THE INFLUENCE OF ACTIVE MATERNAL SMOKING DURING PREGNANCY ON BIRTH WEIGHTS IN CYPRUS

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SUMMARY

Cigarette smoking during pregnancy has been causally associated with an increased risk of both intrauterine growth retardation and preterm delivery but most strongly with low birth weight. No such study to date had ever dealt with the Cypriot population. In interviews with their gynaecologists 65,530 pregnant women were asked between January 1990 and August 1996 to answer two questions, whether they had been smoking before and whether they had been smoking during pregnancy. Data from 59,014 births were considered to have valid birth weight data for this investigation. In 81.2% of the cases the mother explicitly declared that she had neither smoked before or during pregnancy whereas in 1.4% of the cases the mother said that she had smoked both before and during pregnancy and in 1.4% of the cases the mother said that she had smoked before but not during pregnancy. Finally, in 15.3% of the cases no answer to "smoking question" was given, whereas in 0.7% of the cases the answer that was given was deemed as not clear. The average birth weight of babies born to women who had stopped smoking was insignificantly different than that of those born to never smokers. The average birth weight of babies born to women who smoked during pregnancy was lower compared to babies born to non smokers' babies by 92 grams, 66 grams, and 109 grams for all babies, singleton boys and singleton girls respectively. The greatest effect to their mean birth weights was observed in babies whose mothers did not answer the question on smoking. Their babies had birth weights lower than non smokers' babies by 203 grams, 197 grams, and 201 grams for all babies, singleton boys and singleton girls respectively.

Key words: smoking, birth weight, premature delivery, Cyprus

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INTRODUCTION

Cigarette smoking during pregnancy has been causally associated with an increased risk of both intrauterine growth retardation and preterm delivery (1) but most strongly of low birth weight. It has been estimated that smokers have a 54% to 130% increase in the risk of low birth-weight (2) (birth weight of less than 2,500 grams) or a weight decrement of 150–200 grams at birth, compared with those of non-smokers (3). Of course there is also the question of passive smoking, persons exposed to environmental tobacco smoke are exposed to most of the same constituents as those contained in mainstream smoke, although obviously the pattern and amounts of exposure differ (4). Studies have shown a 20% to 40% increase in the risk of low birth-weight or a weight decrement of 25–40 grams at birth, compared with those of women not exposed to environmental tobacco smoke (4).

According to the World Health Organization, at present, about 12% of women worldwide smoke cigarettes. In developed countries, about 15% of women smoke, and in developing countries, about 8% smoke. Two surveys of smoking prevalence were performed in Cyprus eight years apart, the first one was a part of a large stratified household survey by the Statistical Office of the Ministry of Finance (5) and was performed in 1989 with 10,849 subjects and the second was conducted in 1997 by the Ministry of Health on a smaller scale (only 1,976 subjects) but used the same methodology and sampling frame (6). Over these eight years, the prevalence of smoking in men seems to have decreased from 43% to 39% while the prevalence of smoking in women increased slightly from about 7% to almost 8%. According to the 1989 survey, intensity of smoking is high among Cypriot smokers, 73% of all male smokers and 50% of all female smokers smoke more than 10 cigarettes per day while 39% of all male smokers and 14% of all female smokers smoke more than 25 cigarettes per day. The 1989 survey also indicated that 20.1% of males and 2.1% of females were ex-smokers. Although smoking among Cypriot women is one of the lowest in Europe (5–8) and indeed ranking quite low worldwide, smoking among the youth and teenagers is one of the highest in Europe (8–9) and no data exist separately for the girls in the corresponding ages. Table 1 shows smoking prevalence in some European countries, including Cyprus (10–14).

To date no study has investigated the patterns of maternal smoking during pregnancy in the republic of Cyprus or the association, if any, between this and the occurrence of low birth weight or preterm delivery.

