ORIGINAL ARTICLE

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Tobacco-related Foetal Origin of Adult Diseases Hypothesis – population studies in Poland

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Abstract

Epidemiological studies in Poland show that tobacco smoking by adolescents at reproductive age is still frequently observed. This concerns both boys and girls. The study was based on all-Polish population studies of health behaviours of adolescents aged 14-24 (Youth Behavioural Polish Survey – YBPS) conducted in 2011, and the Pregnancy-related Assessment Monitoring Survey (PrAMS). More than 12% of pregnant women do not discontinue smoking in association with becoming pregnant and expose the foetus to tobacco smoke, despite being aware of the hazardous effect of smoking on the health of the mother and child. Smoking in pregnancy is mainly observed among mothers with a low education level and those aged under 23. According to the Baker's Foetal Origins of Adult Health and Diseases Hypothesis, exposure of the foetus to the components of tobacco smoke results in many perturbations in the form of a lower birth weight, prematurity, worse state of neonates after birth, and higher susceptibility to contacting civilization diseases at the age of adulthood. The results of studies confirm some observations. Polish studies clearly confirmed a lower birth weight of babies delivered by mothers who smoke; however, earlier termination of pregnancy and worse status of neonates after birth were not observed. According to the Baker's hypothesis, a lower birth weight of babies delivered by smoking mothers during the further life cycle exposes the offspring to the risk of contracting civilization diseases. The efforts undertaken by public health authorities should be biased towards education of the population at reproductive age about the hazardous effect of smoking on the health of the foetus and the offspring born. Women at reproductive age should be encouraged to discontinue smoking in association with the planning of pregnancy and in pregnancy.

Key words

Barker's Foetal Origin of Diseases Hypothesis, epigenetics; IUGR – intrauterine growth retardation, pregnancy outcome, tobacco, foetal smoke exposure, transgenerational epigenetic inheritance

INTRODUCTION

It has been empirically proven that the conditions in which the foetus develops during the foetal period exerts an effect on becoming ill with civilization diseases in adulthood [1]. In the relevant literature, the term "Baker's hypothesis" is used for determining the effect of environmental factors during the period of intrauterine life on the etiology of chronic diseases at the age of adulthood: stroke, arterial hypertension, coronary heart disease and type 2 diabetes[2]. Inhalation of tobacco smoke is among the factors affecting the development of the foetus by mothers who smoke in pregnancy.

THE MOST IMPORTANT COMPONENT OF TOBACCO SMOKE IS NICOTINE

Nicotine absorbed by inhalation by a pregnant woman enters her blood stream within 30-60 seconds [3]. Subsequently, nicotine penetrates through the placenta into the blood stream of the foetus. It is also found in the amniotic fluid, from which it penetrates through the skin into the foetus [4, 5]. The clearens of nicotine and cotinine (the main component of nicotine metabolism) increases in pregnant women [6]. This results from an increased blood flow through the liver, and an increase in the enzymatic decomposition of both nicotine and cotinine in the mother [7, 8, 9]. However, the metabolism in the liver of the foetus is slower, which leads to a longer period of nicotine half-life in the organism of the foetus. This is confirmed by higher concentrations of nicotine observed in the tissues of the foetus, compared to the mother [10, 11]. Thus, the tissues and cells of the foetus are exposed to higher concentrations of nicotine for a longer time, which enhances the negative effect of nicotine on the organism of the foetus. The dividing cells of the foetus are also more susceptible to the effect of foreign substances, such as nicotine. Therefore, exposure of the human foetus to nicotine affects both the growth and development of the foetus. It has also been confirmed that the long-term effect of nicotine leads to genetic instability [5, 12, 13], and cigarette smoking by the mother leads to elevation of the level of oxidative stress markers, both in the mother and the offspring [14, 15]. The toxicity of nicotine also consists in inducing the release of oxidants [11, 16, 17].

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TOBACCO SMOKING BY PREGNANT WOMEN AND INTRAUTERINE GROWTH RESTRICTION (IUGR)

The effect of nicotine on the foetus leads to the restriction of intrauterine growth (foetal intrauterine dystrophy), irrespective of the term of delivery [18]. Low birth weight of the neonate is the result of the effect of nicotine on the structure and function of the placenta, and disturbances in the supply of oxygen and nutrients to the foetus via the placental barrier. Nicotine also activates nicotinic acetylochine receptors, resulting in the constriction of blood vessels, and consequently, in the reduction of oxygen supply to the organism of the foetus, leading to the impairment of its development [10, 19, 20]. Smoking causes a decreased oxygen flow from the uterine muscle into the foetus via the placental barrier, which also disturbs development of the foetus [19]. Tobacco smoking by a pregnant woman results in an increase in the amount of carbon dioxide in her body, which also reduces the oxygen supply to the foetus and inhibits its growth [19]. Also, many studies show that smoking causes a considerable increase in the thickness of the placental membrane villi, leading to the limitation in gas and nutrients exchange via the placenta, and subsequently, to foetal development disorders [21, 22]. In addition, smoking affects the development of the trophoblast and results in reduced blood diffusion between mother and foetus [22, 23]. Disorders in trophoblast differentiation under the effect of tobacco smoke occur as early as at the beginning of the development of the placenta [24, 25].

MOTHER'S SMOKING DURING PREGNANCY, AND OBESITY IN OFFSPRING

It is commonly known that tobacco smoking significantly restricts foetal growth [26], and low birth weight exerts an effect on the incidence of obesity in later life [27, 28]. It is emphasized that this is due to the phenomenon of so-called 'catch-up growth' after delivery [28, 29, 30]. Tobacco smoking in pregnancy directly results in a lower birth weight of the offspring, and neonates with low birth weight are more susceptible to chronic diseases after birth, and later in adulthood.

