Araştırma Makalesi
Research Article

Evaluating the effects of smoking during pregnancy and maternal anemia on neonatal parameters

SİGARA KULLANIMININ VE MATERNAL ANEMİNİN FETAL DOĞUM AĞIRLIĞI ÜZERİNE ETKİLERİ VE YENİDOĞAN SONUÇLARININ DEĞERLENDİRİLMESİ

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ABSTRACT

Aim: It is well-known that smoking and anemia have unfavorable effects on the fetus. For this reason pregnant women should always be advised to stop smoking, should be screened for anemia and be given iron replacement therapy. Our aim in this study was to evaluate the negative effects smoking and maternal anemia have on the birth weight and neonatal outcomes.

Materials and methods: 1021 women who delivered in our clinic were included in the study. Those included were either smokers and anemic or non-smokers but anemic. Neonatal outcomes such as birth weight and week, Apgar scores, umbilical cord lactate level, bilirubin values, and intensive care needs were compared.

Results: In the study population, smoking habit was detected with a rate of 10.8% and anemia at a rate of 30.3%. When compared to non-smokers, birth weight (3079.4 (415.8) vs 3272.3 (442.1), [P<0.001]) and birth week (39.3 (1.0) vs 39.6 (1.0), [P=0.029]) were found to be statistically significantly lower in the smokers group. It was observed that smoking did not make a statistically significant difference in terms of APGAR scores, lactate and bilirubin levels, and neonatal intensive care need among the smokers and non-smokers group. Moreover, to make sure smoking was not masking the effects of anemia, the non-smoker group was divided into anemic and non-anemic subgroups. Despite that, anemia did not result in statistically significant differences between the subgroups.

Conclusion: Pregnant women should be advised to quit smoking as it has significant effects on the fetus.

Keywords: Anemia, Pregnancy, Smoking, Neonatal Outcomes.

ÖZ

Giriş: Sigaranın ve aneminin gebelik ve fetus üzerine olumsuz etkileri bilinmektedir. Gebelikte sigaranın bırakılması, ayrıca anemi taraması ve demir replasmanı önerilmektedir. Amacımız sigara ve aneminin doğum ağırlığı ve yenidoğan sonuçları üzerine etkisini araştırmaktır.

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DEU Tıp Derg 2024;38(3): 133-142
J DEU Med 2024;38(3):133-142
doi: 10.18614/deutip.1327188

Gönderim tarihi / Submitted: 20.07.2023
Kabul tarihi / Accepted: 07.10.2024

Gereç ve Yöntem: Kliniğimizde doğum yapan 1021 kadın sigara içenler, anemisi olanlar, sigara içmeyenlerden anemisi olanların doğum ağrılığı ve haftası, Apgar skorları, umbilikal kord laktat seviyesi, bilirubin değerleri, yoğun bakım ihtiyaçları gibi yenidoğan sonuçları açısından kıyaslandı.

Bulgular: Çalışma populasyonunda sigara alışkanlığı %10,8 ve anemi %30,3 oranında tespit edildi. Sigara alışkanlığı olanlarda olmayanlarla kıyaslandığında istatiksel anlamlı olarak doğum ağırlığı (3079,4 (415,8) vs 3272,3 (44,.1), [P<0,001]), doğum haftası (39,3 (1,0) vs 39,6 (1,0), [P=0,029]) daha düşük bulundu. Sigaranın APGAR skorları, laktat ve bilirubin seviyesi, yenidoğan yoğun bakım ihtiyacı açısından istatiksel anlamlı fark yaratmadığı izlendi. Sigaraya bağlı olabilecek riskleri ortadan kaldırmak için sigara içmeyen populasyondaki anemi grubu oluşturuldu. Maternal aneminin ve sigara içmeyen gruptaki maternal aneminin yenidoğan sonuçlarında anlamlı değişikliğe sebep olmadığı görüldü.

Sonuç: Gebe kadınlara sigara bırakması tavsiye edilmelidir.

