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Tobacco influence on the neonatal outcome

Elizabeta Zisovska[1], Liljana Lazarevska[2], Nevena Pehcevska[1], Gabriela Tavcioska[3]

[1]Clinic for Gynecology and Obstetrics, Skopje, Republic of Macedonia; [2]Institution for Public Health, Skopje, Republic of Macedonia; [3]General Hospital, Prilep, Republic of Macedonia

Correspondence to: Elizabeta Zisovska, Department of Neonatology, Clinic for Ginecology and Obstetrics, Marshal Tito Street 6-2/16, 1000 Skopje, Republic of Macedonia. E-mail: zisovska@yahoo.com

Abstract

Background: Cigarette smoking, active or passive, is related to adverse perinatal outcomes, increased risk of spontaneous abortions, preterm delivery, low birth weight, malformations, placenta previa, and abruption. It is also known to have adverse effects on the fetus and newborn, as well as affecting breastfeeding. The literature data gave the initial idea to identify some possibly smoking-influenced conditions on perinatal/ neonatal outcome indicators.

Patients and Methods: Newborns and their mothers admitted to Gynecology& Obstetric Clinic, Skopje, Macedonia were selected to participate in the study. The patients were divided into 3 groups: the first group consisted of newborns unexposed to tobacco smoke, the second group were newborns born to mothers who smoked more than 20 cigarettes per day, who did not try to quit smoking during the pregnancy, and the third group were newborns born to the mothers who don't smoke, but were in close contact with other smokers (intensively exposed to the tobacco smoke).Methods used: epidemiological, clinical examinations, biochemical analysis and statistical analysis of the results.

Our results clearly demonstrated that maternal smoking had a significant effect ($p<0.01$) on indictors for perinatal/neonatal outcomes such as: prematurity combined with low birth weight (3,3% vs 12% for the first and second group respectively, and 3,3% vs 9,7% for the first and third group respectively), Apgar scores <6 in the 5-th minute (5,3% vs 13,7% for the first and second group respectively, and 5,3% vs 12,7% for the first and third group respectively), elevated NRBC (2,3% vs 14,7% for the first and second group respectively, and 2,3% vs 12,7% for the first and third group respectively), and for pregnancy outcomes, anemia and premature rupture of the amniotic sac membranes. The following indicators were also significantly affected ($p<0.05$) by maternal smoking: respiratory distress, cord blood gases, prematurity rate, and for the pregnancy outcome placental abruption and anemia of pregnancy. There was also a statistically significant difference between the results in the unexposed group and both exposed groups.

Although smoking and tobacco cannot be considered unique factors influencing the worse perinatal/neonatal outcomes, our study suggests that cigarette smoking is the most frequent, and completely preventable risk factor for adverse neonatal outcomes.

Key words: newborn, cigarette smoke, outcome, prematurity

Background

Smoking and tobacco exposure are events that only secondarily produce harmful physical effects. There is evidence that cigarette smoking is related to some adverse perinatal outcomes, however it is not just active smoking that plays a role [1]. This problem has at least three facets related to the deleterious effect associated with the fetus and newborn: (1) direct cigarette smoking during pregnancy; (2) the effect of environmental cigarette smoke (second-hand, passive smoking); and (3) the effect of smoking while breastfeeding.

Nicotine from cigarettes reduces the blood flow from the uterus to the placenta, decreasing the flow of blood to the baby and thus injuring the baby's brain. Every cigarette a pregnant woman has increases the level of carbon monoxide in her bloodstream, which replaces oxygen in her blood, so the amount of available oxygen through the umbilical cord is reduced [2]. Also, the majority of pulmonary parameters are lowered in smokers that have implications on the overall blood oxygen supply [3]. Maternal exposure to cigarette smoke is associated with a doubled risk of persistent pulmonary hypertension of the newborn (PPHN), in which infants starve for oxygen. In a Californian