METHODS

The Department of preventive medicine of the Faculty of medicine of Masaryk University in Brno (Czech Republic) performed a retrospective study on the Cypriot population studying the effects of maternal smoking during pregnancy on birth weights

Table 1. *Smoking prevalence in some European countries (including Cyprus). Source of data: ref. 7–14. Only regular (daily) smokers included*

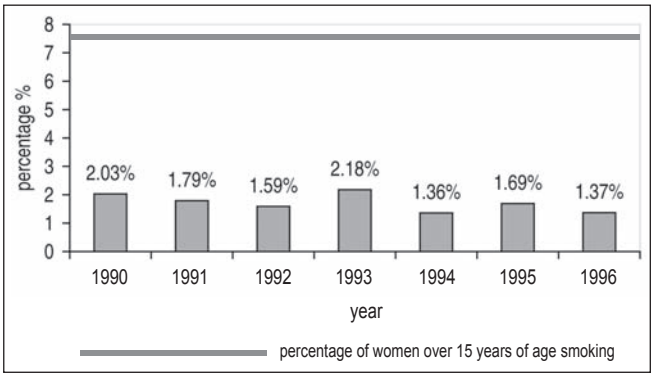
United Kingdom		Czech Republic		France		Greece	
Adult (18 years+) (10)		Adult (18 years+) (11)		Adult (18 years+) (12)		Adult (18 years+) (13)	
Male	29%	Male	28%	Male	39%	Male	46%
Female	28%	Female	12%	Female	27%	Female	28%
11-15-year-olds (14)		11-15-year-olds (14)		11-15-year-olds (14)		11-15-year-olds (14)	
Male	8%	Male	7%	Male	8%	Male	5%
Female	11%	Female	5%	Female	10%	Female	5%
Cyprus							
Males (15 years+) (7)		Females (15 years+) (7)		Youths (10–11 years) (9)		Youths (12–14 years) (9)	
38.5%		7.6%		3.6%		16%	

and preterm delivery, based on data that was obtained for more than 65,000 births for the time period between January 1990 and August 1996 from the database of a non-governmental Cypriot foundation the 'Centre for Preventive Paediatrics' (which checks pregnant women for possible congenital diseases such as Down's syndrome, hypothyroidism and phenylketonuria). All the data that this Cypriot foundation had on newborn babies in Cyprus were obtained directly from the paediatricians and gynaecologists that were involved in each birth. The data about newborns (birth weight, longevity of pregnancy, twinning, sex etc.) were based on the doctors' personal observations, while the smoking history of the mother was documented during private interviews between the doctor and the mother during which the mother stated if she had smoked before and/or during pregnancy. More precisely, 65,530 births (or an approximate 99% of all births in Cyprus in the same period) were investigated of which 59,014 births (90%) were considered to have valid birth weight data for this investigation. In our statistical analysis we considered 'low birth weights' to be weights **lower than 2,500 grams** whereas, since no data existed about the exact gestation time, preterm delivery was taken as stated by the doctors i.e. as **less than 38 weeks**.

In 47,909 (81.2%) of the cases the mother explicitly declared that she had neither smoked before or during the pregnancy whereas in 823 cases (1.4%) the mother said that she had smoked both before and during the pregnancy and in 833 (1.4%) cases the mother said that she had smoked before but not during the pregnancy. Finally, 9,057 women (15.3%) did not answer the question on smoking, whereas in 392 cases (0.7%) the answer that was given was not clear. According to the data obtained for this study approximately half of the women that are known from previous studies to smoke (approximately 3.3% of all valid answers) admitted to have smoked until prior to their becoming pregnant and less than a quarter (approximately 1.7% of all valid answers) admitted to have smoked during their pregnancy (Fig. 1 and 2).