Anahtar Kelimeler: Anemi, Gebelik, Sigara, Yenidoğan Sonuçları

Follow up of fetal growth and development is very important to estimate fetal well-being. Low birth weight is an important risk factor for perinatal morbidity and mortality. In addition to the placenta which has direct effects on the fetal growth and well-being, there are also other factors like maternal chronic systemic diseases, maternal infections, nutrition, bad habits like smoking and excess maternal weight gain during pregnancy which also affect the fetal development (1). Unfortunately, smoking during pregnancy is our generation's biggest public health problem. It is known that smoking during pregnancy has adverse effects on the mother and fetus. As a result of campaigns done to prevent smoking during pregnancy, smoking in the United States have decreased from 13.2% in 2006 to 7.2% in 2016 (2). It is not possible to estimate the true prevalence as cigarette consumption varies significantly based on the social structure. The use of cigarettes and tobacco products is associated with increased maternal, perinatal and neonatal morbidity and mortality. In a study conducted in the United States, a total of 5%-8% preterm births, 13%-19% of intrauterine growth restriction in term newborns, 5%-7% of preterm birth-related deaths and sudden infant death syndrome cases were reported in the country and 23-34% of them were associated with prenatal smoking (2).

Anemia is a public health problem among the females in the reproductive age. A study done in our country showed that smoking especially in the 3rd trimester resulted in newborns with low birth weight. Whereas the same study showed that high maternal hemoglobin levels are correlated with higher birth weights (3). Therefore, maternal anemia is correlated with increased perinatal morbidity and mortality. A longer hospital stay after delivery, preeclampsia, placenta previa, and therefore cesarean delivery are more common among anemic women (4). Anemia is associated with preterm birth, being small for gestational age, low fifth-minute Apgar score, and an increased risk of perinatal and neonatal death (4). In addition, maternal anemia is associated with an increased risk of ablation placenta, postpartum hemorrhage, and fetal malformations. It has been shown that the risk of maternal shock, need for intensive care, maternal death, fetal growth restriction, and stillbirth increases in moderate and severe anemia (5).

The aim of our study was to compare the effects of smoking and anemia on neonatal outcomes like neonatal birth weight of those born after the 37th gestational week.

MATERIALS AND METHODS:

After obtaining approval from the hospital's clinical research ethics committee (2022/0215), pregnant

women and newborns who gave birth in our clinic between 01.01.2021 and 31.12.2021 were retrospectively screened.

The females included in the study were those who gave birth at their or after the 37th week of pregnancy with a body mass index between 18.5-30, those who gave birth to a single live neonate by vaginal delivery or C-section. Our exclusion criteria were pregnant women who gave birth before 37 weeks of gestation, stillbirths, those with a body mass index below 18.5 or above 30, pregnant women with systemic disease (preeclampsia, gestational diabetes, gestational hypertension, hypo-hyperthyroidism, hematological disease, etc.), multiple pregnancies, uterine or fetal anomalies.

In the study, gestational week was calculated according to the last menstrual period (LMP). However, in cases with inconsistent LMP, it was calculated according to the first trimester ultrasound scan. Maternal anemia was defined as a hemoglobin (Hb) level below 11 mg/dL. Based on the prenatal maternal hemoglobin levels, the participants were divided into two groups. Those with a hemoglobin below 11 g/dL were in the anemic group and those with a hemoglobin value equal to or above 11 g/dL were in the non-anemic group. The newborns were divided into 3 groups according to their birth weight as small for gestational age (SGA) if birth weight was below 2500 g, as large for gestational age (LGA) if birth weight was over 4000 g, and as appropriate for gestational age (AGA) if birth weight was between 2501-3999 g. Body mass index (BMI) was calculated according to the prenatal weight of the pregnant women. Participants included in our study had a body mass index (BMI) between 18.5 and 30 as according to the World Health Organization's obesity classification a BMI of 18.5 is underweight a BMI above 30 is obesity. Patients who smoked before pregnancy but quit during pregnancy were placed in the non-smoker group.