study it was reported that 27.3 percent of the mothers of children with PPHN had smoked during pregnancy, compared to 14 percent of the mothers of normal controls.Also maternal smoking significantly increases the risks of spontaneous abortions, preterm delivery or low birth weight [4], as well as fetal malformations including: cleft lip, cleft palate, missing fingers or toes [5], optic nerve hypoplasia and visual impairment, placental abruption andplacenta previa. Maternal cigarette smoking during pregnancy increases the risk of neurodevelopment impairment during later childhood, because the nicotine causes the developing brain to develop millions of extra acetylcholine receptors in the cortex, striatum, and cerebellum regions, which will unnaturally regulate the pre-birth flow of more than 200 neurochemicals within the unborn child's mind and body, including dopamine, serotonin and adrenaline.

Also, parents should avoid exposing their baby, born or unborn, to second-hand smoke by keeping the living room smoke-free for the pregnant or breastfeeding mother and her baby. Breathing second-hand or "side-stream" smoke poses health risks. Over 600 medical reports have been published linking passive smoking to diseases.The breathing in of tobacco smoke by non-smokers can lead to middle ear infections and bronchitis, pneumonia, asthma and other chest conditions in children. It is also linked to sudden infant death syndrome (SIDS)[4]. Passive smoke, which is emitted from the burning end of the cigarette, contains higher concentrations of chemicals than the main stream smoke, and these chemicals in the bloodstream chemically bind to proteins and the genetic material of cells, DNA, forming adducts. Exposure of children to environmental tobacco smoke (ETS) increases the risk of having night cough and respiratory infections, especially during the first 2 years of life. Long-term breastfeeding may have a protective effect on ETS-increased risk of lower respiratory tract illness. Especially infants with lower birth weights had a high risk of recurrent otitis media during the first year of life when the mother was a heavy smoker. Passive smoking has been reported as a risk factor in meningococcal disease and tuberculosis in young children [2].

Second-hand smoke influences breastfeeding as well. Active smoking reduces milk supply, reduces milk quality, reduces the likelihood of breastfeeding, as well as the length of time that a baby is breastfed for, because cigarette smoking affects prolactin, the hormone involved in the establishment and maintenance of breastfeeding. Exposure to second-hand smoke also appears to compromise breastfeeding.

If a mother smokes cigarettes, her baby can still enjoy the benefits of breastfeeding. If the mother smokes fewer than twenty cigarettes a day, the risks to her baby from the nicotine in her milk are small. Heavy smoking can reduce a mother's milk supply and causes symptoms such as nausea, vomiting, abdominal cramps, and diarrhea. The half-life of nicotine is ninety-five minutes. For this reason, a mother should avoid smoking just before and certainly during a feeding [6]. Maternal smoking has been linked to early weaning, lowered milk production, and inhibition of the milk ejection ("let-down") reflex. Smoking also lowers prolactin levels in the blood.

Republic of Macedonia is one of the countries cited as having a very high percentage of smokers, especially female tobacco smokers. According to the WHO Report on The Global Tobacco Epidemic, 2009, the National survey in Macedonia in 2008 reported that there were 9.8% (95% CI 7,2-13,1) women active smokers, the majority of them potentially pregnant women and mothers [7]. Although there is a Law for tobacco banning, the number of tobacco smokers has not reduced in the last few years.This fact, as well as awareness of side effects from passive and active smoking to the siblings, became the pivotal issue that underscored the need to further investigate the influence of smoking on neonatal health.

A few years ago a study on Tobacco influence on perinatal outcomes was conducted at the Clinic for Gynecology and Obstetrics in Skopje, Macedonia [8]. Following the findings of that study, there was an attempt to broaden the spectrum of indicators to should be investigated. The aim of this cross sectional study was to evaluate the association of maternal active and/or passive smoking and a number of perinatal indicators. The investigation period was immediately postpartum, and during the early neonatal period.The objectives were:

1. To present the perinatal outcome of previous and current pregnancies of the mothers of investigated newborns
2. To present anthropometric and maturity indicators for the same newborns
3. To present the clinical and biochemical parameters of the investigated newborns