Many epidemiological cohort studies confirmed the effect of smoking in pregnancy on the development of obesity after birth. For example, in an offspring delivered by mothers who smoked during the foetal period, a significant increase in obesity was noted at the ages of 16 and 33 [31]. This effect was greater in the offspring of pregnant women who habitually smoked large quantities of cigarettes, compared to the offspring of those delivered by mothers addicted to nicotine to a medium degree. Similar results were obtained in other studies [32]. An increase in obesity risk was also observed in offspring aged 5-7 years, delivered by mothers who smoked. Epidemiological studies directly show that the risk of obesity at the age of 4-5 years is twice as high in children delivered by mothers who smoke, irrespective of birth weight [33]. The researchers noted a higher weight gain after birth in the offspring of mothers who smoked, which seems to be the cause of obesity at childhood age. This is a consequence of the phenomenon of 'mismatch' described in the Barker's Foetal Origins of Diseases. It was observed that even in neonates with a normal birth weight delivered by mothers who smoked, the risk of obesity is higher [34, 35]. The studies also show that the cessation of smoking in pregnancy, and then returning to the habit after pregnancy, protects against the development of obesity in the offspring at the age of 5-7 years [36]. This suggests that irrespective of genetic factors and factors related to the life style, intrauterine exposure of the foetus to tobacco smoke exerts a direct effect on the energetic equilibrium in the offspring, which is manifested by the tendency towards obesity at the age of childhood [36, 37]. Also, studies carried out among American Indians on the effect of tobacco smoking by mothers during the foetal period on obesity in the offspring indicated that the offspring exposed to tobacco smoke during the foetal period was more susceptible to obesity at the age of 3 years, compared to those delivered by mothers who did not smoke during pregnancy [37]. This shows that tobacco smoking by mothers, irrespective of the inhibition of foetal growth, has an effect on the development of obesity in their offspring at childhood age [18, 38].

It is of interest from the aspect of public health whether the exposure of the foetus to tobacco smoke during the first weeks of pregnancy (until the moment when the woman knows that she is pregnant) exerts an effect on the development and growth of the embryo and the foetus, and later predisposition to obesity. As confirmed by the studies, smoking by the mother for both the entire period of pregnancy and in the first trimester of pregnancy had an unfavourable effect on the foetus [39]. This suggests that the first three months of pregnancy are a sensitive period in ontogenesis, when epigenetic changes take place under the effect of tobacco smoke which causes the susceptibility of the offspring to obesity. Such relationships were confirmed in offspring aged 3 years [40]. This indicates that women who smoke should discontinue the habit prior to conception.

TOBACCO SMOKING BY PREGNANT WOMEN AND RISK OF DEVELOPMENT OF TYPE 2 DIABETES IN THE OFFSPRING

Cohort studies which covered a population of 17,000 births were among the earliest epidemiological studies to detect the relationship between tobacco smoking by pregnant women, and the risk of development of diabetes in early adulthood [31]. In the presented study, a relationship was found between the risk of falling ill early with diabetes and exposure to tobacco smoke during the foetal period. Mothers who smoked 10 cigarettes daily in pregnancy delivered offspring who were four times more susceptible to type 2 diabetes in early adulthood than the offspring of mothers who did not smoke, which was confirmed by other studies [41].

TOBACCO SMOKING BY PREGNANT WOMEN AND RISK OF ARTERIAL HYPERTENSION IN THE OFFSPRING

Tobacco smoking by pregnant women also results in a greater susceptibility to arterial hypertension in adulthood. Many studies show the effect of smoking in pregnancy on the occurrence of low birth weight in the offspring, which results in the risk of cardiovascular diseases, including hypertension [42]. It was also noted that tobacco smoking in pregnancy may exert an independent effect on the occurrence

of hypertension in the offspring, which was confirmed in the studies of 6-year-olds delivered by mothers who smoked [43]. Similar observations were made among 5-year-olds delivered by mothers who smoked during pregnancy [44].

TOBACCO SMOKING BY PREGNANT WOMEN AND DEVELOPMENT OF THE UPPER AIRWAYS IN THEIR OFFSPRING

Prenatal exposure of the foetus to tobacco smoke results in an increased risk of the development of chronic obstructive pulmonary disease at the age of adulthood [45]. Disorders connected with pulmonary function in individuals whose mothers smoked cigarettes during pregnancy are caused by disorders in the development of the small diameter airways (bronchioles) [46, 47, 48]. Many studies indicate that children exposed to tobacco smoke during pregnancy are characterized by an excessive reactivity of the bronchi and predisposition to asthma [49, 50]. This is due to the impairment of pulmonary function and disturbed air flow via the respiratory bronchioles [51]. The effects of foetal exposure to tobacco smoke are of a permanent character and are observed from childhood to adulthood [52]. Limitations in lung function result from a decrease in the number of alveoli and bronchioles, which is caused by an impaired alveolization of the lungs [53]. There is scientific evidence that exposure of the foetus to tobacco smoke has an effect on lung function in adulthood, irrespective of the style of life after birth [45, 54].

TOBACCO SMOKING BY PREGNANT WOMEN AND SUDDEN INFANT DEATH SYNDROME

It has been reported that sudden infant death syndrome is directly related with tobacco smoking by mothers during pregnancy. The effect of tobacco smoking on the occurrence of this syndrome does not depend on the position in which the baby slept, or the material standard of the family in which it was reared [55].

TOBACCO SMOKING BY PREGNANT WOMEN AND PREDISPOSITION TO INFECTION AND OCCURRENCE OF CONGENITAL DEFECTS IN THE OFFSPRING

It has been reported that the exposure of foetuses and babies to tobacco smoke results in an increase in falling ill with infectious diseases, e.g. infections of the airways, middle ear, and sinuses, in early childhood [56, 57, 58, 59]. Scientific reports also indicate that congenital defects are more frequent among infants delivered by mothers who smoke [60].

TOBACCO SMOKING BY PREGNANT WOMEN, EPIGENETIC PROCESSES AND HEALTH OF FUTURE GENERATIONS

During intrauterine life the characteristics of the phenotype of an individual are formed [61]. Although the effect of the environment on the phenotypic changes has not been sufficiently recognized, the opinion is uncontested that the exposure of the foetus to hazardous agents transmitted by the organism of the mother induces changes in gene expression (epigenetic) which decide the predisposition of the organism to chronic diseases after birth and in adulthood [62, 63, 64, 65]. Exposure of the mother to environmental factors and placental function plays a major role in the formation of the embryo and development of the foetus [66, 67].