The newborn outcomes of birth week, birth weight, Apgar Scores at the first and fifth minutes, umbilical cord blood lactate levels, need for neonatal intensive care, transient tachypnea of neonate and neonatal bilirubin levels were compared.

Statistical Methods

Data analysis was made with the help of SPSS 26.0 program and was studied with a confidence level of 95%. We used frequency or percentage (n(%)) to quantify our categorical (qualitative) variables. For our numerical (quantitative) variables mean, standard deviation (Mean±sd), minimum, maximum and median (M) statistics are given. Mann Whitney U test, Pearson Ki Square test and Fisher's exact chi-square test were applied. A p value below 0.05 was considered statistically significant.

RESULTS

By taking our inclusion criteria into consideration, a total of 1049 patient admissions between 01.01.2021 and 31.12.2021 were scanned, 28 patients who gave birth before 37 weeks of gestation were excluded from the study, and a total of 1021 patients were included.

General data and laboratory results are summarized in Table 1. The mean age of the pregnant women was 27.7, the mean gravida was 2.4, the mean parity was 1.1, the mean week of delivery was 39.5, and the mean birth weight was 3251.7 gr. In the study population, smoking habit was detected with a rate of 10.8% and anemia at a rate of 30.3%.

Table 1: General Data and Laboratory Results

	Mean (SD)	Median (min; maks)
AGE (n=1021)	27.7 (5.7)	27.0 (17; 46)
GRAVIDITY (n=1021)	2.4 (1.4)	2 (1; 10)
PARITY (n=1021)	1.1 (1.1)	1 (0; 9)
MEAN BIRTH WEEK (n=1021)	39.5 (1.0)	39.8 (37; 42.8)
MEAN BIRTH WEIGHT (n=1021)	3251.7 (443.2)	3270 (815; 4665)
SMOKING (n=1021) SMOKER n (%) NON-SMOKER n (%)	 110 (10.8) 911 (89.2)	
MEAN HEMOGLOBIN VALUE (n=980)	11.6 (1.4)	11.7 (6.2-15.9)
MEAN HEMATOCRIT VALUE (n=980)	35.4 (3.7)	36 (22- 49)
HEMOGLOBIN VALUE (n=980) <11 g/dl n (%) ≥11 g/dl n (%)	 297 (30.3) 683 (69.7)	
GENDER OF NEONATE MALE n (%) FEMALE n (%)	 504 (49.4) 517 (50.6)	
MEAN APGAR SCORE (1ST MINUTE) (n=1021)	7.9 (1.1)	8 (0-10)
MEAN APGAR SCORE (5TH MINUTE) (n=1021)	9.2 (1.0)	9 (0-10)
UMBILICAL CORD MEAN LACTATE LEVEL (n=962)	3.2 (2.0)	2.8 (0.1-31.0)
MEAN BILIRUBIN (n=972)	4.3 (3.2)	3.8 (0.1-43)
MEAN HEMOGLOBIN VALUE OF ANEMIC NEONATES (n=297)	9.9 (0.8)	10.1 (6.2-10.9)
NEED FOR INTENSIVE CARE UNIT(ICU) NEED n (%) NO NEED n (%)	 17 (1.7) 989 (98.3)	
MEAN NUMBER OF DAYS IN ICU (n=17)	4.8 (3.5)	4 (1- 16)
TTN (TRANSIENT TACHYPNEA OF NEONATE) 0 (absent) n (%) 1 (present) n (%)	 983 (97.6) 24 (2.4)	

Table 2 presents the neonatal outcomes of those born from smokers compared to nonsmokers and anemic compared to non-anemic mothers. Besides, to ensure that smoking doesn't mask the effects of anemia, a group of anemic and non-anemic, in total 911 participants who don't smoke were included in the study.

