Eskisehir Medical Journal
Eskişehir Tıp Dergisi

Eskisehir Med J. 2024; 5(1): 23-28.
doi: 10.48176/esmj.2024.158.

Original Article / Araştırma Makalesi

THE EFFECT OF CAFFEINE INTAKE LEVELS DURING PREGNANCY ON NEWBORN HEALTH

GEBELİKTE KAFEİN TÜKETİM DÜZEYİNİN YENİDOĞAN SAĞLIĞI ÜZERİNDEKİ ETKİSİ

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ABSTRACT

Introduction: Caffeine is a commonly used ingredient nowadays all over the world but the consumption of caffeine during pregnancy has been an uncertain topic about the impact on birth and childhood. So, we aim to examine the caffeine intake habits during the trimesters of pregnancy and to analyze the effects of caffeine levels on newborn health.

Methods: 42 women were included in the study. The Socio-demographic Characteristics Evaluation Questionnaire was completed in the first interview and, during this same interview; the Daily Caffeine Intake Levels Evaluation Form was given to be updated in assigned weeks and days. The Birth Information Form was completed after witnessing the birth and a review of the mother's files.

Results: The average daily caffeine intake levels were 509.8±353.2 mg and 193.7±116.5 mg pre-pregnancy and on average during the pregnancy period. There was no correlation between any type of socio-demographic findings and the average caffeine intake at any period of the pregnancy period, included the pre-conceptional period. It was also found that birth weight and height, and the 1 and 5 minute Apgar score decreased when caffeine intake was higher in the trimesters of the pregnancy.

Conclusion: More studies using standardized methods and a meta-analysis of these studies may help to discover the relationship between caffeine and pregnancy outcomes, neonatal and childhood health.

Keywords: Caffeine, intake, pregnancy, newborn, nursing

ÖZET

Giriş: Kafein günümüzde tüm dünyada yaygın olarak kullanılan bir bileşendir, ancak gebelik sırasında kafein tüketiminin doğum ve çocukluk üzerindeki etkisi belirsiz bir konu olmuştur. Bu nedenle, bu çalışmada gebeliğin trimesterleri boyunca kafein alım alışkanlıklarını incelemeyi ve kafein düzeylerinin yenidoğan sağlığı üzerindeki etkilerini analiz etmeyi amaçladık.

Yöntemler: Çalışmaya 42 kadın dahil edildi. Sosyo-demografik Özellikleri Değerlendirme Anketi ilk görüşmede dolduruldu ve aynı görüşme sırasında; Günlük Kafein Alım Düzeyleri Değerlendirme Formu belirlenen hafta ve günlerde güncellenmek üzere verildi. Doğum Bilgi Formu, doğum olduktan ve annelerin dosyaları incelendikten sonra doldurulmuştur.

Bulgular: Günlük kafein alım düzeyleri gebelik öncesi ortalama 509,8±353,2 mg ve gebelik süresince ortalama 193,7±116,5 mg idi. Herhangi bir sosyo-demografik bulgu ile gebelik öncesi dönem de dahil olmak üzere gebelik döneminin herhangi bir dönemindeki ortalama kafein alımı arasında bir korelasyon bulunmamıştır. Ayrıca, gebeliğin trimesterlerinde kafein alımı arttıkça doğum ağırlığı, boyu ile 1. ve 5. dakika Apgar skorunun azaldığı bulunmuştur.

Sonuç: Standart yöntemler kullanılarak yapılacak daha fazla çalışma ve bu çalışmaların meta-analizi, kafein ile gebelik sonuçları, yenidoğan ve çocuk sağlığı arasındaki ilişkinin keşfedilmesine yardımcı olabilir.

Anahtar Kelimeler: Kafein, tüketim, gebelik, yenidoğan, hemşirelik

INTRODUCTION

Caffeine is a commonly used ingredient nowadays all over the world. Despite widespread caffeine consumption, there is insufficient knowledge about its effects. Caffeine has a wide clinical spectrum and it may have different effects on different groups, such as adults, pregnant women, or babies. Although it is used to stay awake and cope with stress in significant amounts, and it has beneficial effects on some health issues, e.g., cardiovascular diseases, liver diseases, cancers (1), a person may need to seek treatment for substance use disorder if s/he cannot control the use of caffeine. Caffeine also affects fecundability, and it should be recommended that its consumption be reduced during pregnancy due to the impact on neonatal outcomes. In spite of such harmful effects on infants, caffeine has been used in neonatal intensive care units to prevent apnea (2).

