IMPACT OF TOBACCO SMOKING DURING THE PREGNANCY ON THE PERINATAL OUTCOMES

Ph.D Thesis

Andrea Fogarasi-Grenczer

Doctoral School of Pathology
Semmelweis University

Supervisor: Péter Balázs, MD., Ph.D., professor

Official Reviewers: Zsófia Mészner, MD., Ph.D., director general
Péter Vajer, MD., Ph.D., assistant professor

Haed of the Final Examination Committee:
Júlia Hajdú, MD., Ph.D., professor
Members of the Final Examination Committee:
Tímea Tóth, Ph.D., associate professor
Ágnes Tóth Kovácsné, Ph.D., associate professor

Budapest
2015

INTRODUCTION

In the last few decades, many interventions have been carried out in order to stop the smoking epidemic; however, the significance of public health problems caused by smoking have not decreased in Hungary. The main reason for this is that almost one third (29%) of early deaths (<65 years) are caused by smoking (Vitrai et al., 2012). Tobacco smoke is the first harmful material which is able to affect the health of non-smoking people living in the environment of the smoker, causing serious damages in the health of the children and adult family members who live together with the smoker (Balku et al., 2013). A very special case of secondhandsmoking is smoking during pregnancy. As a result of this, the fetus can be seriously injured in the expectant mother's body. Due to the high number of harmful components and to complex biological effects of tobacco smoke, the consequences cannot only occur perinatally, but it can also influence later life periods, decreasing the possibility of a healthy life. (Eriksen et al., 2015)

There are several aspects which justify the significance of the force to deal with smoking during pregnancy. Primarily, the smoking habits of young people are determinative, as they become smoking women and men in fertile age. Currently, 24% of 13-15-year-old teenagers smoke; 9.5% of them smoke on a daily basis. In the same age group, the proportion of participation in prevention programs declined (by 20%) by 2013, which is about 44% (Balku, 2013). The proportion of regular smokers reaches 32% by the age of 17 (Német, Költő, 2010). The highest rates concern those capable of child-bearing or who are fertile, as 29% of women at the age of 18-34 and 42% of men are regular smokers (ELEF, 2014). These facts emphasize the role of the importance of primary prevention started at an early age, the protection of non-smokers, the regulation of marketing activites, and the role of tax policy.

Those women who continue smoking during their pregnancy form a very special group. In this group, the most difficult field of careis cessation support, as these women did not consider the motivation which would have been the protection of their child concerning giving up smoking. Their proportion during their first registering was the following in the past two decades:

- in 1997 17% (Szauer, 2000),
- between 1999 and 2009 14% of them on average (Moravcsik-Kornyicki, 2013) and
- in 2014 – with a significant increase – 21.6% smokes on a daily basis.

- in 2014, 42.3% smoked in the counties of Northern Hungary (GYEMSZI, 2014).

At the time of learning about pregnancy, based on international results, about 45-55% of smoking women decide to give up smoking (American College of Obstetricians, 2010), but following delivery, unfortunately, the proportion of those relapsingwithin six month is very high (about 40%), which highlights the continuous need of support of this group (Kendzor, 2010) (CDC, 2015).

There are complex reasons in the background of the emergence of smoking. There is a strong correlation between its proportion and the income level of households, because smoking is more frequent in families with the lowest income. The level of income is mainly influenced by the level of education. In poor or impoverishingfamilies, the occurence of individual or family crisis is frequent; however, the system of ways of handling conflicts is insufficient. Therefore, personal crisissituationsmust be regarded as factors which maintain smoking addiction (Scharle, 2012).

The prevalence of smoking shows differences in all age groups of the Roma and the non-Roma population. In fertile age, 66% of Roma women smoke regularly (Ádány, 2011). Smoking during pregnancy concerns Roma women in a much higher proportion as opposed to the non-Roma. In Northern Hungary, 47.3% of Roma expectants smoke throughout the first period of their pregnancy (Balázs et al., 2014).