Material and methods

During the study the anamnestic and clinical data were extracted from the maternal history of the delivered women admitted to the Clinic for gynecology and Obstetrics in Skopje, Macedonia; clinical and biochemical indicators of the

newborns in the first 7 postnatal days were extracted from the neonatal history of their newborns. Only mothers for whom it was at least their second pregnancy were included in the study, aiming to correlate the perinatal outcome of their previous pregnancies. The sample size was determined (calculated) by the package The *survey system*, web site www.surveysystem.com/sscalc.htm, setting confidence level 95%, confidence interval 0,05, and population of 5000 (approximatively the study was comprised of 900 pairs of mothers and babies, 300 in each group. The newborns were divided into three groups: the first group of newborns were born to mothers that did not smoke and were not exposed to intensive smoking in their surroundings during the pregnancy (not exposed group). Newborns born by the mothers who smoke more than 20 cigarettes per day, and who had not try to quit smoking during the pregnancy constituted the second group, and the third group was composed of newborns born by the mothers who did not smoke, but were in close proximity to smokers (they were exposed intensively to tobacco smoke).The indicators investigated were: anamnestic data-obstetric history of miscarriages, stillbirths, previous premature delivery, perinatal history (placenta previa, abruption of the placenta, premature rupture of the amniotic sac membranes, gestational age at delivery, assessed by Dubowitz score [9], assessment of growth, respiratory, neurological and hematological status, and level of blood oxygenation (blood oxygen saturation, heart rate, partial blood oxygen pressure, and partial blood carbon dioxide pressure). The statistical significance of the difference was investigated separately between the three groups, but it is worth mentioning that as some factors were not taken into consideration such as socioeconomic situation, place of living, etc., there is a risk for potential bias. The statistical analysis was performed using the statistical software package StatPac (www.statpac.com/statistics-calculator/). We started with the null hypothesis that the groups were really the same, and that the observed discrepancy between sample means was due to chance (statistical hypothesis testing and the use of two-tail p-value).Although we have performed such statistical analysis, the limit of the statistics lies in the impossibility of controlling the confounding factors.

Results

900 newborns were included, divided into the three above mentioned groups: 300 successively born babies whose mothers didn't ever smoke or had smokers in their closer surrounding (unexposed group), 300 newborns in the second group, and 300 in the third group. Excluded were the newborns of the mothers who declared that they smoke less than 20 cigarettes or smoke occasionally. The sex distribution among the newborns is presented in the Figure 1, and it shows no difference between the groups .

In Table 1 and Figure 2 obstetric data of perinatal outcome of their previous pregnancies are presented. The data show statistical significance in the difference between the exposed groups (second and third) and the non-exposed group of newborns. The difference had high statistical significance between the first and the second, as well as between the first and the third group. Also, there was statistically significant difference between the second and the third group. Statistical test of correlation was not performed, because it cannot be stated for certain that tobacco smoke is

Figure 1. Sex distribution of the investigated newborns.