The consumption of caffeine during pregnancy has been an uncertain topic in the literature concerning the impact on birth and childhood. In the literature the safe dosage of caffeine consumption remains unclear. While some authors concluded that there was no relationship between caffeine intake and miscarriage at any amount (3), another study

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Received date: 11.03.2024 **Accepted date:** 23.03.2024

Cite as: Kaya Y, Tokgöz VY Dalyan E, Tanır HM. The Effect of Caffeine Intake Levels During Pregnancy on Newborn Health. Eskisehir Med J. 2024; 5(1): 23-28. doi: 10.48176/esmj.2024.158.

showed that women who consumed more caffeine might have a greater increased risk of gestational problems (4), and a further study suggested a low birth weight, stillbirth, or small gestational age for women who consumed less caffeine (5). There has been no consensus about the safe dosage of caffeine intake during pregnancy between organizations related to maternal and neonatal health. A caffeine intake <200 mg /per day has been allowed for pregnant women by The American College of Obstetricians and Gynecologists (6), Dietary Guidelines for Americans (7), the European Food Safety Authority (8), and the UK National Health Service (9), despite the fact that up to 300 mg/day of caffeine intake in healthy pregnant women was not associated with any adverse effects (10). While it has been shown that a 100 mg/day caffeine intake could increase the risk of low birth weight, spontaneous abortion, or stillbirth (11,12). A 22nd-week pregnant woman who took 4000 mg caffeine in a single dose during a suicide attempt and was later treated with hemodiafiltration, reported that she gave birth in the 38th week to a healthy child (13). Reviews have also suggested that the evidence about the relationship between restricting caffeine intake and pregnancy, fetal, or neonatal outcomes was insufficient (11,14). The various results about the effects of caffeine on all relevant outcomes could be related to the CYP1A2 enzyme. The CYP1A2 enzyme's function is to metabolize caffeine in the human body. This enzyme's function during pregnancy can be affected by modulators associated with pregnancy and the fetal environment. It has been shown that the CYP1A2 enzymatic reaction could show 'inter-individual variation' (15), which causes different responses in pregnant women. Those who have higher CYPA12 enzyme activity have more pregnancy risks than those with lower CYPA12 activity (16).

To our knowledge, there are limited studies that have researched the impact of caffeine intake on the Apgar scores of newborns in the literature. As a result, in this study, we aim to examine the caffeine intake habits during the trimesters of pregnancy and to analyze the effects of caffeine levels on newborn health.

METHODS

The study was planned with a descriptive research design and data collected between February 2021 and July 2021. The measurements were performed during the pregnancy and the information was collected in the postconceptional period.

After obtaining approval from the ethics committee and after an institutional review, the research population was gathered which consisted of the women who had applied to Eskisehir Osmangazi University, Faculty of Medicine, Department of Obstetrics and Gynecology Polyclinic because of their pregnancy. The study sample included 49 women who were aged 18 and older, were non-smokers and were non-drinker. Furthermore, they did not have any chronic disease, had a healthy pregnancy so far, had not reached the ninth week of pregnancy, and agreed to participate in the study. All human subjects provided written informed consents with guarantees of confidentiality.

In this research, the data were gathered through face-to-face interviews by the researcher who designed the questionnaire and calculated the measurements. When a chronic disease was encountered in any period of the pregnancy, or when the pregnancy ended, these cases were excluded from the study. Three forms designed by the researcher were used in this research: The Sociodemographic Characteristics Evaluation Questionnaire, The Daily Caffeine Intake Levels Evaluation Form, and The Birth Information Form.

The Sociodemographic Characteristics Evaluation Questionnaire was completed during the first interview by the women who had come to the polyclinic to receive service and met the requirements of the study. This form included open-ended and close-ended questions regarding the woman and her partner's ages, educational backgrounds, occupations, duration of marriage, the type of family, monthly income, and any conditions special to the pregnancy.