During pregnancy, the intrauterine life is considered to be sensitive, critical in a teratological term. During the period of organogenesis, the intensive development of organs happens. From the 12th week on, the development of organs is of quantitative nature, but in the central nervous system, there is still qualitative development. Those damages which occur as a result of smoking are dose-dependentin case of the embryo/fetus (Ádám, Rigó, 2009). There are more than 7000 harmful components in tobacco smoke, which also enter the blood circulation through the placenta. These are responsible for the disordersof the placenta or the lungtissue, they have a negative effect on the secretory organ and on the development of the nervous system; they also cause worseningstreamingconditions in the umbilical cord, and because of this, in the fetal organs. The fetal carbon-monoxide level reduces the oxygen level of the blood and tissues, and as a result of this, it causes hypoxia. As a result of maternal smoking, the occurence of preterm birth, low birth weight, retardation in the womb, and still birth cases increase (Chhabra et al., 2014, Räisänen et al., 2014). It can cause further serious problems if, following the delivery, the mother or her family members smoke in the environment of the infant or the growing child. Environmental tobacco smoke exposure

caused by this, according to the previous term "passive smoking", increases the risk of cardiovascular diseases, tubercolosis, infectious ear diseases, and SIDS in the developing organism, and it is also responsible for the occurence of several other symptoms (ASH research report, 2014).

AIMS

The aim of the examination was to get to know some factors of smoking during pregnancy in Hungary. The results of the research can provide an opportunity to make primary prevention programs which support cessation more efficient regarding both the devices and methods through the professional analysis of the characteristic features of the expectant population.

THE DETAILED AIMS OF THE RESEARCH

1. To get to know the proportions of non-smoking and smoking expectant population in the disadvantaged and underprivileged counties of Hungary.
2. To reveal the variables of some demographical, sociological, economic background, to get to know the correlations, and to publish the results.
3. To test the predictors of smoking during pregnancy in order to be able to make a questionnaire adapted to Hungary to learn about the risks of smoking for experts who participate in pregnant care.
4. To clarify the effects of smoking during pregnancy on the fetal biometry, involving other multipler controll variables.
5. The measurement and the identification of dependency level risks and their effects on perinatal outcome results.
6. Curriculum development. To build the results into the syllabus of the courses in higher education. To develop the knowledge and the skills of students to be able to provide cessation support with the precise presenting of the characteristics of pregnant population who smoke during their pregnancy.

METHODS

Antecedents

Hungary is in a disadvantaged position from many aspects concerning the comparison of international frequency of smoking and the consequences of smoking (Eriksen, 2015, KSH, 2014). Because of this, via the Fogarty International Center, the National Institute of Drug

Abuse, and the National Istitute of Health (NIH), the Federal Government of the United States of America also supported an extended smoking research program in Hungary between 2008 and 2013 organized by Davidson College (USA, NC) and Semmelweis University (G. N: 1R01 TW007927-01). Out of the nine subprojects of the program, this study shows the reasons for smoking during pregnancy and its main perinatal outcomes.

General methods

Through a retrospective cohort study, with a structured interview questionnaire, we carried out data collection in North East Hungary, in Borsod, Szabolcs, Heves and in Nógrád County. There were five data collections in the four countries between 2009 and 2012, as we carried out data collection in Szabolcs County in two different years (in 2009 and in 2012) (marked as Szabolcs-I, Szabolcs-II).

The ethical permission was given by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics(TUKEB 103/2009). We asked four health visitors working in the counties to make the personal interviews. Firstly, we provided a written description of the aims of our research for the employers of the health visitors who took part in the examination, and we asked for their consent to let the health visitors take part in the survey. Following the acquisition of the necessary permissions, in every single village, we prepared the health visitors for the tasks they had to carry out through the interview on our own. We put great emphasis on this, as the role of health visitors in interview making was of key importance for the research, as the data collection had to be done in a consistent way.

The Importance of Standard Methods During Data Collection:

The examination of pregnant women's health behavior can cause the difficulty that – due to the negative social judgement of smoking during pregnancy – the mother might not provide real, reliable data. We tried to eliminate or reduce this difficulty with the fact that, in every case, the mother was interviewed by the person who took care of her throughout her pregnancy and after delivery, as well.