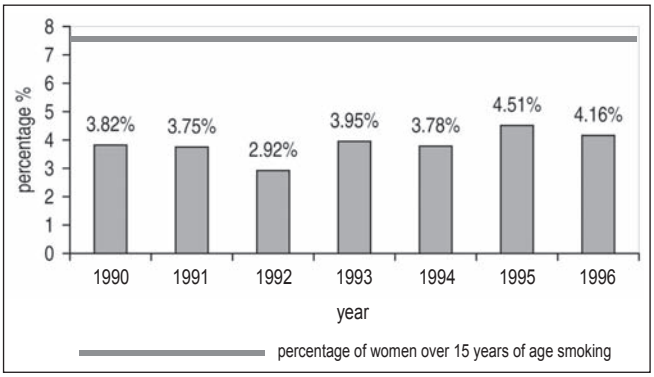
Treating our data, the mean birth weights were calculated separately for the different groups of children and the difference between two of these mean values was then calculated with a 95% confidence interval. If the confidence interval included the 'zero' value then the difference between the mean values of the two groups was not significant (i.e. 0 would be a possible value for the difference). Similarly the increase, from one group to another, in the chance of an underweight or premature baby was calculated together with the equivalent odds ratio and its 95% confidence interval. This time the odds ratio was considered insignificant if the confidence interval included the 'unit' value (i.e. the ratio 1:1 would be a possible value).

Many more factors other than smoking influence the birth weight of a baby as well as the gestation period but data were available to us only for a couple of these factors i.e. the baby's gender and if the birth was multiple or singleton. In order to further identify and pin-point smoking as a cause of low birth weights and premature births in our population we then removed these variables from our data and recalculated the same test statistics as before.



*The line indicates the "expected" percentages according to ref. 5, 6

Fig. 1. *Percentage of mothers smoking during pregnancy by year (based on original data from the study).*



*The line indicates the "expected" percentages according to ref. 5, 6

Fig. 2. *Percentage of mothers smoking before pregnancy by year (based on original data from the study).*

Table 2. *χ^2 test for the hypothesis that the distribution of smoking per district was proportional to that districts population (N = 823)*

	Actual %		Expected %		$\frac{(O_i - E_i)^2}{E_i}$
Ammohostos	4	37	6	49.4	3.10
Larnaka	14	119	18	148.1	5.73
Lemesos	33	272	28	230.4	7.50
Lefkosia	41	339	39	321	1.01
Pafos	7	56	9	74.1	4.41*
Total	100	823	100	823	21.75

**well above the 95% level of the χ^2 test which indicates significant difference between actual and expected"values*

Table 3. *Distribution of sexes between different groups*

	Not smoking before or during pregnancy (N = 47,909) %	Smoking before but not during pregnancy (N = 833) %	Smoking before and during pregnancy (N = 823) %	No answer (N = 9,449) %	1961–1999 Cyprus average %
All births					
Boys	51.8*	49.5*	53.2*	52.5*	51.7
Girls	48.2*	50.5*	46.8*	47.5*	48.3
< 2,500 grams					
Boys	43.7	24.2	35.8	47.9	
Girls	56.3	75.8	64.2	52.1	

**insignificantly different than expected for 95% CI χ^2 test)*

Table 4. *Confidence intervals for the differences of the mean birth weights and the odds ratios of underweight and premature babies for different groups in comparison to non smoking mothers*

	Not smoking before or during pregnancy	Smoking before but not during pregnancy	Smoking before and during pregnancy	No answer
Mean birth weight (grams)	3,254	3,258	3,162	3,051
Difference from non smoking mothers 95% CI		4 [–29–37]*	92 [59–125]	203 [189–217]
% of underweight babies	4.3 %	3.9 %	6.4 %	16.2 %
% change from non smoking mothers		7.8 %	51.2 %	276.7 %
Odds ratio 95% CI		0.93 [0.65–1.32]*	1.54 [1.16–2.04]	4.35 [4.05–4.67]
% of premature babies	4.4 %	4.5 %	10.5 %	26.5 %
% change from non smoking mothers		2.2 %	141.2 %	502.3 %
Odds ratio 95% CI		1.02 [0.73–1.43]*	2.58 [2.05–3.25]	7.9 [7.29–8.56]

**indicates insignificant values*

RESULTS

The number of babies in our data born to mothers smoking during their pregnancy as spread across the different districts seems to be significantly different (Table 2) from the actual distribution of births over the same districts, i.e. higher for districts with larger urban populations and smaller for districts with larger rural population, as shown in Figs. 3–5. [Figures 3 and 4 are based on original data from the study, while the population census (15) served as a data source for Fig. 5.] But this might just be an indication in general of higher numbers of smoking women in the cities. In contrast, the distribution of the ratio of boys to girls was not significantly different for the different groups as compared to the 1961–1999 Cyprus average, while the equivalent ratio restricted to underweight babies was significantly different (Table 3).