The Daily Caffeine Intake Levels Evaluation Form was given during the first interview, and the women were asked to fill out the form on assigned weeks and days to record their daily caffeine consumption. The form also required the women to provide details regarding their consumption pre-pregnancy. They were asked to submit these forms when they came for a checkup after they had updated their form for the last time. In order to select a week in each trimester that would be chosen for analysis, a random draw was made which resulted in the 9th week of gestation in the first trimester, the 22nd week of gestation in the second trimester, and the 34th week of gestation in the third trimester being selected. A further draw was then made to select which day's caffeine intake would be used in the selected weeks and Friday was drawn. Their amount of consumed caffeine was calculated by the researcher after they had returned the form, and both the total amount and trimester average amount were computed according to the information recorded by the women.

The Birth Information Form was completed after the birth by examining the mother's files. This form included the infant's birth week, birth weight, height, and Apgar scores.

Continuous data are presented as Average ± Standard Deviation and categorical data in percentages (%). The Shapiro-Wilk test was used to analyze if the data follows normal distribution. To compare the groups which did not correspond with the normal distribution, the Kruskal-Wallis H test was used for the cases with groups numbered three and above, the Mann Whitney-U test was used for two. To compare the values in different measurements, the

Wilcoxon test was used when the group number was two, and the Friedman test was also conducted. Spearman's rank-order correlation was calculated to detect the direction and strength of the association between variables. Pearson's chi-squared test was used to analyze generated crosstabs. IBM SPSS Statistics 21.0 program was used for the analysis. The value $p<0.05$ was used to determine results as statistical significance.

RESULTS

From the original study sample of 49; 5 women, whose pregnancy resulted in a miscarriage, and two others, who had left the forms incomplete, were excluded from the study, which gave a total of 42 participants who were included in the study. It was found that the average age of women was 28.8±4.6 years, the average times pregnant was 2.0±1.3, the week of delivery for women was 37.7±0.7 on average, the average birth weight was 3409.0±343.6 g, the average birth height was 49.5±0.9 cm, and the average 1-minute and 5-minute Apgar scores were 9.3±0.6 and 9.6±0.5, respectively.

When the daily caffeine intake levels of the women participating in the study were examined, they were found to be 509.8±353.2 mg per day in the pre-pregnancy period, 173.5±159.9 mg per day in the first trimester, 206.4±114.3 mg per day in the second trimester, 195.7±139.7 mg per day in the third trimester, and an average of 193.7±116.5 mg per day during the pregnancy (Table 1). When the average caffeine intake levels were compared, it was observed that there was a statistically significant difference between groups and found that the highest caffeine intake was in the pre-pregnancy period (Table 1).

It was found that while the infant's birth weight and height increased as caffeine intake in the pre-pregnancy period and trimesters decreased; the 1-minute and 5-minute Apgar score decreased as caffeine intake increased in the trimesters of the pregnancy (Table 2).

Table 1. Daily Average Caffeine Intake Levels (mg) and Comparison of the Intake Levels Between the Gestational Periods

Caffeine intake	Mean±SD
Pre-pregnancy (1)	509.8±353.2
First Trimester (2)	173.5±159.9
Second Trimester (3)	206.4±114.3
Third Trimester (4)	195.7±139.7
Pregnancy average (5)	193.7±116.5
Between groups	(2-1) p = 0.000*; (3-1) p = 0.000* (4-1) p = 0.000*; (5-1) p = 0.000*

* Wilcoxon signed Rank test

DISCUSSION

Caffeine's metabolization rate begins to decrease in the first trimester and this downward trend continues until the birth (17). In addition, the blood-placental barrier cannot prevent caffeine's passage from the mother to the fetus because of the lipophilic nature of caffeine (18), the fetus itself does not have an enzyme to metabolize the caffeine (15). As a result, all caffeine taken by women crosses directly to the fetus without any metabolization process. Caffeine and its metabolites could be thought to cause vasoconstriction in the placenta as a historical attitude (19,20). However, an emergent study showed that acute coffee consumption only affected the amniotic fluid volume rather than fetal renal artery blood flow (21). Despite the possible harmful effect on both mother and her baby, 51.7-97 % of women continue to take in caffeine during their pregnancy (22,26) and maintained caffeine consumption at the same level as in their pre-pregnancy period (26). In a recent study, the consumption of caffeine was 59.2 ± 61.5 and 54.3 ± 55.4 mg/day in the first and third trimester, respectively, though the decline of the amount and daily use of caffeine were not statistically significant (24). In our study, the daily average caffeine intake levels were 509.8±353.2 mg and 193.7±116.5 mg in the pre-pregnancy and pregnancy period. In addition, the decrease of caffeine intake started in the first trimester and continued to the third trimester. Some studies have found that the intake levels were decreased once the pregnancy was learned, however, the level of caffeine intake in the third trimester was nearly the same as that in the pre-pregnancy period (27-29). Contrary to this, in our study, the caffeine consumption level in the pre-pregnancy and three trimester periods, without any health advice program being given, were found to be statistically significant and these significances were not related to any demographic findings.