Sample

The complete target population consisted of expectant mothers and newborns registered in the areas of health visitors (N= 22,325), and the response rate was 76,71% (N= 16,336). The participants of our resrearch were mothers who gave birth to their babies within one year, and they had live birth cases. Our data collection also concerned those mothers who gave birth to twins, but throughout the procession, we considered the fact that in the samples of infants in

international publications on smoking during pregnancy, there are only single pregnancies (Vogazianos et al., 2005).

The Data Sheets of the Questionnaire and the Grouping of Questions

We used two data sheets in our data collection. The first data sheet (Data sheet I.) was filled in by the health visitor, based on the documentation of the person in care (examinations and the results of some laboratory screening tests, obstetrical, neonatological final reports, newborn reports of hospitals) and based on the reports of the results of screening tests of consultations during pregnant care and based on the results of home visits.

The group of questions of Data sheet I.

- demographical data
- data of pregnant care
- the most important data of the newborn (biometry, APGAR values, infant illnesses and diseases, developmental disorders)
- BMI of the mother, illnesses prior to and during her pregnancy
- health behavior during the time of taking into care (mainly the features of smoking)

Data sheet II.: Interview done by the health visitor in the mother's home, with six groups of questions

- general social and economic data (national self-identification)
- the health status of the mother (prior to and during pregnancy)
- the data of obstetrical anamnesis
- the data of the newborn (biometry, number of days spent in hospital, breast feeding, congenital and acquired disorders)
- the features of smoking of the expectant (39 questions) and her environment (18 questions) (the internationally validated questionnaire of Fagerström Nicotine Dependency)
- the measurement of the mother's mood during data collection with the help of the internationally validated EPDS (Edinburgh Postnatal Depression Scale) questionnaire

Methods of Analysis

The data were registered and analyzed with IBM SPSS v. 20.0 program for statistical analysis.

In descriptive statistical analyses, the categorical variables are with the distribution coefficients, out of which the dichotom variables were done based on internationally accepted definitions. In the complex statistical analyses, the checking of the relationship between the categorical variables was done with Chi-squared test, in case of the comparison of the expected values of continuos variables, it was done with two-sample t-test. The identification of the odds ratio of smoking during pregnancy and abstinence during pregnany happened with 95% confidence interval with the involvement of different variables. In case of complex analyses, I applied binary logistic regression analysis in order to be able to determine what kinds of socio-economic, demographic, and other maternal variables influence significantly the development of smoking during pregnancy and its giving up. I applied linear regression analysis to estimate which maternal variables have the greatest effect on the weight of the newborns and to determine the strength of the effects of maternal smoking and environmental tobacco smoke exposure.

RESULTS

The Introduction of the Statistical Results of the Whole Sample

During the data collection in five counties, N= 16,336 individual interviews were made, and the proportion of answers was 76.71% in the examined years in the examined areas.
The average age of the whole sample was 28.3 (StD±6,08) years, min.: 13 years, max.: 49 years. 46.7% lived in towns, 51.4% in small towns, and 1.9% lived in areas without access to health care. 51.7% of the expectants is married, 42.9% of them lives in cohabitation, 3.9% of them is single, and 1.6% of them is divorced or widower. 3.6% of them is under 18, 80% of them is between 18 and 34 years, 12.8% is between 35 and 39 years, and 3.6% is ≥40 years.

64.2% of the whole sample is non-Roma, 34.6% is Roma, and 1.2% of them is the member of a nationality living in the territory of Hungary or outside the territory of Hungary. The proportion of primary education (8 grades) or education level under that is 36.8%, 18% of them is skilled worker, 25.5% of them has school leaving exams, 19.7% of them attended higher education. 42.7% of the sample was active worker priort to her pregnancy, 23.5% was unemployed, and 33.8% did not work (maternity grant/student/disabled). 44% of the whole sample lives in deep poverty (limit <30000 HUF/month/family member), 28.1% of them lives in poverty, 24.7% of them has average income, and the income of 3.2% of them is higher than the average.