Epigenetic processes take place at the beginning of the development of an organism – from a single fertilized zygote to the development of complicated cells and tissues [68]. In humans, the first division of the fertilized zygote takes place within 24-30 hours after fertilization. The genome of the fertilized zygote is activated between days 1-3 after fertilization, and the implantation of the blastocyst in the uterine wall occurs, on average, 7 days after fertilization. Formation of the placenta begins more or less from day 8 after fertilization, while the differentiation of cells begins 2 weeks after fertilization. Organogenesis ends between weeks 8-9 after fertilization, after which the period of foetal development begins [69].

Changes in the epigenome are the main mechanism, as a result of which prenatal exposure creates the risk of diseases at an older age. The best recognized epigenetic mechanism in humans and other mammals is DNA methylation. It is considered that this is an epigenetic dosimeter which evidences the prenatal exposure to toxic substances, which may lead to health impairment for the entire lifetime [70].

The most sensitive periods of individual human development occur at the initial stage when the methylation patterns generate the development of cells with wide developmental potential throughout the entire lifetime. The periods are as follows: periconception, embryonic, and early organogenesis. The reproductive cells of both the father and the mother are exposed to epigenetic processes, as are the cells of the embryo prior to the implantation in the uterus, and differentiating cells during the post-implantation period of the embryo in the uterus [71]. These periods are characterized by dynamic demethylation, followed by remethylation of the cells. Thus, the prenatal exposure of reproductive cells and the embryo to tobacco smoke may exert an effect on DNA methylation, the phenotype, and predisposition to chronic diseases during throughout the entire life cycle [72, 73].

It was found that arsenic, one of the metals detected in tobacco smoke, is associated with global DNA hypometylation in the studies in vitro [74] and on animal models [75, 76], Cadmium, another metal detected in tobacco smoke, causes DNA hypomethylation and the proliferation of cells [77] which, when accumulating in the placenta, results in the lower birth weight of the foetuses [78]. Polycyclic aromatic hydrocarbons (PAH), which are also components of tobacco smoke, also exert an effect on DNA methylation [79]. Global DNA hypomethylation was also confirmed in epidemiological studies of elementary and junior high schoolchildren exposed *in utero* in foetal life to tobacco smoke [80]. Similar observations have been made in other studies [81, 82, 83].

There is increasing evidence that the environment in which an egg or sperm develops during the periconceptional period, and later the embryo and foetus, decides about the phenotype, the traits of which may be transmitted from generation to generation [84]. Thus, the embryo and then the foetus, when exposed to the effect of tobacco smoke components, changes its phenotype through changes in gene expression without violating their sequence [85, 86].

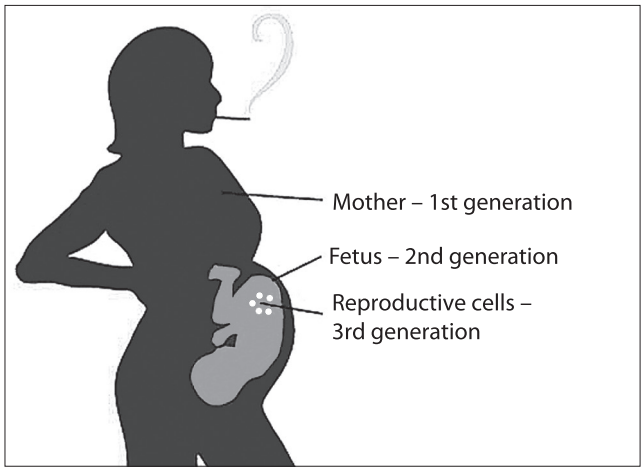

Figure 1. Inhalation of tobacco smoke by a pregnant woman exposes three future generations to its negative effects. The mother is exposed to the direct effect, whereas in the foetus and its reproductive cells these changes are most frequently of the type of epigenetic inheritance [87]

There are hypotheses that epigenetic changes associated with the effect of the environment (including tobacco smoking) on the embryo and foetus, affect the phenotype of the cells and organs of the F1 generation, and subsequently the reproductive cells of the F2 generation. This confirms that tobacco smoking by the mother exerts an effect on the phenotype of the baby, and the phenotype of the baby and its reproductive cells, i.e. phenotype of the F2 offspring [86, 88].

OBJECTIVE – RESEARCH HYPOTHESIS

In the presented study it was assumed that tobacco smoking by parents during the periconceptual period, and by women in pregnancy, may exert an effect on health and susceptibility to civilization diseases among adult offspring and future generations (Fig. 1). The study was based on the Foetal Origins of Adult Health and Diseases Hypothesis – Barker's Hypothesis, and randomized 2011 all-Polish studies of health and health behaviours of adolescents, together with all-Polish population studies conducted during the period 2009-2010 concerning the effect of the state of health and health behaviours of pregnant women on the state of neonates after birth. The studies were carried out based on the all-Polish Health Monitoring System – PL.

METHODS

The analysis covered the following:

1. Results of an all-Polish population study (Youth Behavioural Polish Survey – YBPS) conducted in 2011 among junior high and secondary school adolescents and university students aged 14-24. The sampling frame was the database of the Ministry of National Education (MEN), especially 'Identification of data of schools and educational facilities according to the data by the System of Educational Information (SIO) of 30 September 2010 (No. 2010.09.30/01).

For the purposes of the survey, the sample of post-secondary school adolescents was selected by means of two-stage sampling: at the first stage, a school was selected, while at the second stage – a class for the study. The sample was of a cluster character: all the schoolchildren present in the class selected were qualified for the study by means of a specially designed anonymous questionnaire.

The schools for the study were grouped according to:
- size of the province (three groups according to the number of the population),
- types of provinces into two groups: 1. towns possessing the status of a province, 2. other provinces;
- type of commune into two groups: 1. urban communes (or quarters), 2. rural communes;
- regions into 16 groups,
- type of school into 4 groups: 1. Junior high school; 2. General secondary school; 3. Profile secondary school; 4. Secondary technical school;
- class (age-group) in an individual school.