Comparing first birth weights for smoking and non smoking mothers for the whole population (Tables 4–5) indicated that there

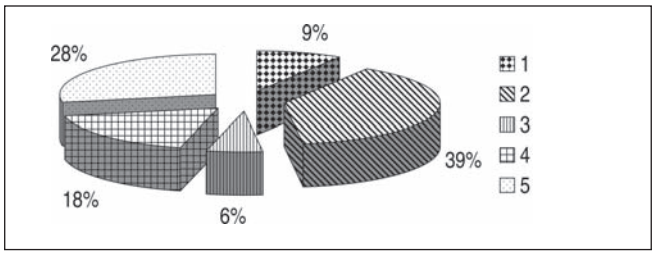


Fig. 3*. Births by district (1990–1996) based on original data from the study.*

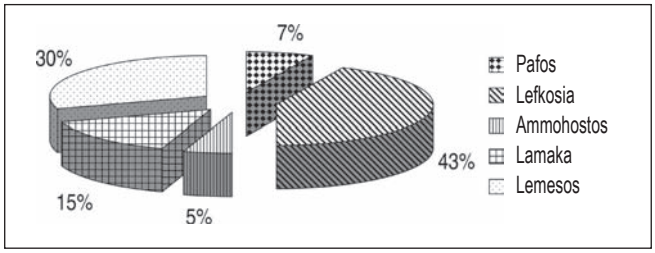


Fig. 4. *Births to smoking mothers by district based on original data from the study.*

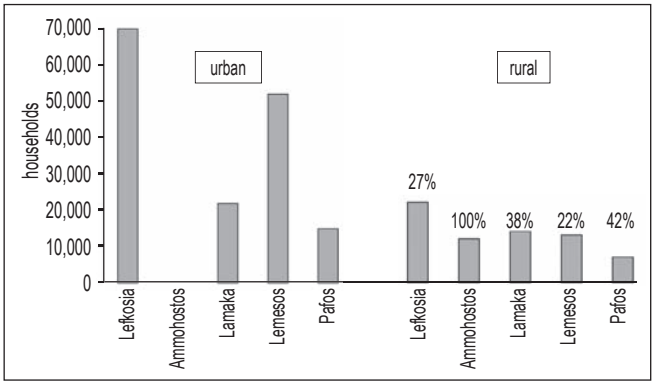


Fig. 5. *Households by district. Data for the construction of the bar chart were taken from the public information office of the Republic of Cyprus – Census of population 2001 (15).*

Table 5. *Crude odds ratios for underweight and premature babies for different groups in comparison to non smoking mothers*

	Smoking before and during pregnancy		Not smoking before or during pregnancy		Crude odds ratio [95% CI]
< 2,500 grams	53	6.4%	2,040	4.3%	1.54 [1.16-2.04]
> 2,500 grams	770	93.6%	45,869	95.7%	
All babies	823		47,909		
Premature	84	10.5%	2,072	4.4%	2.58 [2.05- 3.25]
Not premature	713	89.5%	45,320	95.6%	
All babies	797		47,392		
	Smoking before but not during pregnancy		**Not smoking before or during pregnancy**		**Crude odds ratio [95% CI]**
< 2,500 grams	33	4%	2,040	4.3%	0.93 [0.65– 1.32]*
> 2,500 grams	800	96%	45,869	95.7%	
All babies	833		47909		
Premature	36	4.5%	2,072	4.4%	1.02 [0.73–1.43]*
Not premature	770	95.5%	45,320	95.6%	
All babies	806		47,392		
	No answer		**Not smoking before or during pregnancy**		**Crude odds ratio [95% CI]**
< 2,500 grams	1,467	16.2%	2,040	4.3%	4.35 [4.05–4.67]
> 2,500 grams	7,590	83.8%	45,869	95.7%	
All babies	9,057		47,909		
Premature	1,145	26.5%	2,072	4.4%	7.9 [7.29 – 8.56]
Not premature	3,170	73.5%	45,320	95.6%	
All babies	4,315		47,392		

