Introduction

Previous research found much evidence of parental influences on many types of adolescent behavior [1], in particular tobacco smoking [2,3]. Smoking behavior of parents may have an impact on different periods of child’s life: fetal period, infancy, childhood, adolescence, and early adulthood [4]. Several studies have investigated the influence of maternal smoking during pregnancy on offspring smoking in retrospective reports [5,6], and some of them have shown that this association was present only among daughters [7].

Longitudinal studies may be considered a more reliable source of data; however, they also did not give final evidence about the association of maternal smoking during pregnancy and adolescent smoking. Study by Fergusson et al. found the significant association between maternal smoking and conduct disorder symptoms in late adolescence, but not adolescent smoking [8]. Several studies have investigated the influence of maternal smoking during pregnancy on offspring smoking in retrospective reports [5,6], and some of them have shown that this association was present only among daughters [7].

Methods: The present analysis is based on data from the Ukrainian component of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC). Main exposure was smoking by mother. Smoking status of the adolescent and age of smoking initiation, reported at the 16-years-old follow-up, were outcome measures. Data were analyzed using multivariate binary logistic regression model separately for boys and girls.

Results: Of 2148 women who agreed to participate, 1020 were available for complete follow-up until their study children were 16-years-old. The odds of current smoking among girls whose mothers smoked during pregnancy was higher (OR = 2.48, CI = 1.09-5.64) compared to girls with non-smoking mothers. Boys whose mothers currently smoked, but didn’t smoke during pregnancy, had twice higher odds (OR=2.08, CI = 1.16-3.74) to be smokers, compared to boys with mothers who never smoked. After control for confounders, the risk of early initiation of smoking by adolescent girls was still higher (OR= 2.05, CI=0.94-4.48) among girls whose mothers smoked during pregnancy.

Conclusions: Prenatal tobacco exposure was associated with increased risk of early initiation of cigarette smoking and current smoking by adolescent girls, but not by boys. The possible explanation is that biological influences are more important for girls, but boys are more susceptible to social influences.
adolescence or late adolescence), the behavior studied (e.g. initiation of smoking versus the development of dependence) and level of confounding that was controlled. Not all the above studies controlled for current maternal smoking, which is an important factor in role modeling. As a result, many discrepancies are observed in the reviewed literature regarding the presence and the nature of the association between prenatal tobacco exposure and smoking during adolescence. Moreover, in all these studies data originate exclusively from high-income countries; no studies are available from low- and middle-income countries.

Our study uses data about smoking by mother before pregnancy, during pregnancy and their current smoking to examine the risk of tobacco smoking and early initiation of smoking by their adolescent children in a middle-income country. We hypothesize that maternal smoking during pregnancy and after it is associated with adolescent smoking initiation or continuation, or both.

Methods

Study setting and population

The present analysis is based on data from the Ukrainian component (the details of this study have been described previously [17] of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC). Briefly, it is a prospective cohort study of women and babies aimed at identifying features of the environment that affect the health and development of children [18]. Of all the pregnant women in Dneprodzerzhinsk, a city in Dnepropetrovsk oblast in south-central Ukraine, we invited those who between 1992 and 1994 visited antenatal clinics, planned to continue their pregnancy, and were permanent residents of the city [19]. Of 4398 women who met study eligibility criteria, 2148 (49%) women agreed to participate, and 1020 of these women were available for complete follow-up until their study children were 16 or 17-years-old.

Data collection

Data about outcomes, exposures and potential confounders were obtained through self-completed questionnaires distributed by medical staff from local primary health care facilities. Mothers completed questionnaires about their smoking habits before pregnancy, during pregnancy (this data collection took place in 1992-1994), and at the child’s age of 16-17 years old. In 2010-2011, when the study children became age 16, they completed questionnaires about their tobacco smoking, and were permanent residents of the city [19]. Of 4398 women who met study eligibility criteria, 2148 (49%) women agreed to participate, and 1020 of these women were available for complete follow-up until their study children were 16 or 17-years-old.

Outcome measures

The two study outcomes are child’s smoking status and age of smoking initiation. Each measure was determined from the answers on the above-mentioned questionnaire that was completed by the 16 or 17 year old study children. The questions were: "On how many occasions (if any) during your lifetime have you smoked cigarettes?" and "How frequently have you smoked cigarettes during the LAST 30 DAYS?" To establish the age when adolescent smoked first cigarette the question was asked "When (if ever) did you FIRST do each of the following things (smoke your first cigarette)?"

These questions were taken from the European Survey Project on Alcohol and Other Drugs (ESPAD) questionnaire [20]. The test-retest reproducibility and high internal consistency of the ESPAD questionnaire were shown in the previous studies [21,22].

Exposure measures

Mothers responded study questionnaires to report their smoking before pregnancy and during pregnancy. These questions were derived from Avon Longitudinal Study of Parents and Children [23], “Did you smoke regularly last 9 months?”, “How many cigarettes in a day did you smoke usually: (1) At the start of pregnancy (2) When first felt the baby move (3) In the last 2 weeks?”. Current smoking by mother at the child’s age of 16 years old was derived from the answers on the question "How often did you smoke cigarettes during last 30 days?"