The expectants' first registering by health visitors happened on gestation week 11.07

(StD±4,6). The proportion of unexpected pregnancies is 32.5%. The number of previous pregnancies was 2.42 (StD±2.01), and the number of deliveries was 1.91 (StD±1.46). The average of gestation weeks did not differ significantly in the different counties, the average was 38.7 weeks (StD±1.88). Based on the results of the five data collections, the biometrical data of births were similar in the counties. The average of birth weights was 3210 grams, and the difference between the averages of the lowest and highest birth weights was 72.9 grams. The average of birth weight is the highest in Borsod (3248 grams), and it is the lowest (3175 grams) in Szabolcs II.

Based on the dichotomy of the smoking and non-smoking, the differences of demographic, social, and economic results were the followings:

- → the proportion of mothers under 18 is 2.6%/4.5%, in the other age groups between the ages of 18-34 years 80%/81,9%, between the ages of 35-39 years 13.9%/9.8%, ≥ 40 years 3.5%/3.8%
- → the number of children living in families 1.28/1.85
- → living in towns: 50.9%/35.0%, living in small towns 47.5/61,9%, living in areas without access to health care: 1.6%/3%
- → smokes during pregnancy on average: non-Roma: 33.7%, Roma: 64.5%, of other nationality: 1.8%
- → the proportion of non-smoker expectants living in marriage: 59.5%, smokers living in marriage: 29.4%
- → lives in cohabitation: 36.0%/63%, single: 3.2%/5.2%, divorced or widower: 1.3%/2.4%
- → primary education or under that level: 25.1%/70%, skilled worker: 17.9%/18.5%, school leaving exam: 31%/9.7%, attended higher education 26%/1.8%,
- → active worker: 51.6%/16.9%, unemployed 19.1%/36.1%, was at home (maternity grant/student/disabled): 29.3%/47%
- → lives in deep poverty: 33.3%/73.7%, lives in poverty: 31.4%/19.1%, is with average income: 31.3%/6.4%, above average income: 4%/0.8%
- → is not satisfied with her income: 82.1%/93.3%

Data in Connection with Smoking

Directly before pregnancy, 38% (6117 mothers) of the whole sample smoked on a daily basis, with the frequency of 8.7 smoked cigarettes/mother/day. Out of the smokers, 35.6% decided

to give up smoking when they learned they were pregnant, 64.4% (3936 mothers) continued smoking. 32% (1269 mothers) continued smoking with the same number of smoked cigarettes per day, while 68% (2667 mothers) reduced the number of smoked cigarettes per day. The outcomes of the Fagerström dependency levels among expectants are the followings:

- → very low dependence 28.9% (1226 mothers)
- → low dependence 35.6% (1510 mothers)
- → low to moderate dependence 26% (1104 mothers)
- → strong dependence 8.7% (371 mothers)
- → very strong dependence 0.7% (31 mothers)

41.6% of mothers who smoked during their pregnancy tried to give up smoking (unsuccessfully, as they continued smoking throughout their pregnancy), and 58.4% of them did not even try to give up smoking. Only 2% asked for help to be able to give up smoking. Figure 1. shows the average and the distribution of the number of smoked cigarettes per day

