

## THE EXPOSURE OF THE FOETUS AND THE BREAST-FED NEWBORN OF WOMEN SMOKERS TO CARCINOGENIC ELEMENT NICKEL

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**Summary.** *The carcinogenic element nickel, which is present in nickel carbonyl compounds found in tobacco smoke, is almost totally absorbed through the respiratory tract during cigarette consumption. Our research study was aimed at determining to what extent cigarette smoking in reproductive women affects the exposure of the fetus and the breast-fed newborn to nickel. The method: the research was based on the analysis of 255 samples of biological material. Nickel content was determined by the electrothermal atomization technique, on a Perkin Elmer AAS M-1100. The results obtained indicate that nickel content in the blood of reproductive women smokers (0.05-0.33 µg/l) is higher than the content of this metal in the blood of non-smoking women (0.01-0.27 µg/l). Nickel content in the placentas of women who consume cigarettes is also higher (<0.01-1.23 µg/l) than the content of this metal in the placentas of non-smoking women (<0.01-1.01 µg/l). The concentration of nickel in the umbilical cord blood of smoking women (<0.01-0.11 µg/l) only slightly differs from the nickel content in the umbilical cord blood of women who do not smoke (<0.01-0.06 µg/l). There was a positive correlation regarding nickel content in the placenta and umbilical cord blood ( $r=0.817$ ). The presence of nickel in the maternal milk was also determined, confirming that women smokers had a higher content of nickel (<0.01-1.34 µg/l) than non-smoking women (<0.01-0.93 µg/l). It is highly important that would-be mothers discontinue the smoking habit long before the act of conception, and especially during pregnancy and breast-feeding.*

**Key words:** *Nickel, women, smoking, foetus, human milk*

### Introduction

Nickel enters the human body through food, air, water, objects for everyday use, and seldom in some other way. The higher contamination of the living environment by nickel, the higher exposure of each individual to this metal. Nickel is partly excreted from the organism (through urine, feces, sweat or in some other way) and partly remains in the organism for some time manifesting its biological effects.

It is believed today that very small amounts of nickel that enter the body through food increase erythropoiesis. During its evolutionary development, the human digestive tract acquired the capacity of absorbing only small amounts of nickel taken in through food (cca. 1%), which significantly contributes to human organism protection (1,2). However, if nickel enters the body through the respiratory system, the absorption percentage of this metal may be very high (75-100%). Whether a total or selective absorption will take place in the respiratory system depends on many factors, and primarily on the chemical and physical characteristics of the nickel compounds that man is exposed to (3,4). Gas forms of nickel compounds such as nickel carbonyl present in tobacco smoke are quickly and easily absorbed. After inhaling, nickel carbonyl rapidly reaches the lung circulation and, through blood, all other body organs and systems. Solu-

bility of nickel carbonyl in the lung alveolar membranes is of paramount importance for its penetration.

Experiments on non-human subjects, as well as some studies among the human population, have shown the possibility of transplacental transfer of nickel from the expectant mother onto the offspring. Transplacental transfer represents the starting point of the fetus exposure to this metal, which will be perpetuated after birth owing to the exposure of the child to environmental effects (exposure through maternal milk, for example). For this reason, exposure of women to secondhand smoke during pregnancy, especially in an early phase, may represent a serious health hazard. Placental transfer is conditioned by the gestation period, as well as by nickel content in maternal blood. Some significance may also be attributed to specific differences inherent to the placental structure and implantation, which may also affect the transfer of nickel through the placental barrier (5).

### Aim of the study

This research study is aimed at determining nickel content in a smoking-mother's organism, and transplacental exposure of the fetus and the breast-fed newborn to this carcinogenic element.

## Methods

The study involved an analysis of a total of 255 samples of biological material (59 blood samples, 63 placental samples, 63 umbilical cord blood samples, 70 human milk samples). Blood samples were taken from healthy women in the reproductive period who were not affected by workplace exposure to nickel. Placental samples and umbilical cord blood samples were taken immediately after delivery at the Gynecology and Maternity Clinic in Nis, and the samples of human milk were obtained from the women in childbed at the Clinic. The sampling and collection of anamnesis data was performed by the clinicians.

The samples were placed in polyethylene containers with covers previously rinsed with deionized water. Rubber (talcum powder-free) gloves were used to prevent the sample contamination by sweat. The chemical analysis of the samples was carried out at the Institute of Public Health in Nis. The samples were exposed to high temperatures (400°C), and afterwards treated with nitrogen acid. The nickel content was determined by the electrothermal atomization technique, on a Perkin Elmer AAS M-1100. The validity of the obtained results was checked by triple repetition of the analyses.

The research results were processed using mathematical and statistical methods, while the obtained values were expressed in percentiles (C25 = 25th percentile, C50 = 50th percentile, or medium, C75 = 75th percentile). The comparison of the obtained results was performed by Mann-Whitney Rank Sum Test (since the data in question did not have a normal distribution), while the values  $p < 0.05$  were treated as statistically significant.