The sample of schoolchildren was selected from the above-mentioned list of schools and educational facilities (database of the Ministry of National Education of 30 September 2010) which was the sampling frame. At the first stage of selection, the scope of the educational facilities from the list was limited to four types of schools (junior high school, general secondary school, profile secondary school, and secondary technical school), schools were then selected by means of the Statistica and SPSS statistical systems procedures. The sample covered 569 schools from 379 provinces in Poland. The examinations covered all the schoolchildren present in a selected class at a selected school.

The class was selected automatically by means of the EXCEL programme. The advantage of the procedure is that it unequivocally selects the class for the study, which may be checked later. In addition, the resulting numbers are selected in such a way that the random character of the selection of the class in a given age-group is maintained.

The survey was carried out by trained surveyors – employees of provincial sanitary-epidemiological stations. The questionnaire forms were completed by the schoolchildren independently during a lesson. The mean time of completing the questionnaire was 40 minutes. The questionnaires were collected by the surveyors, who subsequently introduced their results into the reply forms within the electronic system of health monitoring managed by the Institute of Rural Health. A total of 10,083 correctly completed questionnaire forms were obtained and then subjected to statistical analysis. According to the definition by the Central Statistical Office (CSO) reproductive age is the age at which a woman is biologically capable of giving birth to a child. In CSO statistical practice, reproductive age (for the temperate climate zone in Poland) of 15-49 is assumed [89]. The presented analysis covered respondents at reproductive age – aged 16 and over.

The questionnaire for the study of students slightly differed from that used for the study of schoolchildren, due to differences in the methods of studying schoolchildren and students. Students were investigated by means of a questionnaire in an electronic form, available on the specified website of the Institute of Rural Health. Access to the questionnaire was provided, and the possibility to complete it by students from the entire territory of Poland. Simultaneously, an information action was conducted concerning the possibility to complete the questionnaire. The survey was anonymous; however, additional data were collected concerning the educational facility and the place

of the respondents' residence (commune). This was used for stratification of the sample and the precise correction of the composition of individual groups of students in the sample.

The correction procedure was conducted by two methods: 1) by elimination (so-called sampling-out) of excessively investigated respondents and questionnaires containing mistakes and repetitions, i.e. a structural correction of the sample; 2) the all-Polish additional data allowed the ascribing of weights to individual questionnaires and the standardization of the sample according to the additional variables. While performing more comprehensive calculations, two procedures were applied, because the first simplified statistical calculations, however, decreased the level of significance of the estimation of parameters and results of testing, whereas the second procedure, which was more troublesome to apply for statistical calculations but used a larger sample (obviously after the elimination of errors). In order to check the compatibility of data from the questionnaire for students with the all-Polish data, this data was compiled with information supplied by the Main Statistical Office concerning higher education facilities in Poland. The differences were considerable and statistically significant. Thus, it was decided to correct the sample of students by corrective elimination (sampling-out) of a relatively small part, making its percentage composition more similar to the all-Polish data according to regions, gender and age (using distribution by age and regions, and according to gender and age). The correction procedure was performed by means of SPSS statistical package.

Subsequently, the questionnaires were statistically analyzed at the Department of Statistics and Analyses at the Institute of Rural Health.

2. The results of population studies conducted with the use of questionnaires within the monitoring of mother and child health – Pregnancy-related Assessment Monitoring System (PrAMS-BabyMo). In 2009, following the Pregnancy Risk Assessment Monitoring System – a surveillance project collecting data on maternal attitudes and experiences before, during and shortly after pregnancy, which has been carried out in the USA since 1987, for the first time monitoring studies in this area were conducted in Poland. The studies were of a pilot character. In 2009, a questionnaire was carried out by the face-to-face method, and from 2010 by the method of independent completion of the questionnaire form (self-questionnaire) by mothers who after delivery stayed in hospitals with their newborn babies. The second section of the questionnaire was completed by the qualified medical staff (physician, nurse or midwife). Every year, the scope of questions directed to the mothers and medical staff was expanded. Figure 1 presents the chronology and methodology of the studies. Since 2011, the studies have been of a prospective character. Mothers were asked to define the form of communication, and 40% of the mothers expressed their consent to participate in further studies. It is planned to conduct a survey by communication by e-mail (74%), telephone (19%) or by mail (7%), 6 months after delivery, and subsequently, when the child is aged 1, 2, 4, 6, 10, 14, 18 years. These are the dates for obligatory examinations of children and adolescents in Poland, so-called well-child care check-up, performed by paediatricians exercising prophylactic care of children. At present, the Institute of Rural Health develops a computer platform for the health monitoring of children and adolescents, based on consulting rooms taking care of children throughout Poland. In the future, it is planned to create 2-3 population cohorts, and conduct an expanded survey with the collection of biological material and its storage. The survey will be of a prospective character.

The survey was conducted by surveyors-employees of Provincial Sanitary-Epidemiological Stations. Mothers hospitalized after delivery provided replies to the questions in the first section of the questionnaire, whereas the second section was completed by medical staff (physician or nurse)