**indicates insignificant values*

Table 6. *Confidence intervals for the differences of the mean birth weights and the odds ratios of underweight and premature singleton boys for different groups in comparison to non smoking mothers*

	Not smoking before or during pregnancy	Smoking before but not during pregnancy	Smoking before and during pregnancy	No answer
Mean birth weight (grams)	3,334	3,345	3,269	3,138
Difference from non smoking mothers 95% CI		10 [-36–57]*	66 [22–110]	197 [165–229]
% of underweight babies	2.8%	2.0%	3.1%	13.9%
% change from non smoking mothers		43.1%	12.5%	396.4%
Odds ratio 95% CI		0.69 [0.34–1.40]*	1.13 [0.65–1.97]*	5.62 [4.79–6.59]
% of premature babies	3.6%	4.01%	6.7%	16.8%
% change from non smoking mothers		10.0%	84.2%	366.7%
Odds ratio 95% CI		1.12 [0.68–1.90]*	1.90 [1.28–2.82]	5.4 [4.66–6.25]

**indicates insignificant values*

was a very significant difference of 92 grams between babies born to mothers that did not smoke before or during their pregnancy and mothers that smoked during their pregnancy. In addition, smoking during pregnancy significantly increased the chance of delivery of an underweight baby in comparison to babies born to non smoking mothers and similarly significantly increased the chance of premature birth by smoking women in comparison to non smoking women. Interestingly, babies born to women that gave up smoking before being pregnant were not significantly different than babies born to women that never smoked and were almost 96 grams heavier than babies born to mothers smoking during pregnancy. Another interesting feature was that babies for which mothers did not answer whether they had been smoking or not had a very significant decrease of 203 grams in their birth weights in comparison to non smoking mothers as well as a very significant increase in the occurrence of underweight and premature babies.

First we separated singleton boys (Tables 6–7) from the general population. This time there was a smaller but still significant difference of 66 grams between singleton boys born to mothers that did not smoke before or during their pregnancy and mothers that smoked during their pregnancy. In addition, although the chance of an underweight singleton boy to a mother smoking before and during pregnancy was again bigger than in case of non smoking mother this time the difference was smaller and non significant. Similarly the chance of a premature birth of singleton boy was increased in smoking mothers and although it was significant it was once more smaller than for the whole population. The results

Table 7. *Crude odds ratios for under weight and premature singleton boys for different groups in comparison to non smoking mothers*

	Smoking before and during pregnancy		Not smoking before or during pregnancy		Crude odds ratio [95% CI]
< 2,500 grams	13	3.1%	668	2.8%	1.13 [0.65–1.97]*
> 2,500 grams	401	96.9%	23,240	97.2%	
All babies	414		23,908		
Premature	27	6.6%	856	3.6%	1.90 [1.28–2.82]
Not premature	379	93.4%	22.856	96.4%	
All babies	406		23,712		
	Smoking before but not during pregnancy		**Not smoking before or during pregnancy**		**Crude odds ratio [95% CI]**
< 2,500 grams	8	2%	668	2.8%	0.69 [0.34–1.40]*
> 2,500 grams	402	98%	23,240	97.2%	
All babies	410		23,908		
Premature	16	4%	856	3.6%	1.12 [0.68–1.90]*
Not premature	383	96%	22,856	96.4%	
All babies	399		23712		
	Smoking before but not during pregnancy		**Not smoking before or during pregnancy**		**Crude odds ratio [95% CI]**
< 2,500 grams	229	13.9%	668	2.8%	5.62 [4.79–6.59]
> 2,500 grams	1,417	86.1%	23,240	97.2%	
All babies	1,646		23,908		
Premature	273	16.8%	856	3.6%	5.4 [4.66–6.25]
Not premature	1,351	83.2%	22,856	96.4%	
All babies	1,624		23,712		