The statistical analysis was performed using SPSS® for Windows, release 8.0 (SPSS Inc., Chicago, IL, USA).

## Results

The obtained research results have shown that the nickel content in blood samples of women in the reproductive period who consume cigarettes (0.05 - 0.4 µg/l) is higher than the content of this metal in the blood of non-smoking women (0.01 - 0.27 µg/l), though the difference is not statistically significant ( $p > 0.05$ ) (Table 1).

The placental nickel content among the women who consumed cigarettes is also higher (the concentrations ranged from the values below the detection limit to 1.23 µg/l) than the content of this metal in the placenta of non-smoking women (the values ranged from the undetectable to 0.01 µg/l) (Table 2), and no statistically significant difference was determined ( $p > 0.05$ ).

The nickel concentration in the umbilical cord blood of smoking women (< 0.01 - 0.11 µg/l) only slightly differs from the nickel content in the umbilical cord of non-smoking women (0.01 - 0.06 µg/l) (Table 3).

There was a positive correlation regarding the nickel content in the placenta and umbilical cord blood ( $r = 0.817$ ) (Table 4).

The presence of nickel was also confirmed in maternal milk (Table 5), in which a higher concentration of nickel was found among smoking women (the concentrations ranged from the undetectable to 1.34 µg/l) than among non-smoking women (the concentrations ranged from the undetectable to 0.93 µg/l). The statistical difference was not significant ( $p > 0.05$ ).

Table 1. Concentration of nickel in blood of women smokers and non-smokers

	Number of samples	Percentiles					Mann-Whitney Rank Sum Test
		Min	C25	C50 µg/l	C75	Max	
Women smokers	28	0.05	0.07	0.09	0.18	0.34	n.s.*
Women non-smokers	31	0.01	0.03	0.07	0.12	0.27	

\* does not differ significantly  
( $p < 0.05$  was considered as the criterion of statistical significance)

Table 2. Concentration of nickel in placentas of women smokers and non-smokers

	Number of samples	Percentiles					Mann-Whitney Rank Sum Test
		Min	C25	C50 µg/l	C75	Max	
Women smokers	29	< 0.01	0.09	0.31	0.86	1.23	n.s.*
Women non-smokers	34	< 0.01	0.13	0.22	0.41	1.01	

\* does not differ significantly  
( $p < 0.05$  was considered as the criterion of statistical significance)

Table 3. Concentration of nickel in umbilical cord blood of women smokers and non-smokers

	Number of samples	Percentiles					Mann-Whitney Rank Sum Test
		Min	C25	C50 µg/l	C75	Max	
Women smokers	29	< 0.01	< 0.01	0.03	0.08	0.11	n.s.*
Women non-smokers	34	< 0.01	< 0.01	0.02	0.05	0.06	

\* does not differ significantly  
( $p < 0.05$  was considered as the criterion of statistical significance)

Table 4. Correlation of nickel content between the placenta and the umbilical cord blood

	Number of samples	Min	Percentiles				Max	Sperman Rank Order Correlation
			C25	C50	C75	µg/l		
Placenta	58	<0.01	0.07	0.26	0.72	1.28	r=0.817	
Umbilical cord blood	64	<0.01	<0.01	0.08	0.18	0.58	p<0.05	

Table 5. Concentration of nickel in human milk of women smokers and non-smokers

	Number of samples	Min	Percentiles				Mann-Whitney Rank Sum Test
			C25	C50	C75	µg/l	
Women smokers	31	< 0.01	0.03	0.12	0.21	1.34	n.s.*
Women non-smokers	39	< 0.01	< 0.01	0.05	0.13	0.93	

\* does not differ significantly  
(p<0.05 was considered as the criterion of statistical significance)

## Discussion

Women in the reproductive period are exposed to various environmental sources of nickel (air pollution, contaminated food and drinking water, objects for everyday use). It is believed that women in the reproductive period are particularly exposed to various objects for everyday use that contain nickel (jewelry, watches, kitchen crockery and cutlery, then various tools, metal coins). Iatrogenic exposure to nickel is also a possibility (using implants made of nickel-containing compounds, certain medicaments, infusion liquids). Cigarette smoking is only one of the risk factors that may, to a different extent, contribute to increased exposure and intake of this carcinogenic element (5,6).

Regardless of the manner in which nickel enters a human organism, after absorption it reaches the blood, attaches itself to protein carriers and arrives at all the organs and tissues in the organism of a woman. Its distribution and retention in specific organs depends on the extent and kind of exposure, as well as on the level of elimination (through urine, feces, sweat, maternal milk) (7,8,9).