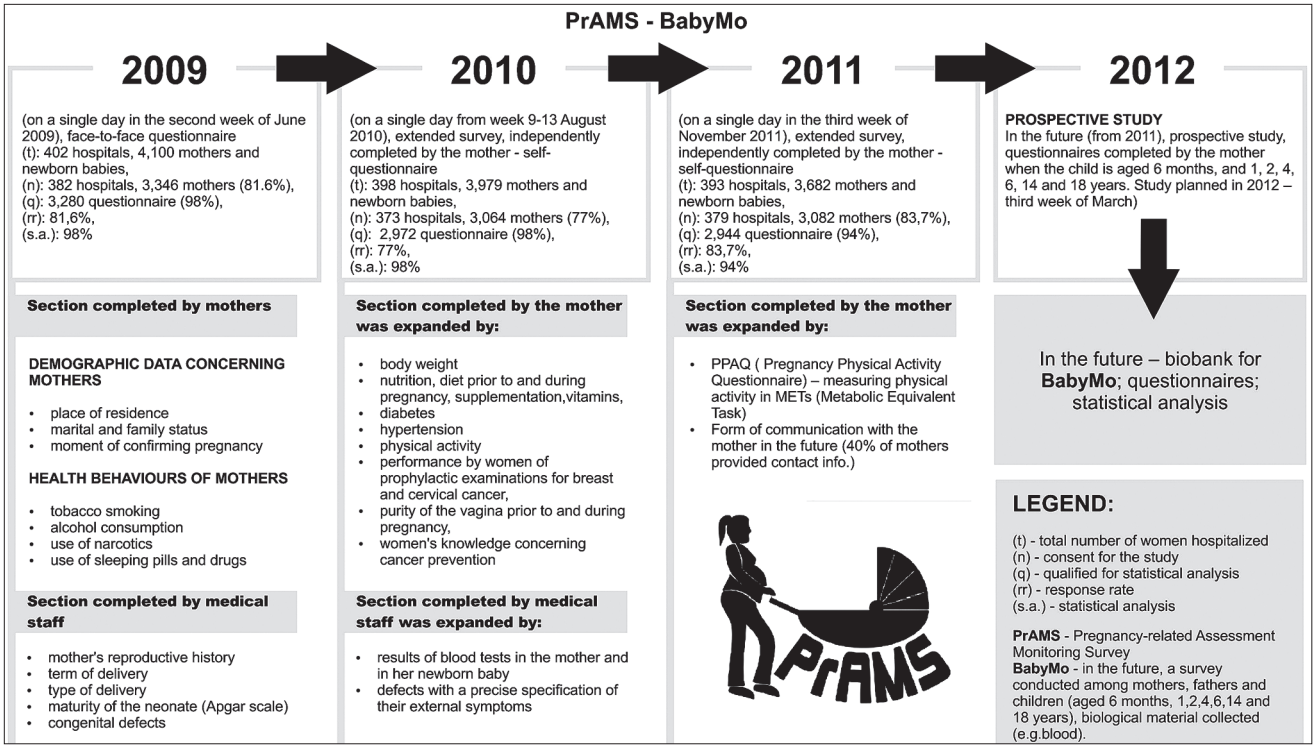

Figure 2. Chronology and methodology of studies

providing care of the mother and her baby, based on medical records (pregnancy chart and history of hospitalization). Consent for the study was obtained from the Bioethical Commission. In each hospital, consent for conducting the study was obtained from its manager. The survey was preceded by sending obstetricians a letter supporting the study, signed by the National Consultant for the Matters of Obstetrics and Gynaecology.

STATISTICAL ANALYSIS

Statistical analysis was performed with the use of the statistical package *Statistica 8.1 PL*. The variables were presented by means of frequency tables, tables with descriptive statistics, and contingency tables. The relationships between categorial variables were analyzed with the use of Pearson's chi-square test. Analysis of the relationships between interval variables were performed by ANOVA test, or, if the assumptions of the parametric method were not satisfied, the non-parametric Kruskal-Wallis one-way analysis of variance was applied.

RESULTS

Tobacco smoking is prevalent among the Polish population at reproductive age. The frequency of smoking in the sample of 11,676 schoolchildren and students examined was 21.4% and changed with age, reaching the highest percentages in the group aged 18-19 (Tab. 1). At this age, 31-32% of males and 24-26% of females are smokers (Fig. 3). It should be anticipated that in the nearest years the offspring will be especially exposed to tobacco smoke during periconceptional and intrauterine period. Due to this situation, during these sensitive periods there may occur unfavourbale epigenetic changes resulting in susceptibility of the offspring to chronic diseases in adult life. At the age of 20 and over, a decrease was noted in the frequency of tobacco smoking among males and females. Nevertheless, 20% of males and females at this age smoke cigarettes, which may also exert an unfavourable effect on their offspring.

Table 1. Tobacco smoking among schoolchildren and students aged 15-24

Age		smokers	total
15	n	226	1,912
	%	11.82%	
16	n	342	1,755
	%	19.49%	
17	n	329	1,257
	%	26.17%	
18	n	388	1,401
	%	27.69%	
19	n	357	1,267
	%	28.18%	
20	n	281	1,187
	%	23.67%	
21	n	194	907
	%	21.39%	
22	n	150	751
	%	19.97%	
23	n	151	725
	%	20.83%	
24	n	81	514
	%	15.76%	
Total	n	2499	11,676
	%	21.40%	

Chi-square exact test, p=0.00001

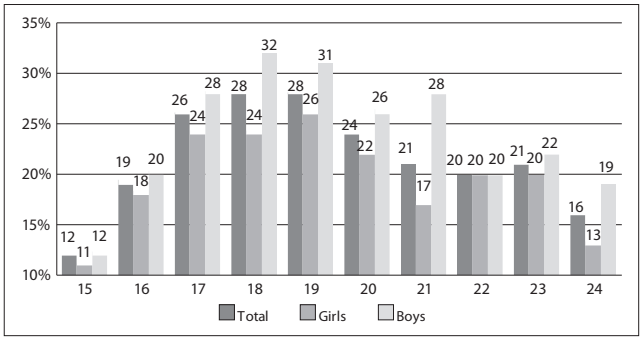

Figure 3. Percentage of tobacco smoking among schoolchildren and students aged 15-24

The replies provided by pregnant women to the questions concerning tobacco smoking are consistent with the replies by adolescents at reproductive age. At the moment of conception 25% of females smoke. The majority of women discontinue smoking in pregnancy; however, 12% of women smoke cigarettes during the third trimester of pregnancy, i.e. throughout the entire period of pregnancy (Tab. 2, Fig.4).