Potential confounders

Based on the literature about factors that are associated with tobacco smoking [24,25], we have chosen six potential confounders to be controlled for in the multivariate analysis. These three came from the questionnaire completed by 16 year old children: current level of family income; current family type; type of school the child currently attended. These three came from the mother: year of child’s birth (1993, 1994, or 1995); education level of mother and father.

Statistical analysis

Our main aim was to assess the relation between factors that we classified as exposures and outcomes. For this purpose we have used the odds ratio, with a 95% confidence interval, in both bivariate and multivariate analysis. We began by reducing the above described study variables into forms satisfactory for our purpose. For example, from the information on smoking status of study children and age at smoking initiation, we made two binary outcome variables: “Current smoking” and “Smoking initiation at age of 13 or younger”. This specific age of smoking came from some previous studies based on the average age of smoking and drinking initiation among children in Eastern Europe [26,27]. Those children who reported smoking sometimes (less than once a week), regularly (at least once a week), or daily were classified as current smokers.

We also constructed one exposure variable based on the information about smoking by mother before pregnancy, during pregnancy and during last 30 days. There were three categories of women: (1) non-smokers; (2) those who smoked before pregnancy and currently, but not during pregnancy; (3) smokers.

Our initial analysis examined the relation between the smoking status of mother and the two study outcomes of smoking status of child and first age of smoking. This was done separately for male and female children using binary logistic regression analysis. We then used bivariate analysis to examine the relation between the above-mentioned potential confounders and the study outcomes/determinants. Next, we included the exposure variable and the potential confounders one by one into the multivariate logistic regression models with only one confounding variable in each model to see attenuation effect attributable specifically to certain...
variable. Finally, multivariate binary logistic regression analysis was conducted, controlling for potential confounders that were selected on the basis of prior evidence in research and on the results of the previous step in this study analysis.

All the data analysis was conducted with SPSS software using crosstabs and binary logistic regression program components.

**Results**

**Descriptive statistics of the study sample**

Of the 1020 study children who were followed until age 16, 33% (160/478) of the boys and 24% (113/470) of the girls started smoking at age 13 or younger. At the time of data collection, 24% (119/500) of boys and 16% (80/501) of girls were current smokers, i.e. smoked sometimes (less than once a week), regularly (at least once a week), or daily. The proportion of mothers who reported smoking before, during and after their pregnancy was low – 9% (39/417) among mothers of boys and 11% (44/410) among mothers of girls. Of the 827 mothers who answered all questions about smoking, 166, or 20%, smoked at some time of their life but not during their pregnancy (Table 1).

**Regression analysis**

In the bivariate analysis, girls whose mothers smoked during pregnancy as well as in other periods of life had thrice higher odds to be current smokers and twice higher odds to start smoking at the age of 13 years or younger, compared to those girls whose mothers didn’t smoke or smoked only before and after pregnancy. Current smoking by boys was associated with mother’s current smoking, but not with her smoking during pregnancy (Table 2).
In the multivariate analysis, current level of family income, current family type, current type of school a child attends, and year of child’s birth appeared to be confounders and were controlled for. Education of mother and father were also included into the model, although didn’t attenuate the association between prenatal tobacco exposure and adolescent smoking. The odds of current smoking among girls whose mothers smoked during pregnancy was more than twice (OR = 2.48, CI = 1.09-5.64) higher compared to girls with non-smoking mothers. Boys whose mothers currently smoke, but didn’t smoke during pregnancy, had twice higher odds (OR=2.08, CI = 1.16-3.74) to be smokers, compared to boys whose mothers never smoked. The association between mother’s smoking during pregnancy and early initiation of smoking by adolescent girls was slightly attenuated (OR= 2.05, CI=0.94-4.48).

**Discussion**

Our study demonstrated that prenatal tobacco exposure was associated with increased risk of early initiation of cigarette smoking and current smoking by adolescent girls, but not by boys. Current smoking by boys at adolescence was associated with current smoking by mother. The findings of this study are in line with the results of several studies in high-income countries about the presence of gender differences [28] with regard to mother’s smoking during pregnancy as a risk factor of early smoking initiation and current smoking among adolescents.

**Explanations for and implications of the study findings**

There may be several explanations of the means by which mother’s smoking during pregnancy influences the subsequent smoking by adolescent.

First, nicotine might directly affect fetal neural development, mainly through its action on acetylcholine receptors, which are present very early in the fetal brain [29].

Second, many epidemiological studies support a relationship between maternal smoking during pregnancy and adverse neurobehavioral effects later in life [30]. Among such conditions, a conduct disorder may play a mediating role between mother’s smoking during pregnancy and child’s smoking initiation later in life [31]. However, it is important to note that these effects are difficult to separate from numerous confounding environmental and genetic factors, and that types and number of confounding variables and corrections for their effects vary across studies. For example, women who smoke during pregnancy are more likely to be depressed, anxious, or to have other mental health problems that could affect parent-child interactions and/or impose a genetic influence on the development of the child [30].