**indicates insignificant values*

Table 8. *Confidence intervals for the differences of the mean birth weights and the odds ratios of underweight and premature singleton girls for different groups in comparison to non smoking mothers*

	Not smoking before or during pregnancy	Smoking before but not during pregnancy	Smoking before and during pregnancy	No answer
Mean birth weight (grams)	3,203	3,204	3,094	3,002
Difference from non smoking mothers 95% CI		1 [-44–46]*	109 [62–156]	201 [168–324]
% of underweight babies	4%	4.5%	7.1%	16.5%
% change from non smoking mothers		-11.9%	78.4%	312.5%
Odds ratio 95% CI		1.14 [0.71–1.84]*	1.84 [1.22–2.78]	4.78 [4.11–5.57]
% of premature babies	3.5%	4.6%	9.0%	17.5%
% change from non smoking mothers		-24.5%	157.6%	400%
Odds ratio 95% CI		1.34 [0.83–2.16]*	2.73 [1.87–3.97]	5.86 [5.03–6.83]

**indicates insignificant values*

for the mothers that had been smoking before but not during pregnancy as well as for the mothers that did not answer the question were very similar to those of the whole population.

Then we separated singleton girls from the general population (Tables 8–9). This time there was a larger difference of 109 grams between singleton girls born to mothers that did not smoke before or during their pregnancy and mothers that smoked during their pregnancy. Both chances of underweight and premature singleton girls were once more significantly greater for smoking mothers and the differences were now greater than for the whole population. Again the results for the mothers that had been smoking before but not during the pregnancy as well as for the mothers that did not answer the question were very similar to those of the whole population.

DISCUSSION AND CONCLUSION

The most widely accepted hypothesis about the mechanism of smoking influencing the intrauterine growth retardation is *intrauterine hypoxia* (16), i.e. a deficiency in the amount of oxygen reaching body tissues situated within the uterus. The hypoxia could occur as a result of factors associated with smoking such as: 1. increased levels of carbon monoxide (CO) in the blood,

Table 9. *Crude odds ratios for underweight and premature singleton girls for different groups in comparison to non smoking mothers*

	Smoking before and during pregnancy		Not smoking before or during pregnancy		Crude odds ratio [95% CI]
< 2,500 grams	25	7.10%	888	4%	1.84 [1.22–2.78]
> 2,500 grams	327	92.90%	21,424	96%	
All babies	352		22,312		
Premature	31	8.99%	773	3.5%	2.73 [1.87–3.97]
Not premature	314	91.01%	21,374	96.5%	
All babies	345		22,147		
	Smoking before but not during pregnancy		**Not smoking before or during pregnancy**		**Crude odds ratio [95% CI]**
< 2,500 grams	18	4.52%	888	4%	1.14 [0.71–1.84]*
> 2,500 grams	380	95.48%	21,424	96%	
All babies	398		22312		
Premature	18	4.62%	773	3.5%	1.34 [0.83–2.16]*
Not premature	372	95.38%	21,374	96.5%	
All babies	390		22147		
	Smoking before but not during pregnancy		**Not smoking before or during pregnancy**		**Crude odds ratio [95% CI]**
< 2,500 grams	247	16.5%	888	4%	4.78 [4.11–5.57]
> 2,500 grams	1,246	83.5%	21,424	96%	
All babies	1,493		22,312		
Premature	256	17.5%	773	3.5%	5,86 [5,03 – 6,83]
Not premature	1,208	82.5%	21,374	96.5%	
All babies	1464		22,147		

**indicates insignificant values*

2. reduction of blood flow, and 3. inhibition of respiratory enzymes (16).

Our data confirmed the generally observed facts about foetal growth retardation and the higher risk of premature delivery influenced by smoking during pregnancy. These trends in general are exactly what we would expect: Babies born to women that did not smoke before or during the pregnancy had a higher mean birth weight than babies born to women that smoked during pregnancy. Reasons for other results like the distribution of babies born to smoking mothers per district and the distribution of the ratio of boys to girls especially for underweight babies were not very clear.