Table 2. Tobacco smoking 3 months prior to conception and during the third trimester of pregnancy

		During pregnancy			
Before pregnancy		none	<5 cigarettes	>5 cigarettes	Total
none	n	1,987	4	0	1,991
	%	99.80%	0.20%	0.00%	75.02%
<=5 cigarettes	n	173	77	2	252
	%	68.65%	30.56%	0.79%	9.50%
>5 cigarettes	n	175	110	126	411
	%	42.58%	26.76%	30.66%	15.49%
Total	n	2,335	191	128	2,654
	%	87.98%	7.20%	4.82%	100.00%

Chi-square exact test: p=0.00001

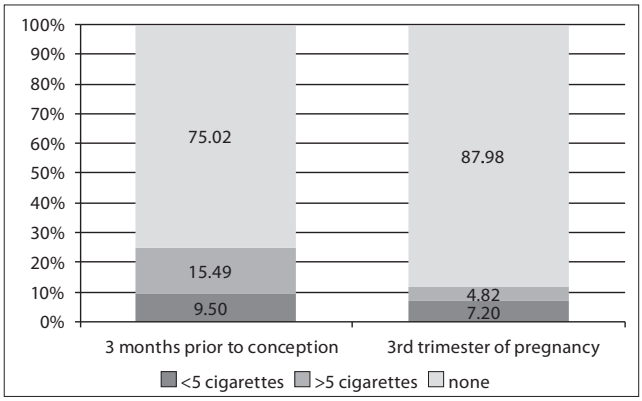

Figure 4. Tobacco smoking 3 months prior to conception and during the third trimester of pregnancy

No differences were observed according to the type of delivery (vaginal or by Caesarean section) between women who smoked and those who did not smoke in pregnancy (Tab. 3, Fig.5).

Table 3. Tobacco smoking 3 months prior to conception and during the third trimester of pregnancy

		vaginal	Caesarean	Total
none	n	1,441	790	2,231
	%	64.59%	35.41%	87.56%
<=5 cigarettes	n	107	79	186
	%	57.53%	42.47%	7.30%
>5 cigarettes	n	92	39	131
	%	70.23%	29.77%	5.14%
Total	n	1,640	908	2,548
	%	64.36%	35.64%	100.00%

Chi-square exact test: p =0.05489

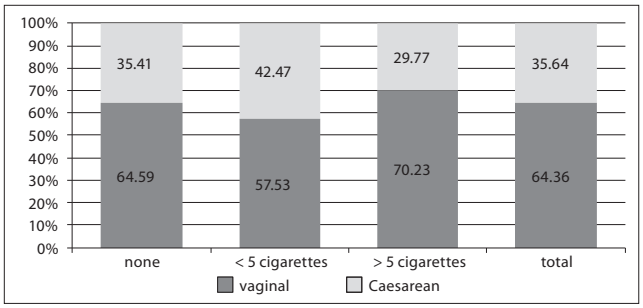

Figure 5. Tobacco smoking during pregnancy and type of delivery

The percentage of pregnant women smoking at any stage of pregnancy decreased with age. More than 27% of the youngest mothers aged under 23 smoked cigarettes at any stage of pregnancy (Fig. 6). The smallest percentage of pregnant women who smoked at any stage of pregnancy was noted in the age group over 34.

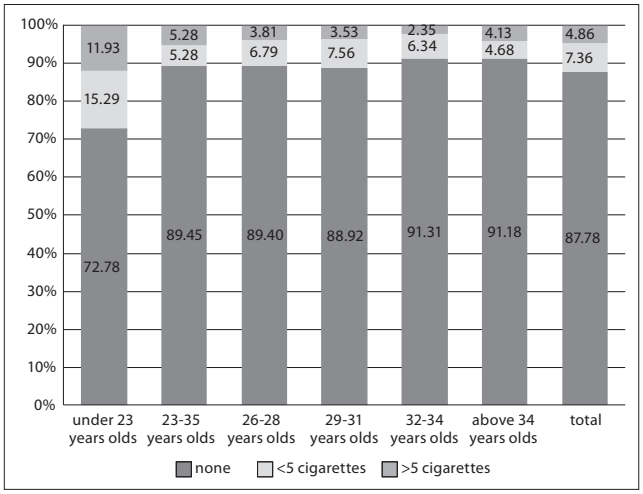

Figure 6. Tobacco smoking during pregnancy and mother's age

Nearly a half of pregnant women with elementary school education smoked during pregnancy. Cigarette smoking in pregnancy decreased with the level of mother's education – more than 20% of mothers with elementary school education smoked more than 5 cigarettes daily at any stage of pregnancy, compared to only 1.3% of mothers with university education. Only 59% of mothers with elementary school education and more than 95% of those with university education never smoked during pregnancy (Fig. 7). No significant differences in tobacco smoking were observed at any stage of pregnancy according to place of residence (Fig. 8).