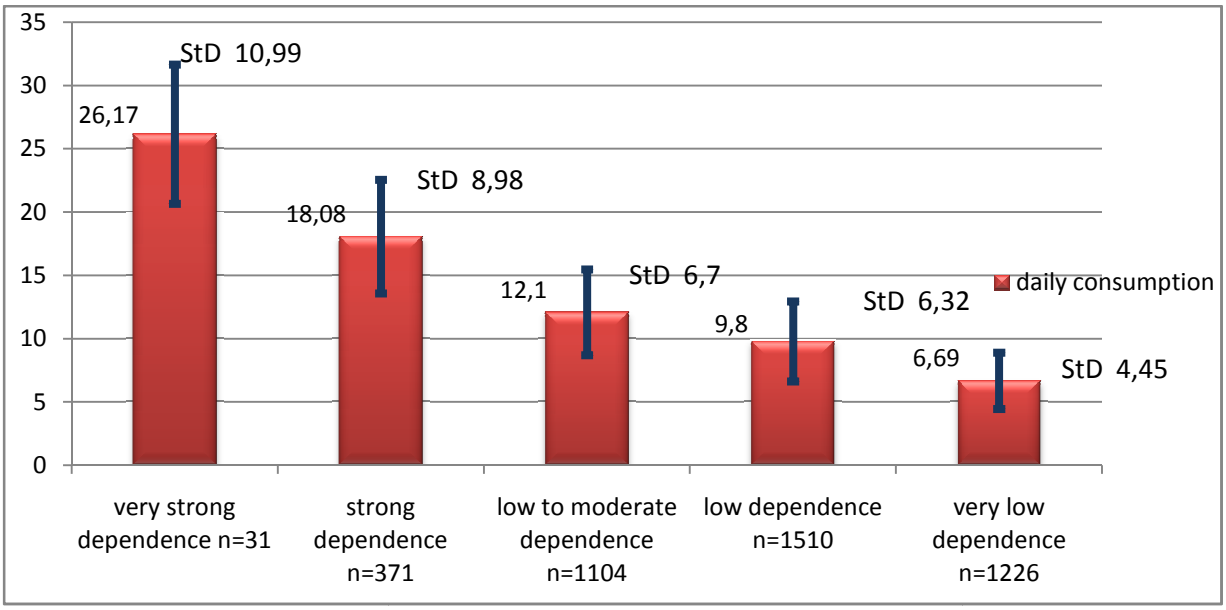

Figure 1. The average number of smoked cigarettes per day according to the categories of Fagerström dependence. (N=4242)

Perinatal Outcome Results

In the non-smoking sample, the frequency of preterm births, low birth weight, stillbirths, developmental disorders is much lower as opposed to the results of the smoking sample. There are significant differences in the groups with different dependency levels. With the increase of dependency level, the proportion of all the perinatal indicators significantly grows (Table 1).According to the strength of the dependency level, the average of gestation weeks is lower at birth. While in the group smokers, delivery happens on gestation week 38.8 (± 1.78)

on average, it is on week 37.8 (±2.5) in the group of strong dependence. In the group of non-smokers, 4% ofall preterm births happen on week ≤28. Among smokers, the proportion is the highest in the group with low to moderate dependence (8.1%).

Table 1. Obstetrical outcomes among non-smokers and among smokers based on the different dependency levels according to Fagerström.

SMOKING STATUS	PTB[1] (%)	LBW[2] (%)	Previous stillbirth (%)	Congenital malformation (%)	Time of registration (StD)
Non-smoker (n=11313)	6,6	6,5	1,1	3,8	10,7 (4,0)
Smoker, very low dependence (n=1226)	9,2	13,5	1,9	4,4	12,2 (5,2)
Smoker, low dependence (n=1510)	11,3	14,4	2,1	3,9	12,5 (5,6)
Smoker, moderate dependence (n=1104)	13,5	17,4	3,7	5,3	13,3 (6,0)
Smoker, high/very high dependence (n=402)	17,4	24,4	3,5	7,0	14,5 (6,4)
Total	**11,6**	**15,24**	**2,46**	**4,9**	**12,6 (5,4)**