Table 2: Comparison Between the Neonatal Outcomes of Those Born from Smoker-Anemic Mothers and Non-Smoker Anemic Mothers

	SMOKING STATUS		**ANEMIA**		**NON-SMOKERS (n=911)**	
	SMOKERS (n=110)	**NON-SMOKERS (n=911)**	**ANEMIC (n=297)**	**NON-ANEMIC (n=683)**	**ANEMIC (n=295) Hb<11**	**NON-ANEMIC (n=575) Hb>11**
Mean Birth Week mean (SD) median (min;maks)	39.3±1.0 39.4 (37; 41.4)	39.6±1.0 40 (37; 42.8)	39.6±1.1 40 (37; 42.8)	39.5±1.0 39.8 (37; 42.7)	39.6±1.0 40 (37; 42.8)	39.6±1.0 39.8 (37;42.7)
P	0.029		0.484		0.770	
Mean Birth Weıght mean (SD) median (min;maks)	3079.4 (415.8) 3052 (1350;4300)	3272.3 (442.1) 3290 (815; 4665)	3243.2 (462.8) 3275 (815; 4665)	3258.4 (429.4) 3280 (1150; 4540)	3259.2 (464.9) 3280 (815; 4665)	3279.9 (432.4) 3300 (1150; 4540)
P	<0.001		0.813		0.647	
Mean Weight in Small for Gestatıonal Age mean (SD) median (min;maks)	2154.2 (373.9) 2230 (1350; 2450)	2127.9 (410.6) 2290 (815; 2480)	2138.4 (504.8) 2362.5 (815; 2480)	2145.9 (318.1) 2262.5 (1150; 2475)	2074.8 (554.5) 2310 (815; 2480)	2138.2 (337.4) 2265 (1150; 2475)
P	0.895		0.200		0.468	
Mean Weight in Normal for Gestatıonal Age mean (SD) median (min;maks)	3120.2 (301.1) 3065 (2540; 3800)	3281.3 (338.2) 3292.5 (2260; 3990)	3271.5 (356.7) 3280 (2520; 3970)	3264.0 (328.1) 3280 (2260; 3975)	3281.4 (354.4) 3287.5 (2520; 3970)	3286.0 (329.0) 3300 (2260; 3975)
P	<0.001		0.775		0.864	
Mean Weight in Large for Gestatıonal Age mean (SD) median (min;maks)	4257.5±60.1 4257.5 (4215; 4300)	4209.4±173.6 4170 (4000; 4665)	4204.3±270.6 4080 (4000; 4665)	4211.5±131.9 4215 (4010; 4540)	4204.3±270.6 4080 (4000; 4665)	4207.7±136.2 4202.5 (4010; 4540)

P	0.457		0.220		0.254	
Mean 1st Minute Apgar Score mean (SD) median (min;maks)	7.9 (1.2) 8 (0; 10)	7.8 (1.1) 8 (0; 10)	7.8 (1.0) 8 (2; 10)	7.9 (1.1) 8 (0; 10)	7.8 (1.0) 8 (2; 10)	7.9 (1.1) 8 (0; 10)
P	0.347		0.450		0.571	
Mean 5th Minute Apgar Score mean (SD) median (min;maks)	9.3 (1.1) 10 (0; 10)	9.2 (1.0) 9 (0; 10)	9.3 (0.8) 9 (6; 10)	9.2 (1.0) 9 (0; 10)	9.3 (0.8) 10 (6; 10)	9.2 (1.0) 9 (0; 10)
P	0.234		0.891		0.822	
Mean Umbilical Cord Lactate Level (mmol/L) mean (SD) median (min;maks)	3.1 (1.5) 2.9 (0.2; 8.1)	3.2 (2.0) 2.7 (0.1; 31)	3.3 (2.3) 2.8 (0.5; 31)	3.1 (1.8) 2.7 (0.1; 17)	3.2 (2.4) 2.8 (0.5; 31)	3.2 (1.9) 2.7 (0.1; 17)
P	0.546		0.365		0.639	
Mean Neonate Bilirubin Level (mg/dL) mean (SD) median (min;maks)	3.7 (2.2) 3.6 (0.2; 10.8)	4.4 (3.3) 3.3 (0.1; 43)	4.2 (2.7) 3.6 (0.2; 18.4)	4.4 (3.4) 3.9 (0.1; 43)	4.2 (2.8) 3.7 (0.2; 18.4)	4.4 (3.6) 3.9 (0.1; 43)
P	0.155		0.562		0.492	
Number of Neonates Requırıng ICU n (%)	2 (1.8)	15 (1.7)	4 (1.4)	13 (1.9)	2 (0.8)	13 (2.2)
P	0.706*		0.539*		0.255*	
Mean Number of Days in ICU(n) mean (SD) median (min;maks)	10 (8.4) 10 (4; 16)	4.1 (2.1) 4 (1; 8)	8 (5.6) 6 (4; 16)	3.8 (2.0) 4 (1;8)	6 (2.8) 6 (4; 8)	3.8 (2.0) 4 (1; 8)
P	0.294		0.102		0.305	
Neonatal Transient Tachypnea (n) n (%)	4 (3.7)	20 (2.2)	9 (3.0)	15 (2.2)	6 (2.3)	14 (2.3)
P	0.319*		0.443*		0.962*	