But why was the difference in birth weights of babies born to smokers and non smokers lesser in our population compared with data published in international publications? One possibility is that our data were obtained retrospectively and flawed or biased in some way. Another reason may be the effect of passive smoking. Unfortunately no data were available on passive smoking of pregnant women but the Cypriot law does not provide sufficient protection to any non smokers from passive smoking.

Based on 1980 legislation, which was toughened in 1988, the sale of tobacco products to individuals under the age of 18 and vending machines sales of tobacco products are prohibited. The legislation also prohibits tobacco advertisements on radio and television, although advertisements in printed media and on billboards are allowed. The printing of warnings on cigarette, cigar and tobacco packets and advertisements became obligatory and "normal" European levels of tar and nicotine had to be maintained. According to the same law (17) smoking is prohibited in public places ("public place" meaning a movie theater, a hospital, including rural health centers and emergency facilities, hospital rooms in a private clinic, waiting rooms in a private clinic, a doctor's office and a dentist's office, museums, art galleries, concert halls, cultural centers, public libraries, factories or other food-production or packing facilities, food-preparation areas, classrooms and other shared areas in schools and elevators), excluding specifically designated areas within them, used as smoking rooms. Smoking is also prohibited inside public transportation vehicles (meaning buses, taxis, and chartered buses). Any person violating the provisions in this section could be found guilty of wrongdoing and be subject to a fine of up to five hundred pounds (≈ €850).

Unfortunately no regulation seems to exist about smoking in private companies (where non smoking employees can work in the same area with smoking ones) and the only regulation about bars and restaurants is that any person who runs or owns any restaurant, café or coffee bar should post a visible sign clearly reading as follows: *CAUTION: Smoking is seriously harmful to your health, Ministry of Health*. Again any person violating the provisions in this section could be found guilty of wrongdoing and be subject to a fine of up to five hundred pounds (≈ €850). It is clear therefore that passive smoking is a real danger for pregnant women as it is indeed for any other non smoker in Cyprus.

One final possibility for the reason why our data differed from the internationally accepted ones is that for social reasons women in Cyprus might be 'ashamed' to admit that they are smokers. In this case data for smoking women could have been either included in the 'non smoking' group or in the group of women that gave no answer to the smoking questionnaire. Even more importantly

these women might have been not only heavier smokers than the women that admitted smoking but with generally worst life styles. This hypothesis is supported by the fact that the mean birth weights of babies that were born to women that did not answer the smoking questionnaire had even bigger differences from the 'non smoking mothers population' than babies born to women that admitted to have been smoking both before and during pregnancy (Tables 4–9).

There could be some remarks regarding internal validity of our study and a large potential for selection bias. But, on the other hand, it should be stressed that 100% in our study is indeed the whole of the population of Cyprus as this was a 'population' study covering all birth in Cyprus. The potential for selection bias is unquestionable, but only due to the 15.3% "non-participation rate", which was discussed. The 10% with 'no adequate' information did not appear to be biased (as far as this study was concerned) as the lack of information did not involve smoking but rather information concerning birth-weight, fetal gender, prematurity or twining. The lack of this information made the stratification of the data impossible and hence it caused their exclusion from the study (mentioned in the methods section).

Another remark can be addressed to the effect of potential confounders such as weight of mothers, their age at birth etc. Indeed, further stratification of the population would have been desirable and if performed would have had the potential to reveal much more about the real impact of smoking. Unfortunately such variables were not available to us and therefore further stratification was impossible.

Overall, on the one side, our data have confirmed the generally accepted adverse impact of maternal smoking on birth weights and preterm deliveries, and on the other, Cyprus seems to have been comparatively spared from this health risk for children with only 1.4% of mothers smoking during pregnancy. At the same time the much bigger group of 15.3 % of mothers who did not give their smoking history (probably intentionally) together with the associated worsening parameters regarding babies indicates that the "smoking mother" problem can be in fact much more serious, and simultaneously raises questions about methodology and sets tasks for future research. It seems very important to find approaches for reaching that possibly most risky group of women in Cyprus. From this point of view, our study could serve as a groundwork and impulse for more detailed, systematic and targeted research on the topic.

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