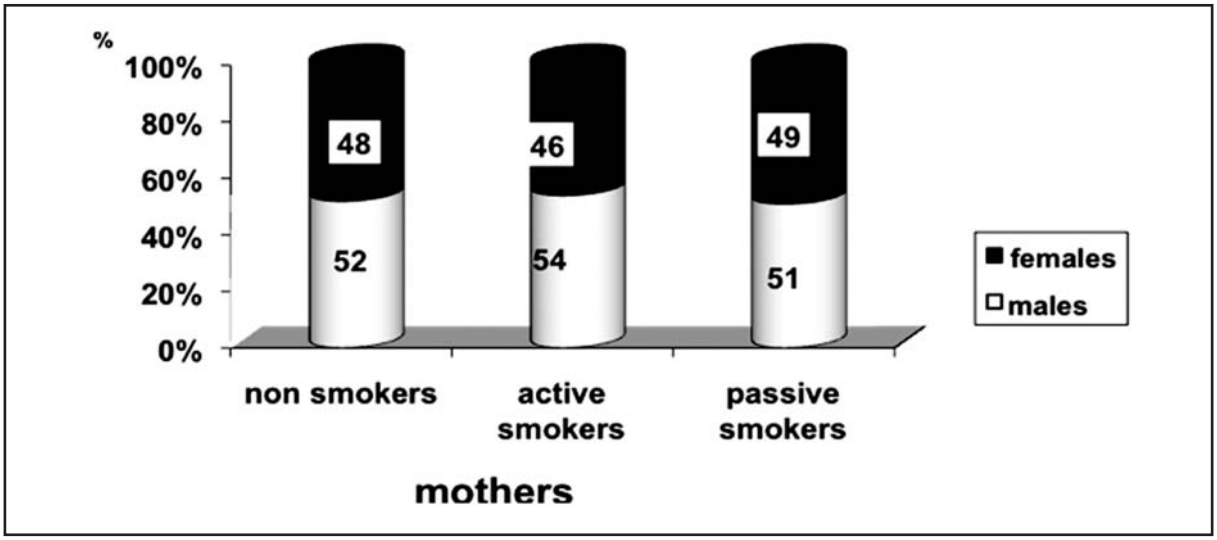
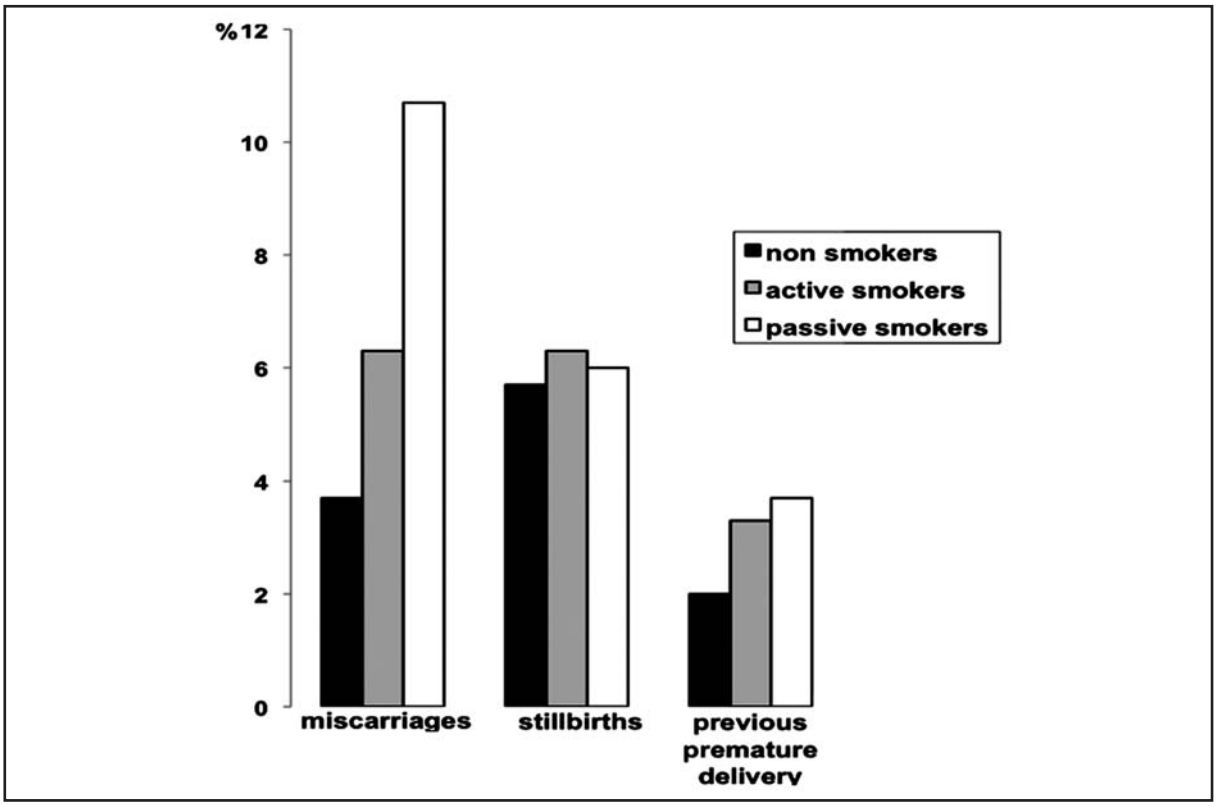


Table 1. Perinatal outcome of the previous pregnancy.