[1] *PTB (< 37 gestational week)* [2] *LBW (≤ 2499 gram)*

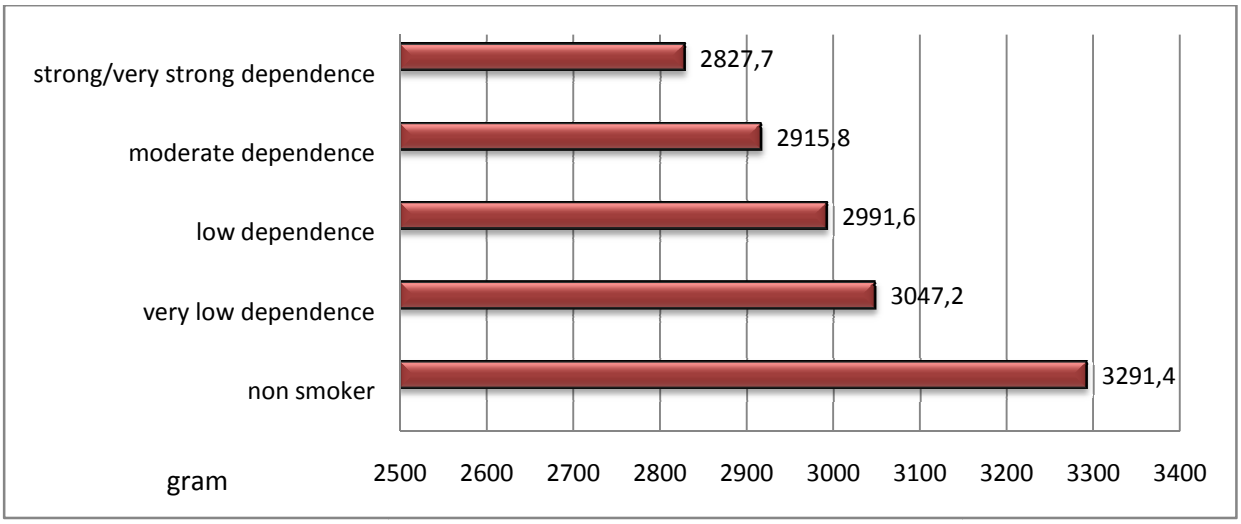

Figure 2. The comparison of weight averages based on the grouping of Fagerström smoking dependency. N=4242

It can be seen on Figure 2 that with the increase of dependency levels, the weight of newborns decreases. The birth weight of non-smoker expectants' babies is higher by 464 grams than strong dependents'. The time of registration of expectants happens later in case of stronger dependency levels, because while it happens on week 10.7 in case of non-smokers, strong dependents only go to their health visitors on week 14.5 for the first time.

The Most Important Data Concerning Roma Nationality

49.2% (4263 mothers) of Roma expectants smokes on a daily basis, as opposed to the non-Roma (10.055 mothers), where the frequency is 15.6%. 35% of the Roma smoke more than 10 cigarettes a day; the proportion of this is 17.1% in the non-Roma group. Out of the Roma expectants, 12.1% gives up or stops smoking, in the non-Roma group, this proportion is 52.1%. 70% of the Roma expectants suffer from environmental tobacco smoke exposure, in case of the non-Roma group, this is 30.8%.

The Results of the 2x2 Contingency Analyses

The analysis was carried out in two models. The first one examined what the chances are of smokers who smoked regularly during their pregnancy as opposed to non-smokers, through some dichotomous maternal variables. In this model, low level of education [OR=10.2 95% CI (9.21-11.36)], the smoking partner [OR= 7.31 95% CI (6.66-8.02)], and unemployment [OR=5.77 95% CI (5.20-6.41)] had the strongest effect, as well as deep poverty [OR=5.61 95% CI (5.16-6.09)], which is strongly related to unemployment.

The second contingency analysis examined what the odds ratio values were on smoking during pregnancy as opposed to giving up smoking, through some dichotomous maternal variables.In this model, low level of education [OR=10.12 95% CI (8.88-11.52)], Roma origin [OR=7.80 95% CI (6.79-9.04)], and not comfortable living circumstances [OR=7.19 95% CI (5.86-8.80)] had the strongest effect.

The Results of Binary Logistic Regression Analysis

In the test model of giving up smoking, besides low level of education [OR=5.63 (2.26-9.73 95% CI)], the partner's smoking [OR=2.29 (1.75-3.01 95% CI)] and unexpected pregnancy [OR=1.76 (1.35-2.28 95% CI)] have a very strong effect, but Roma origin, deep poverty, bad living circumstances also significantly influence the chances of cessation.