The obtained research results have shown that nickel is present in the blood of the woman (both smoking and non-smoking). Other studies elsewhere have shown that the bio-concentration of nickel in the blood and specific tissues primarily depends on the solubility of nickel compounds (5). Our earlier research (10) and research done by other authors (3,11) indicate that smoking is not necessarily accompanied by high nickel content in blood of people, although smokers accumulate somewhat higher concentrations of nickel.

During pregnancy, nickel is carried by blood to the placenta as well. The results of this study prove that nickel is accumulated in the placenta to a certain extent, transferred through the placental barrier unhindered, and carried into the body of the fetus by the umbilical cord blood. A higher concentration of nickel was found in the placenta and the umbilical cord blood among women who consumed cigarettes during pregnancy, but the difference is not statistically significant since other environmental factors also affect the intake and accumulation of nickel in the maternal organism.

The nickel content in the umbilical cord blood is lower than in the placenta since the umbilical cord blood only transports the metal. There is a positive correlation of nickel content between the placenta and the umbilical cord blood which points to the fact that a higher exposure of the expectant mother causes a higher exposure of the fetus. However, it should be stressed that the health hazard to the fetus as an effect of the exposure to this carcinogenic element is significantly higher, even in smaller concentrations, due to the vulnerability of the fetus.

The data available in literature mainly concern the occupational exposure of women in the reproductive period to nickel compounds, while there are relatively few papers investigating non-occupational nickel exposure of expectant mothers and their offspring (12). Knezevic et al. (13) point to a significant relationship between nickel content (and other toxic metals) and a high risk of maternal rejection of the fetus among exposed female workers (a higher percentage of pre-term births and spontaneous abortions, more frequent cases of maintained pregnancy, lower birth weight of newborns among affected workers compared to controls). Authors from Russia (14) stress more frequent congenital abnormalities (cardiovascular defects, skeletal-muscular malformations etc.), as well as miscarriages among workers exposed to nickel at work. Experiments on non-human subjects (15) have also confirmed the transplacental transfer and the deleterious effect of nickel on the fetus.

## Conclusion

The results of this study show that children born to smoking mothers are more exposed to nickel present in maternal blood than children born to non-smoking mothers, which implies a higher health-hazard. If one is reminded that nickel is only one among many toxic and carcinogenic substances present in tobacco smoke, it is reasonable to conclude that the health-hazard to these children is multiplied.

It is highly important that would-be mothers in the reproductive period be encouraged to discontinue the

smoking habit long before conception, and especially during pregnancy and breast-feeding in order to prevent health detrimental effects on the fetus and the newborn,

which may be brought about by an increased exposure to nickel-containing cigarette smoke.

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## EKSPOZICIJA FETUSA I ODOJČETA NA PRIRODNOJ ISHRANI ŽENA PUŠAČA KANCEROGENOM ELEMENTU NIKLU

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**Kratak sadržaj:** Jedna od kancerogenih materija, nikl u vidu niklkarbonila, koja se nalazi u duvanskom dimu, gotovo u potpunosti se resorbuje prilikom pušenja cigarete preko respiratornog trakta. Cilj istraživanja je bio da se utvrdi u kojoj meri pušenje cigareta od strane žena koje su u generativnom periodu utiče na izloženost ploda i odojčeta na prirodnoj ishrani niklu. Metod: U okviru ispitivanja uzorkovano je i analizirano 255 uzoraka biološkog materijala. Determinacija nikla je vršena elektrotermalnom atomizacionom tehnikom, na aparatu Perkin Elmer AAS M-1100. Dobijeni rezultati ispitivanja su pokazali da je sadržaj nikla u krvi žena u generativnom periodu koje konzumiraju cigarete (0,05 - 0,33 µg/l) veći u odnosu na sadržaj ovog metala u krvi žena nepušača (0,01 - 0,27 µg/l). Sadržaj nikla u placenti žena koje su konzumirale cigarete je takodje veći (< 0,01 - 0,23 µg/l) u odnosu na sadržaj ovog metala u placenti žena nepušača (<0,01-1,01 µg/l). Koncentracija nikla u krvi pupčane vrpce žena pušača (< 0,01 - 0,11 µg/l) je nešto niža od sadržaja nikla u krvi pupčane vrpce žena nepušača (< 0,01 - 0,06 µg/l). Utvrđena je pozitivna korelacija u pogledu sadržaja nikla u placenti i krvi pupčane vrpce ( $p < 0,05$ ). U majčinom mleku takodje je utvrđeno prisustvo nikla, pri čemu su žene pušači imale veći sadržaj nikla (< 0,01 - 1,34 µg/l) u odnosu na žene nepušače (< 0,01 - 0,93 µg/l). Neophodno je insistirati na prestanku konzumiranja cigareta kod žena u generativnom periodu koje nameravaju da ostanu u drugom stanju mnogo pre začeca, a posebno tokom trudnoće i dojenja.

**Ključne reči:** Nikl, žene, pušenje, fetus, majčino mleko