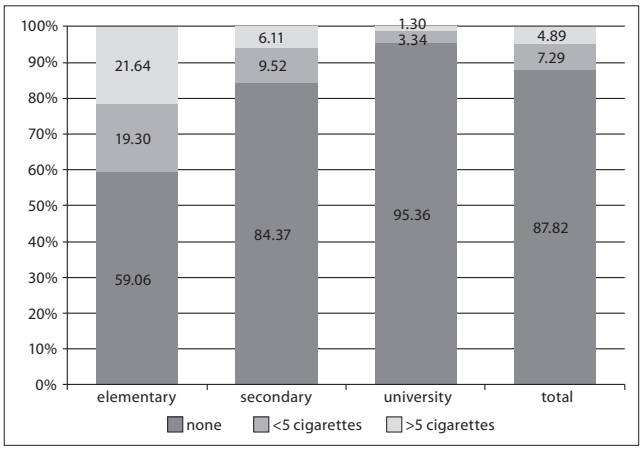

Figure 7. Tobacco smoking during pregnancy and mother's education level

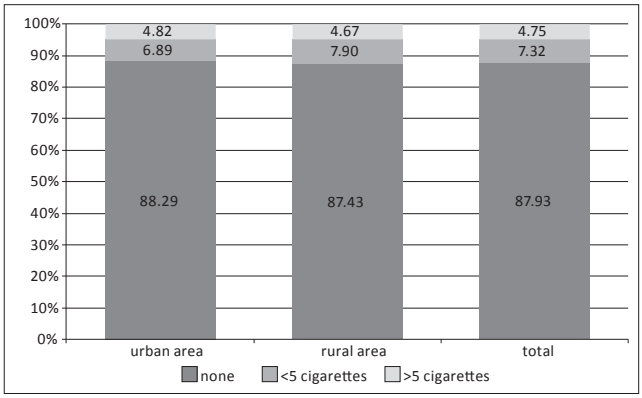

Figure 8. Tobacco smoking during pregnancy and place of residence

Tobacco smoking exerts a negative effect on the birth weight of a newborn. The percentage of newborns with low or very low birth weight decreased with the number of cigarettes smoked by the mother at any stage of pregnancy. 10.62% of infants with low birth weight were delivered by mothers who smoked more than 5 cigarettes at any stage of pregnancy, 9.36% of mothers smoking less than 5 cigarettes daily, and only 6.39% of mothers who never smoked during the course of pregnancy (Fig. 9). An inversely proportional

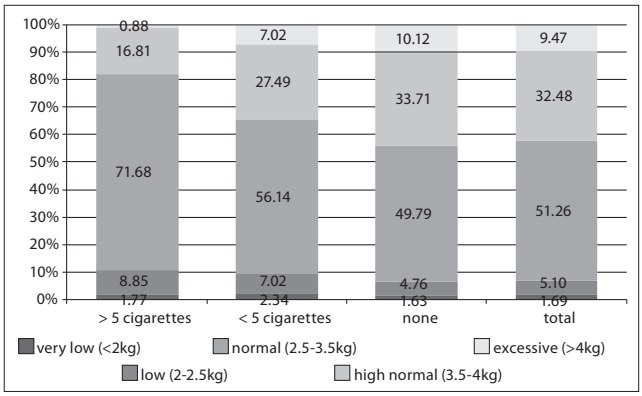

Figure 9. Tobacco smoking during pregnancy and birth weight of the newborn

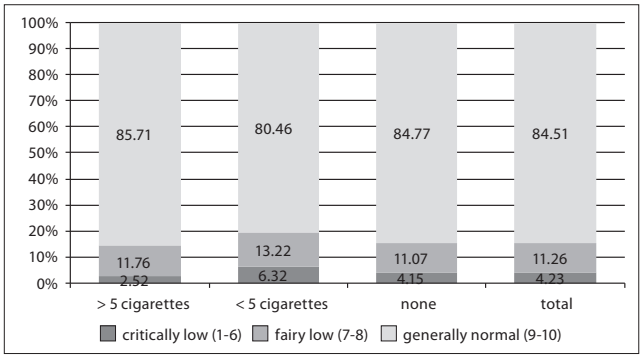

Figure 10. Tobacco smoking during pregnancy and state of the newborn according to Apgar scale

relationship was detected with respect to the percentage of newborns with an excessive body weight (> 4 kg) – women smoking more than 5 cigarettes at any stage of pregnancy delivered less than 1% of newborns with such a birth weight, compared to over 10% of those delivered by women who never smoked in pregnancy. The highest percentage of newborns with a low Apgar score was noted among babies delivered by mothers who smoked less than 5 cigarettes daily at any stage of pregnancy (Fig. 10).

DISCUSSION

The prevalence of tobacco smoking in Poland is still very high [90]. This results in an increased incidence of chronic diseases, which has been confirmed by a number of studies [91, 92, 93, 94, 95]. Despite a decrease in the number of smokers noted after 1990, smoking still remains highly prevalent in the entire population [90]. During this period, the incidence of smoking by females has nearly equalled that observed among males [96]. Mainly the youngest women smoke.

The prevalence of tobacco smoking by pregnant women varies in different countries worldwide: 9.9% in Japan [97], 17% in Australia [98], 30-35% in Spain [99] and approximately 17% in Canada [100]. In the USA, about 10-12% of women declared smoking in pregnancy, despite the decrease in this percentage by nearly 40% within the last decade [101, 102, 103, 104]. The frequency of tobacco smoking by pregnant women depends on their age, social status and race. In selected states in the USA, an increase has recently been noted in the percentage of smoking teenagers who become pregnant [105, 106, 107, 108]. In this country, the percentage of pregnant women aged under 25 who smoke is higher, and also depends on education level, 20% of women aged 20 are smokers, compared to only 9% of smokers among those aged over 35 [109]. 22% of females aged 25 who had a period of education of less than 12 years are smokers, while the percentage of smokers among those with the period of education of over 12 years is 6.5% [110]. At present in the USA, the percentage of smoking women at reproductive age is 22% [104]. The national reports in the USA admit that efforts by public authorities in order to reduce the percentage of women who smoke at childbearing age and pregnant women are relatively ineffective [111]. The goals specified in the official national documents were not attained. In none of the states in the USA was the goal achieved which was assumed in the document: Healthy People 2010 concerning the reduction of the percentage of pregnant women who smoke by 1% by the year 2010. This situation is maintained, despite the fact that in recent years, due to the global actions popularizing knowledge of the hazardous effect of tobacco smoking, a decrease has been noted in the percentage of women smoking during pregnancy in the USA, as well as in the majority of the countries worldwide, including Europe [112, 113, 114, 115, 116]. Nevertheless, within the last two decades, in the majority of countries, tobacco smoking has become increasingly more prevalent among the youngest women [98, 117, 118]. In recent decades, an increase has been observed in the percentage of women who smoke in the youngest age groups, especially in the countries of Eastern Europe [119, 120, 121, 122]. For example, in Romania, the percentage of women who smoke in pregnancy is 24% [123, 124]. The studies conducted in Poland, in the agglomeration of the city of Łódź, showed that the percentage of women who smoke during the period of pregnancy is 25-30%, according to the survey independently completed by pregnant women and examinations of the level of cotinine in blood plasma [125]. The presented studies which covered a large randomized sample of pregnant women did not confirm these observations. The percentage of women who continued smoking in pregnancy was lower. A similar situation has been noted in other countries. In the United Kingdom the percentage of pregnant women who smoke is 17%, the percentage of pregnant women aged under 20 who smoke is 45%, while among those aged over 35 – only 9%. In this country, the percentage of smoking pregnant women who perform physical work is 29%, while among those who occupy the position of a manager – only 7% [126]. Similar relationships have been noted in other countries, e.g. in Canada the incidence of smoking among pregnant women increases with lower education level and lower family income, and is higher among unmarried women and pregnant women aged under 25 [127]. A similar situation is also observed in the countries of the Central and Eastern Europe, including Poland, considering other risk factors, such as alcohol consumption and use of stimulants [128]. Also, pregnant women exposed to smoking at home more often smoke in pregnancy, and more rarely decide to discontinue the habit in association with becoming pregnant [129]. Also, women who abuse alcohol more rarely decide to desist from smoking during pregnancy [130].

