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Association Between Cigarette Smoking and Breast Milk Levels of Nesfatin-1, Irisin, and Oxidative Stress Markers

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Abstract

Background: Breast milk is a very important functional food in the prevention of metabolic and chronic diseases. This study aimed to investigate the effects of smoking during pregnancy on the concentrations of nesfatin-1, irisin, and oxidative stress markers in breast milk.

Methods: This study included two groups of 14 smoking and 14 nonsmoking mothers. Malondialdehyde (MDA) level and superoxide dismutase (SOD) activity were measured according to the spectrophotometric method in breast milk samples. Nesfatin and irisin levels were measured by enzyme-linked immunosorbent assay.

Results: Levels of nesfatin-1 and MDA of the smoking group were significantly higher than those in the control group ($p < 0.001$). The SOD activity of the smoking group was significantly lower than that of the control group ($p < 0.001$). No significant difference was found in the breast milk irisin level between the study groups ($p > 0.050$).

Conclusions: Cigarette smoking increases MDA level and decreases SOD activity in breast milk. Nesfatin-1 levels would increase in accordance with increased oxidative stress, and nesfatin-1 acts as a protective mechanism to limit oxidative damage.

Keywords: breast milk, irisin, nesfatin-1, oxidative stress, smoking

INTRODUCTION

Consumption of tobacco products is a risk factor of the 6 of 8 leading causes of death worldwide.[1] At least 7000 chemical substances are present in a cigarette, and most of them are pharmacologically active, toxic, mutagenic, and carcinogenic. The harmful effects of smoking on humans have been emphasized for a long time.[2,3]

Free radicals and reactive oxygen metabolites produced during smoking are the most important factors in the occurrence of these harmful effects on human health. Free radicals cause oxidative damage on membrane lipids, proteins, carbohydrates, and DNA through various molecular pathways.[4,5] Lipid peroxidation in the membranes is one of the most important mechanisms involved in cell damage due to free radicals. Malondialdehyde (MDA), one of the end products of lipid peroxidation, causes cross-binding, and polymerization of membrane components. This also causes some changes in membrane properties, such as deformation, ion transport, enzyme activity, and aggregation of cell surface compounds.[6,7] Many reports have shown that enzymatic and non-enzymatic antioxidants can reduce the harmful effects of free radicals induced by smoking.[8]

Superoxide dismutase (SOD), an enzymatic antioxidant, catalyzes the conversion of superoxide to hydrogen peroxide and molecular oxygen. SOD plays an important role in controlling the levels of superoxide in cells, thus protecting the cell against free radicals.[9,10]

The increased cigarette consumption among women leads to an increase in smoking-induced risks for pregnancy and health problems in children.[11] Breast milk is easy to digest and a natural nutrient with high bioavailability, which contains all the liquid, energy, and nutrients necessary for the growth and development of newborns. Breast milk and breastfeeding offer various benefits for the baby and the mother, in terms of nutritional, developmental, psychological, social, and economic aspects.[12]

Breast milk is a very important functional food in the prevention of metabolic and chronic diseases. In addition to 87%–90% of water contents, breast milk contains various peptide/protein hormones, such as leptin, adiponectin, resistin, nesfatin, irisin, ghrelin, apelin, and motilin.[13] Nesfatin-1 is a 9.7-kDa peptide discovered in 2006, consisting of 82 amino acids, and it is effective in the physiological control of nutritional behavior. It is involved in the control of body weight by suppressing peristaltic movement of the digestive tract,

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eventually decreasing food intake.[14] It can pass the blood–brain barrier through endogenous and exogenous pathways and reach the brain. By such a capacity, it can exhibit anorexigenic effects on the control of body weight; moreover, it is involved in food intake and several metabolic processes.[15] Irisin is a protein discovered first in muscle tissue, with a molecular weight of 12 kDa, and contains 112 amino acids. Irisin is a myokine released from skeletal muscles and is involved in energy consumption by changing white adipose tissues into brown adipose tissues and protecting people from metabolic diseases with regular exercises.[16] Breast milk contains important hormones such as nesfatin-1 and irisin, which participate in the regulation of energy balance. These hormones may contribute to the regulation of growth and development in newborns and infants, participate in appetite control, and influence the development of metabolic diseases in childhood and adulthood. This study aimed to investigate the effects of smoking during pregnancy on the levels of nesfatin-1, irisin, and oxidative stress markers in breast milk.

METHODS

Study population

Ethics committee approval for the study was obtained from Recep Tayyip Erdogan University Ethical Committee (dated July 1, 2021, no. E.151). The study was conducted in a primary care center in the province of Erzurum, with two groups including 14 smoking and 14 nonsmoking mothers.[17,18] The control group consisted of non-smokers. Sociodemographic data of the participants were collected using the Interview Questionnaire Form (which asks for information about the mother, pregnancy period, baby, and smoking).