Parameters	Non smokers (n=300)	Active smokers (n=300)	p⁰	Passive Smokers (n=300)	p*
miscarriages	11 (3,7%)	19 (6,3%)	<0,05	32 (10,7%)	<0,01
Stillbirths	17 (5,7%)	19 (6,3%)	NS	18 (6,0%)	NS
Previous premature delivery	6 (2%)	10 (3,3%)	<0,05	11 (3,7%)	<0,05

⁰ comparison active versus non smokers ; * comparison passive versus non smokers: NS = non significant.

Figure 2. Perinatal outcome of the previous pregnancy.



the only factor affecting such an outcome.

Table 2 presents the data related to the current pregnancy, and there is obvious statistically significant difference between the occurrence of placenta previa, placental abruption and premature rupture of the membranes (PROM) within 24 hours prior to the delivery in the group of mothers who either actively smoke cigarettes, or live in an environment with high levels of exposure to cigarette smoke. The results in this study slightly differ from those in our previous study [8]. It doesn't mean that the cigarette smoke is the only factor for these conditions, but there is great probability that it has additional negative influence to this adverse effect.

Some perinatal outcomes of the newborns were reviewed and compared between the groups. Anthropometric and maturity indicators are presented in Table 3. The highest statistical significance of the difference (p<0,01) was shown for the mean birth weight (3077 grams in the first group vs 2332 grams for second one), and lower difference between the first and third group (3077 grams in the first group vs 2754 grams for the third one), symmetric intrauterine growth restriction (probably because the women smoke from the very beginning of the pregnancy), and combination of prematurity and growth restriction (3,3% vs 12% for the first two groups and 3,3% vs 9,7% for the first and third group), and also for pregnancy outcomes, anemia as well as premature rupture of the membranes.. The incidence of congenital anomalies and the early neonatal mortality rates were not investigated because of uncertainty of the causal factors related to their occurrence.

Table 4 shows the clinical and biochemical

Table 2. The main indicators of the current pregnancy.

Parameter	Mothers Non smokers (n=300)	Mothers active Smokers (n=300)	p⁰	Passive Smokers (n=300)	p*
Placenta previa	2(0,7%)	3(1%)	NS	2(0,7%) NS	NS
Placental abruption	3(1 %)	7(2,3%)	<0,05	6(2%)	<0,05
PROM	24(8%)	63(21%)	<0,01	45(15%)	<0,01
Anemia in pregnancy	58(19,3%)	89(29,7%)	<0,05	96(32%)	<0,01

⁰ comparison active versus non smokers ; * comparison passive versus non smokers; NS = non significant.

Table 3. The indicators of perinatal outcome of the newborns.

Parameters	Mothers non-smokers (Non-exposed newborns) (n=300)	Mothers active smokers (n=300)	p⁰	Mothers passive smokers (n=300)	p*
Mean BW(grams)	3077±123	2332±215	<0,01	2754±98	<0,05
No/% premature babies	29 (9,7%)	65 (21,7%)	<0,01	52 (17,3%)	<0,05
Number (%) SGA	19 (6,3%)	61 (20,3%)	<0,01	68 (22,7%)	<0,01
Premature+SGA	10 (3,3%)	36 (12%)	<0,01	29 (9,7%)	<0,01
Symmetric SGA	2 (0,7%)	26 (8,7%)	<0,01	25 (8,3%)	<0,01

⁰ comparison newborns of mothers active versus non smokers; *comparison newborns of mothers passive versus non smokers; NS = non significant.

Table 4. Clinical and biochemical indicators of the neonatal wellbeing.