(%): column percentage *: Chi square test

The neonatal outcomes of smokers compared to non-smokers, anemic smokers and anemic non-smoker mothers were compared and presented in Table 2. Mean week of birth was statistically significantly shorter (39.3 (1.0) vs 39.6 (1.0), [P=0.029]) and mean birth weight was statistically significantly lower (3079.4 (415.8) vs 3272.3 (442.1), [P<0.001]) in mothers who smoked compared to non-smokers.

When the birth weights of neonates of the same gestational age from smokers and non-smokers were compared, no difference was found between LGA and SGA, while it was statistically lower in smokers in the AGA group (3120.2 (301.1) vs 3281.3 (338.2), [P<0.001]). No statistically significant difference was found in any of the parameters when the anemic and non-anemic pregnant and non-smokers anemic and non-smokers non-anemic groups were compared.

DISCUSSION

For our study, women who gave birth to a single term fetus either by C-section or normal vaginal delivery (in their 37th week of pregnancy or more) those with a body mass index between 18.5-30 were included. In total 1021 participant's medical records were screened and included in the study. The effects of smoking habits and anemia in pregnant women on newborn outcomes were investigated. It was found that smoking was associated with a decrease in mean week of birth, mean birth weight, and mean normal birth weight (AGA). Anemia did not have a significant effect on newborn outcomes in the anemia group and in non-smokers anemic pregnant's babies.

Cigarettes contain many toxins that affect almost every system in the body. Smoking during pregnancy has significant negative effects on the fetal health. Active or passive smoking during pregnancy is associated with an increased risk of intrauterine growth retardation and low birth weight, therefore smoking cessation in the first and second trimesters reduces the risk of intrauterine growth retardation or low birth weight. Moreover, when compared to active smoking, passive smoking also has a moderately harmful effect on fetal development (7). It has been found that women exposed to passive smoking have an increased risk of giving birth to a low birth weight neonate (OR = 1.404) (8). Smoking is thought to be associated with low fetal birth weight, abortion, stillbirth and neonatal death, preterm premature rupture of membranes, preterm birth, placenta previa, and congenital malformations (9). In addition, in a study investigating the relationship between the amount of cigarettes smoked per day and maternal and perinatal outcomes, it was shown that maternal smoking increases the risk of low birth weight and hospitalization in the neonatal intensive care unit (10). In our study, pregnant mothers who smoked during pregnancy were considered in the smokers group and those who used to smoke before but quit smoking during pregnancy were evaluated in the non-smokers group. However, the amount of cigarettes smoked by each participant in the smokers group could not be evaluated. Consistent with the literature, negative effects of smoking on birth weight were observed. Based on what is mentioned in literature, smoking has a significant effect on mean week of birth, mean birth weight, and mean normal birth weight (AGA) in smokers regardless of smoking dose. However, no significant difference was found in terms of increasing the risk of hospitalization and length of stay in the neonatal intensive care unit.