Mothers who were diagnosed with hypertension, gestational diabetes, hemorrhoids, chronic renal failure, respiratory diseases, anemia, and malignant diseases during pregnancy and puerperium were not included in the study. Mothers whose babies had any health problems were also excluded from the study. Mothers who were between the 1st and 6th months of lactation were informed about the study, and written informed consent was obtained from those who wanted to participate in the study.

Collection of mothers' milk samples and biochemical analysis

From each mother, approximately 10 mL of breast milk was collected in a Falcon tube and stored at −20 °C in a dark environment. MDA, SOD, nesfatin, and irisin levels were measured in breast milk samples. Lipid peroxidation was measured in accordance with the method of Ohkawa et al.,[19] and the level of MDA (end product) in the reaction was measured by a spectrophotometer. Results were given in nmol/mL.

SOD activity was measured in accordance with the method of Sun et al.[20] This was based on the generation of superoxide anion from xanthine catalyzed by xanthine oxidase and then the spectrophotometric measurement of the color intensity of the colored compound created by superoxide anion and nitroblue tetrazolium. Results were given in U/mL.

The levels of nesfatin-1 and irisin in breast milk samples of the patient and control groups were determined by ready-to-use reagents (Chemicon® International Inc., CA, USA) using enzyme-linked immunosorbent assay. Serum levels of nesfatin-1 were given in pg/mL, while serum irisin levels were presented in ng/mL.

Statistical analysis

All data analyses were performed by SPSS for Windows version 17.0. Since the data showed non-normal distribution, Mann–Whitney-U test, a non-parametric test, was used to evaluate the differences between groups. The relationship between the data was evaluated by Spearman's correlation analysis, a non-parametric test; $p < 0.05$ was considered significant.

RESULTS

The sociodemographic characteristics of the study groups are given in Table 1. No significant difference was found between the smoking and nonsmoking groups in terms of age, weight before, and after pregnancy, birth week of the baby, and birth weight of the baby.

Levels of nesfatin-1 and MDA were significantly higher in the patient group than in the control group ($p < 0.001$) (Table 2). The SOD activities of the patient group were significantly lower than those in the control group ($p < 0.001$). The decrease in irisin levels was not significant ($p > 0.050$).

As mentioned in Table 3, MDA levels increased and SOD activities decreased significantly, as the levels of nesfatin-1 increased. Nonetheless, a negative correlation was found between pregnancy weight gain and nesfatin-1 level. In addition, MDA levels demonstrated a significant negative correlation with SOD activity and pregnancy weight gain, whereas irisin presented no significant negative or positive correlation with any other parameters.

DISCUSSION

Cigarette smoking is one of the most common social addictions in our country as it is worldwide, which is potentially harmful to health. Smoking during pregnancy and lactation may negatively affect the growth and development of the baby and decrease the nutritional value of breast milk. In this study, we investigated the

TABLE 1. Sociodemographic characteristics of the participants

	Control group (Mothers who did not smoke during pregnancy)	Experimental group (Mothers who smoked during pregnancy)	*p*
Age (year)	31 ± 9	29 ± 5	>0.05
Weight (kg) 3rd trimester	65 ± 18	66 ± 11	>0.05
Weight before pregnancy (kg)	61.5 ± 24	65 ± 13	>0.05
Birth weights of newborns (g)	3,160 ± 430	3,100 ± 720	>0.05
Birth week of the baby	38 ± 3	37 ± 2	>0.05

Values are presented as mean ± standard deviation (SD).

TABLE 2. Comparison of nesfatin-1, irisin, MDA, and SOD levels between the groups

	Control group (Mothers who did not smoke during pregnancy)	Experimental group (Mothers who smoked during pregnancy)	*p*
Nesfatin-1 (pg/mL)	42.70 ± 4.57	63.68 ± 18.54	<0.001
Irisin (ng/mL)	49.42 ± 8.88	45.63 ± 9.59	>0.05
MDA (nmol/mL)	9.04 ± 2.15	15.02 ± 1.21	<0.001
SOD (U/mL)	77.05 ± 9.46	25.52 ± 13.57	<0.001

MDA, malondialdehyde; SOD, superoxide dismutase

Values are presented as mean±standard deviation (SD).