In the presented studies in Poland, similar relationships were observed. Mainly, the youngest women are smokers while becoming pregnant, and the majority of women who become pregnant discontinue the habit. However, a high percentage of women continue smoking, while simultaneously being aware of the hazardous effect of smoking for both the course of pregnancy and the foetus.

American reports based on randomized studies show that a part of women who plan pregnancy discontinue smoking prior to conception [131, 132]. From among women smokers in this country, 14% discontinue the habit prior to becoming pregnant, a half of them cease smoking in pregnancy, including 75% of those who stop smoking in the first trimester of pregnancy. 10% of women smoke throughout the entire period of pregnancy [133]. Similar percentages are noted in the USA according to the Pregnancy Risk Assessment Monitoring System (PRAMS) [134]. Also in this country, women with a lower education level more often smoke during pregnancy [135, 136, 137]. In American

studies, the phenomenon was observed of reducing the number of cigarettes smoked daily by pregnant women with the advancement of pregnancy. The number of pregnant women who smoked more than 15 cigarettes daily decreased with the age of pregnancy, while an increase was noted in the number of those who smoked less than 15 cigarettes daily [80]. Women who planned pregnancy discontinued smoking one month earlier than those who did not plan pregnancy.

According to the reports from various countries worldwide, more than 60% of women who smoked before becoming pregnant, ceased smoking during pregnancy [138]. These percentages are similar in European countries [133], and slightly lower in the USA (45%) [139, 140, 141, 142].

Low birth weight of neonates and premature births were most frequent among women who smoked throughout the entire period of pregnancy, whereas most rarely occurred among women who did not smoke during pregnancy and before conception. Women who discontinued smoking during pregnancy were also characterized by a lower percentage of babies born preterm and with low birth weight, compared to those who continued smoking for the entire period of pregnancy, this percentage being higher compared to never smokers. This shows that the cessation of smoking at any stage of pregnancy exerts an effect on the term of delivery and birth weight of a neonate. Similar relationships were obtained in the presented study.

Recent reports from England and Wales indicate that the incidence of congenital defects in mothers aged under 20 is higher than among neonates delivered by mothers aged 30-34 (139.8 per 10,000 vs. 116.5 per 10,000). This contradicts the to-date commonly adopted scientific opinions. The researchers investigating the problem explain this situation by a higher percentage of mothers who smoke in the youngest age groups, and the lower percentage of women taking vitamins and folic acid due to a higher percentage of unplanned pregnancies [143]. In the presented study, no such a relationship was observed, which was probably due to the relatively small population of laying-in mothers hospitalized in Poland after delivery.

The limitation of the presented study is that it is based on replies to the self-questionnaire items independently provided by women, or on questionnaires collected by the surveyors. The reports show that the quoted percentage of pregnant women is underestimated, while the declaration concerning the discontinuation of smoking is overestimated. This was confirmed by the study which included a simultaneous examination of the level of cotinine [144, 145, 146]. Comprehensive reviews of literature confirm these observations [124, 147]. However, while comparing data pertaining to independent replies of mothers to the self-questionnaires with the levels of cotinine measured in cord blood of the neonates, a convergence is noted between the replies and the observed levels of cotinine in 94.9% of non-smoking mothers, and 87% in those who smoke [148]. In other studies, it was found that 13% of women who declared that they discontinued smoking prior to becoming pregnant, had a level of cotinine evidencing active smoking, while 25% of mothers who admitted that they ceased smoking in pregnancy had level of cotinine confirming tobacco smoking [148]. However, the reservation is made that these discrepancies may be caused by the passive exposure of pregnant women to tobacco smoke [149]. It is commonly adopted that the studies with the use of questionnaire forms, especially self-questionnaires independently completed by women, are a valuable source of information concerning the prevalence of tobacco smoking among women during the period of pregnancy [150]. In conditions of epidemiological studies which cover the entire Polish population, this is the only method which allows examination of the tobacco smoking habit among pregnant women.

CONCLUSIONS

In Poland, tobacco smoking is still very prevalent among pregnant women. Despite being aware of the hazardous effect of tobacco smoking on the course of pregnancy and the development of the foetus, more than 12% of pregnant women smoke during pregnancy. Smokers are mainly pregnant women from the youngest age groups. Exposure to the components of tobacco smoke results in a lower birth weight of the neonates and their worse state after birth, as measured by means of the APGAR scale. According to the Foetal Origins of Health and Diseases, the observed phenomena may exert an effect on the health of the offspring and future generations. It seems that the increase in morbidity due to civilization diseases which have been observed in Poland during the last decades, may be the result of smoking during pregnancy by mothers of these individuals, which may also be confirmation of this hypothesis [151]. Public health authorities should undertake efforts directed at females at reproductive age, as well as young males, which would enhance their awareness of the negative effects of tobacco smoking during the periconceptual period and in pregnancy. It is recommended that women who plan pregnancy and those who are pregnant should be afforded the possibility to discontinue the tobacco smoking habit. Paediatricians who provide care for neonates and children should familiarize the mothers with the risk of the phenomenon of catch-up-growth after delivery in dystrophic neonates born with low birth weight, because, according to the Baker's hypothesis, this phenomenon is the cause of susceptibility to civilization diseases in later life cycles. The normal trajectory of development may efficiently prevent this phenomenon.

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