Parameters	Mothers non-smokers (Non-exposed newborns)	Mothers active smokers	p⁰	Mothers passive smokers	p*
Apgar score at 5 min <6	16 (5,3%)	41 (13,7%)	<0,01	38 (12,7%)	<0,01
RD	9 (6%)	18 (12,6%)	<0,05	12 (8,6%)	<0,05
pO2 kPa	10,2±1,8	8,3±1,2	<0,05	8,2±0,9	<0,05
pCO2 kPa	5,8±0,4	6,3±3,2	<0,05	6,2±3,7	<0,05
SatO2 %	86±2,3	76±3,1	<0,05	74±3,6	<0,05
pH	7,31 ±0,3	7,20±0,2	<0,05	7,17±0,25	<0,05
Elevated NRBC	7 (2,3%)	44 (14,7%)	<0,01	38 (12,7%)	<0,01

⁰ comparison newborns of mothers active versus non smokers; *comparison newborns of mothers passive versus non smokers; NS = non significant.

parameters of the newborns delivered by

mothers in all three groups. It is obvious that the newborns in both exposed groups have significantly lower Apgar score in the 5-th minute (Apgar scores <6 in the 5th minute was in

5,3% vs 13,7% for the first and second group respectively and 5,3% vs 12,7% for the first and third group respectively). The difference between the two exposed groups is not significant. The occurrence of respiratory distress was significantly more frequent in the exposed groups, and the incidence was higher among the newborns of mothers who were active smokers. The blood-gas analysis in the cord blood showed significantly worse results in newborns born either by mothers who were active smokers or mothers exposed to tobacco smoke. The same impression was found with regards to the number of Nucleated Red Blood Cells (NRBC), which is considered a marker of a chronic intrauterine hypoxia (elevated NRBC in the second group compared to the first group, 14,7% vs 2,3% respectively, and 12,7% for the third group vs 2,3% in the first group).

Discussion and conclusions

According to literature data, maternal smoking increases the risks of spontaneous abortion, as well as for miscarriages (25%)and for stillbirths (40%). It also increases the risk two fold for preterm delivery, which rises to three fold for low birth weight babies. With a similar risk for premature rupture of the membranes, placental abruption and placenta previa. The majority of literature data confirms the strong relationship between the cigarette smoke and the adverse perinatal outcome of newborns. There are uncertainties relating to passive smoking, but some data shows a correlation between the perinatal hypoxia and exposure to cigarette smoke in the environment. Unfortunately, there is evidence that the prevalence of women smokers has continued to increase overthe last 20 years, and therefore it can be expected that more pregnant women are being exposed to tobacco smoke [10]. Exposure to second-hand smoke during pregnancy increases the risk of low birth weight (20%), miscarriage, and premature birth, resulting in 2000 LBW babies being born each year to pregnant non smokers in the UK. It is also harmful if the father smokes around the mother and this may also increase the risk of a baby being born with a lower birth weight [1].The results of our study are in concordance with the findings of other investigators, although the results relating to the effects of second-hand smoking were not as strong. The greatest statistically significant difference was shown in the newborn group of mothers who were active smokers for all of the following parameters: birth weight, both premature+intrauterine growth, respiratory distress, low Apgar score, blood oxygen-saturation and elevated NRBC in cord blood. Compared to the results of newborns born by mothers exposed to tobacco smoke, the results were worse in the latter group for the following parameters: lower pH, higher percentage of growth restricted infants, and some of the parameters of blood gas analysis. There was no significant difference in the obstetric parameters between the two exposed groups. It was recently demonstrated that a marker of fetal hypoxia, the absolute number of circulating nucleated red blood cells (NRBC's), measured at birth, is increased in infants of smoking mothers, but significantly increased erythropoietin was not found [11]. Our results are in accordance with those findings. All of the researchers agree that cigarette smoke is just an additional factor which makes pregnancy unsafe for the growth and development of the fetus, and that environmental exposure to cigarette smoke worsens both short term and long term outcomes., Therefore it cannot be overstated that there a lot of reasons not to smoke during pregnancy and breastfeeding, and that smoking is the most frequent, and completely preventable risk factor for adverse perinatal outcomes of newborns.

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