1 – 1.0)	0.013 [b,c,d]
18-35 years	50.1 (1.8)	2666	49.4 (2.0)	1064	0.7 (0.6 – 0.9)	<0.000 [b,c,d]
>35 years	50.3 (1.8)	167	49.8 (2.2)	47	0.7 (0.1-1.3)	0.034 [d]

	Head circumference (cm)					
	Non-smokers		Smokers			
	Mean (SD)	*N*	Mean (SD)	*N*	Adjusted mean difference (95% CI)[a]	*p*-value
<18 years	34.1 (1.2)	103	33.9 (1.4)	74	0.3 (-0.1 – 0.7)	0.161 [b,c,d]
18-35 years	34.5 (1.4)	2483	34.2 (1.4)	960	0.3 (0.2 – 0.4)	<0.000 [b,c,d]
>35 years	34.8 (1.3)	149	34.3 (1.3)	46	0.6 (0.2 – 1.0)	0.008 [c,d]

[a] adjusted for mothers BMI, weight gain during pregnancy and stature

[b] significant for the parameter BMI (significance level: p<0,05)

[c] significant for the parameter weight gain during pregnancy (significance level: p<0,05)

[d] significant for the parameter stature (significance level: p<0,05)