Sex differences that are observed in our study results may be considered from the point of view of different theoretical frameworks.

One of them is cultural peculiarities in the attitude to smoking by females. Generally, smoking by women and in particular by adolescent girls is less socially acceptable than smoking by boys. Smoking can even become normative at some point in development among young men. That point puts aside the early life risk factors of smoking among adolescent boys, but brings to consideration concurrent factors, like social environment, availability of alcohol, smoking by parents and peers. In contrast, smoking by women is less acceptable in Ukraine; consequently, this is not a normative behavior. Thus, early life factors may have their impact.

Another putative explanation is that these sex differences reflect the distinctive sexual dimorphism of the brain, i.e. hormonal and structural factors, that emerge during fetal development. For example, the release of androgens may protect the male infant against the priming effect of nicotine [7].

**Strengths and limitations**

The longitudinal design may be considered one of the biggest strength of this study. The information about prenatal tobacco exposure of children was reported by mothers during their pregnancy. This partially limits the recall bias, which threatens the validity of those studies which use the retrospective report of study participants. The other strength of this study which is worth mentioning is the use of the reliable tool to measure adolescent tobacco smoking and alcohol use.

The study has its limitations, such as potential underreporting of smoking by mothers during pregnancy. Earlier estimates of accuracy of self-reported smoking among pregnant women vary in their conclusions. Some found significant agreement between self-reported smoking and serum cotinine levels (the major metabolite of nicotine) [10]. In a population-based cohort of pregnant women, half of the women systematically under-reported the amount they smoked [32]. In our study, biological measures of tobacco use were not used, but information was gathered in the clinical setting with a detailed questionnaire.

Table 2: Association of smoking by mother with smoking status and early smoking initiation by adolescents, bivariate and multivariate binary logistic regression, Odds Ratios, Adjusted Odds Ratios and Confidence Intervals (95%). Adjusted for confounding.

<table>
<thead>
<tr>
<th>Smoking by mother</th>
<th>Boys</th>
<th>Current smoking by adolescent, N=815</th>
<th>Girls</th>
<th>Current smoking by adolescent, N=773</th>
</tr>
</thead>
<tbody>
<tr>
<td>N % with outcome</td>
<td>OR (95% CI) AOR (95% CI)</td>
<td>N % with outcome</td>
<td>OR (95% CI) AOR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Non-smoker (reference)</td>
<td>287 19.2%</td>
<td>1.00 1.00</td>
<td>283 13.1%</td>
<td>1.00 1.00</td>
</tr>
<tr>
<td>Smoked before, after pregnancy, but not during</td>
<td>83 36.1%</td>
<td>2.39 (1.40-4.08)</td>
<td>2.08 (1.16-3.74)</td>
<td>81 17.3%</td>
</tr>
<tr>
<td>Smoked before, during and after pregnancy</td>
<td>37 29.7%</td>
<td>1.79 (0.83-3.83)</td>
<td>1.83 (0.80-4.18)</td>
<td>44 29.5%</td>
</tr>
</tbody>
</table>

| Non-smoker (reference) | 271 30.3% | 1.00 1.00 | 267 22.1% | 1.00 1.00 |
| Smoked before, after pregnancy, but not during | 81 39.5% | 1.51 (0.90-2.52) | 1.55 (0.89-2.71) | 79 25.3% | 1.20 (0.67-2.14) | 1.27 (0.67-2.41) |
| Smoked before, during and after pregnancy | 37 40.5% | 1.57 (0.78-3.18) | 1.56 (0.71-3.18) | 38 39.5% | 2.39 (1.13-4.69) | 2.95 (0.94-4.48) |

Loss to follow-up is a further potential limitation. If the exposures and poor outcomes analyzed in this study were less prevalent among those lost to follow up, our results would be biased, overestimating the association between the risk factors and children’s tobacco use in adolescence. However, as we have found that the prevalence of smoking during pregnancy among mothers lost to follow-up did not differ significantly compared to those mothers, who remained in the study, this study seems unlikely.

To increase certainty regarding the causal nature of the revealed associations, and future research might be strengthened with collection of biological markers of smoking by mothers and their offspring.

Practical implications of the study are related to providing additional evidence to support those policy measures which discourage smoking in pregnancy.

Conclusion

This prospective study of mothers and children confirmed the association between prenatal tobacco exposure and adolescent tobacco smoking initiation and continuation among girls.

Funding

This work was supported in part by the Fogarty International Center of the National Institutes of Health (D43TW006653).

Acknowledgment

We are grateful to the families who took part in the study, the medical personnel for help in recruiting them and the whole ELSPAC team in Ukraine, which includes computer and laboratory technicians, interviewers, clerical workers, and research scientists.

References