In the last trimester, a hemoglobin level lower than 11g/dl is defined as anemia and the most common cause of microcytic anemia is iron deficiency. During pregnancy, since maternal, fetal and placental iron consumption increases, prophylactic iron supplementation, and in anemic mothers iron treatment is recommended (11). Despite these recommendations, anemia still remains a common health problem in pregnancy (12). Research showed that severe antenatal or postnatal maternal anemia increases the risk of maternal mortality (OR=2.36) (13). Maternal anemia is also a risk factor for neonatal low birth weight (14).

In moderate anemia (Hb level of 7-8.9 g/dL), the risk of being small for gestational age, below 10th and 3th percentiles is 1.17 and 1.67 fold, the risk of being born with

an Apgar score below 7 at the fifth minute is 1.03 fold and the risk of neonatal death is 2.96 fold. In addition, the risk of fetal asphyxia is also increased by 1.32 fold (4). In a study where 51.5% of the population was anemic (mean Hb level 8.45 g/dL in the anemic group), the frequency of the first and fifth minute Apgar scores being below 5 was statistically significantly higher in the anemic group. Lower Apgar scores and lower birth weight were observed more frequently in the anemic population (15). It was observed that treating anemia with intravenous iron replacement in the last trimester did not improve the fetal birth weight, Apgar scores at the first and fifth minutes, need for neonatal intensive care, or umbilical artery pH (16-17).

In a recent systematic review published in 2022, the evidence for the relationship between maternal anemia and fetal distress, low Apgar score, low umbilical cord pH, and neonatal intensive care unit need or risk of perinatal death was evaluated as inconsistent. Moreover, even in some studies, it was emphasized that high hemoglobin levels increased the risk of perinatal mortality and that special attention should be paid in such situations (18).

In the recent literature, the pathophysiology behind the negative impacts of maternal anemia on neonates was studied at a molecular level. The molecules studied were neuro-trophins, molecules found in the central and peripheral nervous systems and play an important role in learning and memory. It was found that the levels of brain derived neurotrophic factor (BDNF) found in the umblical cord blood of babies born from anemic mothers were significantly lower than the levels of those born from non-anemic mothers (19).

It is believed that the negative effects of smoking in anemic mothers was higher than its effect in mothers with normal hemoglobin levels. The cadmium in cigarettes binds to transferrin and disturbs its structure. Therefore, it decreases transferrin's transport of iron to the fetus causing growth retardation. In other words, smoking has an additive effect with anemia on fetal growth retardation (20).

In our study, we showed the negative effects of maternal anemia and smoking consumption on neonatal parameters. Based on our results, anemia did not have a significant effect on the neonatal results. Moreover, to make sure smoking was not masking the effects of anemia, the non-smoker group was divided into anemic and non-anemic subgroups. Despite of that, anemia did not result in statistically significant differences between the subgroups. This might be due to the fact that despite being anemic, the hemoglobin levels were not very low, or in other words the anemia was not severe. Therefore, a study dividing the anemic mothers into subgroups based on the severity of the anemia might be helpful in determining the lowest level of hemoglobin which would have significant effects on neonates.

The restrictions of our study include the fact that it was retrospective and that the amount of cigarettes smoked per day before and during pregnancy, the duration of smoking consumption, the type of tobacco smoked and weather the mother was an active or a passive smoker was not determined. When it comes to anemia, the time it was diagnosed, whether it was acute or chronic and weather iron supplements were used was also not determined.

Conclusion

It has been shown that smoking during pregnancy has significant unfavorable effects on the fetal birth weight and birth week. However, we believe that more wide spectrum prospective studies should be done taking into consideration the amount of cigarettes smoked per day before and during pregnancy, the duration of cigarette consumption, the type of tobacco smoked, weather smoking was ceased during pregnancy or not and the levels of maternal carbon monoxide which would give more accurate and definite conclusions and results.

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