The Result of the Multivariate Linear Regression Model

Considering many factors at the same time, maternal BMI has the strongest effect on the newborn's birth weight (-185 grams), smoking during pregnancy is also very significant (-178

grams), as well as Roma origin (-131 grams). The combined presence of the further factors (environmental tobacco smoke exposure, bad living circumstances, low level of education) can lead to the decrease of the birth weight by 660 grams.

CONCLUSIONS

- There is no database in Hungary, which shows the proportions of smoking during pregnancy based on trimesters, in a structured way. The health visitor part of our national documentation system (expectant mother's registry sheet, pregnant care book) does not contain questions concerning smoking or addiction anamnesis. This way of exact registration of the expectants is an important public health concern, because, based on the data, it would be possible to draw conclusions concerning the correlations of the health behavior prior to and during pregnancy and concerning the possible perinatal outcomes. The analysis of the results would be vital for the intervention planned for the target population. Standardized data collection could contribute to the fact that Hungary could be present in the European data bank.
- 26.16% of expectants living in the areas of Northern Hungary and on the north of the Great Plains smokes throughout her pregnancy. This ratio is close to the smoking proportions of the whole Hungarian woman population, so fertile women living here are endangered, which must be considered during their pregnant care.
- Smoking during pregnancy is related to the mother's unfavorable social, economic, and demographic situation. Out of the indicators, level of education, level of income, cohabitation, and sinlge status are of great importance. The effects of the aforementioned factors on the presence of smoking during pregnancy can still prevail besides the controlling of many other factors - social, economic, demographic.
- Half of the Roma expectants smoke during their pregnancy, and less of them decide to stop or pause smoking. Their health status and the development of the fetus can be further destroyed by the high proportion (70%) of environmental tobacco smoke exposure. Therefore, in the system of pregnant care, special attention and help are needed in this field, and it would also be necessary to involve mediators to make care more efficient, where the proportion of the Roma is high within the population.
- The perinatal results of some mothers with different dependency levels can show huge differences. Our researches point to the fact that the increase of dependency levels significantly influences the occurrence of preterm birth ratios, low birth weight, still

births, and developmental disorders. Therefore, all the opportunities of nicotine replacement must be thought over in case of low to moderate dependence and strong dependence, with the possible public funding support. We must strive for the reach of total abstinence, but the slightest change (the reduction of the number of smoked cigarettes and environmental tobacco smoke exposure) can also have serious effects. The most important aim is the training of expert skills to be able to provide information in connection with this and to enhance motivation, because efficient work is impossible without special guidance.

- In Hungary, the frequency of smoking, the high ratios of youngs and expenctants, smoking related illnesses, and the occurrence of deaths all highlight the importance of the necessity of changes on macro level. Most of smokers live in disadvantaged position (unemployed, have low level of income, low level of education, bad living circumstances). To overcome psycho-social stress in the medium and long term, the increase of employment, the positive changes of income levels, the reach of higher level of education, and, this way, the changes in the value system of the endangered population could mean the more stable solution.

PUBLICATIONS RELEVANT TO THESIS

Book chapter

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11. Balázs P, Foley KL, Grenczer A, Rákóczi I. (2011) Some Demographic and Socio-economic Features of the Roma and Non-Roma Population Based on the Obstetrical Data of 2009. (Roma es nem-roma népesség egyes demográfiai és szocio-ökonómiai jellemzői a 2009. évi szülészeti adatok alapján). *Magyar Epidemiologia* 8(2):67-75.

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THE LIST OF PRESENTATONS, POSTERS IN CONNECTION WITH THE DISSERTATION

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2. Tarcea M, Abram Z, Grenczer A, Penzes M, Balazs P, Foley K. Active Smoking - a risk behavior for pregnant women from Mures county, Romania, SRNT Europe 15th Annual Meeting, 18th-20th September, 2014, Santiago de Compostela, Spain, Poster session 2 Saturday No. 234. http://2014srnt.sergas.es/Documents.aspx
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