TABLE 3. Correlation table of the parameters

	(1)	(2)	(3)	(4)	(5)
Nesfatin-1 (1)	1	−0.307	0.600**	−0.606**	−0.404*
Irisin (2)		1	−0.125	0.288	0.275
MDA (3)			1	−0.769**	−0.409*
SOD (4)				1	0.326
Weight taken during pregnancy (5)					1

MDA, malondialdehyde; SOD, superoxide dismutase; ** $p < 0.001$; * $p < 0.05$

effects of smoking on breast milk by measuring levels of MDA, SOD, nesfatin-1, and irisin in smoking and nonsmoking mothers. In addition to being an excellent nutritional source for the newborn, breast milk contains antibodies, cytokines, growth factors, antimicrobial substances, and specific immune cells. Thus, breast milk protects the baby against infections until self-immune system develops.[21]

Breast milk was shown to improve the development of the immune system in newborns, besides its primary protective effects against infections of the gastrointestinal, respiratory, and urinary systems.[22] In this study, no significant difference was between smoking and nonsmoking mothers, with respect to the birth weeks and weights of the babies, which may be attributed to the small sample size of our study groups. The exposure of a pregnant woman to environmental cigarette smoke is dangerous, and the inhaled smoke, whether from herself or others, can easily pass to the babies through the placenta, negatively influencing the growth and development of the baby.[23] The effects of cigarette smoking on low birth weight are particularly pointed to carbon monoxide and nicotine. Cigarette smoke contains numerous toxic chemicals that can damage cellular functions. The high content of oxidants in cigarette smoke stimulates the production of free radicals and lipid peroxidation, causing negative effects on certain membrane lipids. In the body, endogenous enzymatic and non-enzymatic defense systems are activated against free radicals induced by exposure to smoke.[24,25] In a previous study, Ermis *et al*.[26] included 60 mothers and analyzed MDA levels and SOD activities in the serum and breast milk samples. They found increased MDA levels and decreased SOD activities in the breast milk samples of the smoking group. Breast milk has high nutritional value and protects newborns from infections and various diseases. Napierala *et al*.[27] reported that cigarette smoking decreases the nutritional quality of breast milk, which affects adversely the breastfeeding process and breast milk. In our study, the smoking group displayed significantly higher MDA levels than the nonsmoking group but significantly lower SOD levels than the control group. Antioxidant enzyme levels, such as SOD and glutathione peroxidase, are high in breast milk during lactation.[28] Noakes *et al*.[29] reported that smoking leads to adverse outcomes on the fetus, with negative effects on life span, and affects the peroxidative/antioxidative status of the newborn. Based on results and results in the literature, the balance between antioxidants and oxidants

appears to be disrupted in smoking mothers, and MDA levels increased and SOD activities decreased as a result of increased free oxygen radicals released from inflammatory cells. Decreased antioxidant enzyme activity and increased lipid peroxidation further enhanced the pathogenicity of cigarette smoking, adversely affecting the development of newborns. In the early phase of their lives, babies can self-regulate milk intake as a response to environmental and nutritional factors.[30] Recently, various peptide/protein hormones were determined in breast milk, such as leptin, adiponectin, resistin, obestatin, nesfatin, irisin, apelin, motilin, and cholecystokinin. Breast milk hormones regulate the activities of various organs until the endocrine system of the newborn starts to function.[31] In our study, nesfatin-1 levels were significantly higher among smokers than among non-smokers. In addition, irisin was lower in the smoking group, but the decrease in irisin level was not significant. In a study by Solmaz *et al*.,[32] nesfatin-1 was protective against oxidative damage because of its antioxidant and anti-inflammatory properties. A study reported the antioxidant and anti-apoptotic characteristics of nesfatin-1 and its anti-inflammatory effects on cells.[33] The present study demonstrated increased nesfatin-1 levels in the breast milk samples of smokers when compared with those of non-smokers because the body becomes reactive against lipid peroxidation as a self-defense mechanism, which can develop in case of oxidative stress. Irisin, having important roles in the regulation of energy consumption, is also critically involved in the development of diabetes, metabolic syndrome, obesity, and inflammation.[34] Zhu *et al*.[35] reported that irisin inhibits apoptosis induced by oxidative stress.

Cigarettes, containing numerous oxidant substances, can induce apoptosis. Sugiyama *et al*.[36] claimed that irisin could have antioxidant effects on oxidative stress induced by cigarette consumption. In our study, irisin levels were decreased in the milk samples of smokers when compared with those in non-smokers, but it was not significant. To our knowledge, no study has investigated the effects of smoking on the levels of nesfatin-1 and irisin. As a result, early phase nutrition may influence growth and development in the short and long term. We observed that exposure to cigarettes during pregnancy and lactation adversely affected the levels of these two hormones and enzymatic antioxidants.

CONCLUSIONS

This study revealed that cigarette smoking is associated with an increase in MDA levels and a decrease in SOD activities in breast milk. Nonetheless, our results indicate that nesfatin-1 levels may increase with increased oxidative stress. On the contrary, no association was found between cigarette and nesfatin-1 in breast milk. Among its limitations, this study has a small sample size and limited area of research. Further comprehensive studies involving more people living in different regions are warranted.

CONFLICT OF INTEREST

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