There is no consistent evidence of an association between caffeine intake and newborn health. A Cochrane database about caffeine intake's effect on reproductive and newborn health concluded that the evidence is insufficient on the avoidance of caffeine to prevent low birth (14). Later, a review included 10 studies, and this showed that the risk of low birth increased with caffeine intake in 7 studies (30-35) A meta-analysis has recently demonstrated that caffeine consumption during pregnancy was associated with a 33% greater risk of lower birth (36). However, a recent study from Poland concluded that there was no relationship between caffeine intake levels and neonatal anthropometric parameters. In this research, 100 pregnant women completed a questionnaire to measure their daily caffeine intake (37). Another study examined the effects of caffeine intake on neonatal health with the blood level of caffeine and its metabolite paraxanthine to exclude the limitation of the self-reported caffeinated beverage consumption. It was found that decreased birth weight and length were statistically significant when associated with plasma caffeine and paraxanthine concentration while the

Table 2. The comparison of the daily average caffeine intake levels pre-pregnancy and in the trimesters with demographic findings

	Caffeine Intake Levels								
	Pre-pregnancy	The first trimester	The second trimester	The third trimester	During the pregnancy	Birth weight	Birth Height	1-minute Apgar	5-minute Apgar
Caffeine pre-pregnancy	1.000								
Caffeine in the first trimester	.328*	1.000							
Caffeine in the second trimester	.370*	.418**	1.000						
Caffeine in the third trimester	.221	.415**	.756**	1.000					
Avg. caffeine intake during the pregnancy	.320*	.739**	.829**	.846**	1.000				
Birth weight	-.399**	-.629**	-.746**	-.638**	-.823**	1.000			
Height	-.540**	-.489**	-.682**	-.576**	-.693**	.852**	1.000		
1-minute Apgar	-.197	-.386*	-.579**	-.635**	-.630**	.398**	.450**	1.000	
5-minute Apgar	-.011	-.241	-.510**	-.587**	-.533**	.353*	.361*	.605**	1.000

Spearmen correlation *p < .005; ** p < .001

low birth risk started from the level of 50 mg caffeine/day (38). In this study, we have shown that birth weight and height decrease with the increase of daily caffeine intake during pregnancy ($p < 0.05$). The association between the caffeine consumption level in the pre-pregnancy period and neonatal health has not been discussed before in the literature. We also found that the birth weight and length decreased with higher caffeine intake levels in the pre-pregnancy period and all the trimesters ($p < 0.05$).

The Apgar score is used to provide a standardized assessment for infants after delivery. The minimum and maximum scores are 1 and 10, respectively. The higher points show the wellness of the infant. In the literature, there are only two studies that have tried to show the association of caffeine intake level and the Apgar score (39,40). The two studies could not show any association. The reason for not being able to show the association between caffeine intake levels and Apgar score, as declared by the authors, was that the percentage of caffeine overconsumption was very low and the average intake level per day was also too low in the study population (40). In our study, for the first time in the literature, we found that there was a negative association between the 1st and 5th minute Apgar score and caffeine intake levels in the pre-pregnancy and all trimester periods on neonatal anthropometric parameters.

In our study, we did not examine the relation between caffeine intake and pregnancy outcomes and childhood problems. A limitation of the study was that the average caffeine intake levels were calculated by the questionnaire form designed by researchers as a result, data collection was self-reported, the individuals' caffeine metabolism was not examined, and the caffeine exposure of the fetus was not estimated. Another limitation was that the pregnant women were not separated into groups according to caffeine consumption levels, such as < or > 200 mg /day, thus we could not conclude any cut-off or safety dosage level for a daily caffeine intake that would help avoid its harmful effects. Strength of this cohort study was that non-smokers, non-drinker, and pregnant women who did not have any chronic illness were included in the study. Furthermore, all conditions that could affect neonatal health were excluded from the study.

This study was the first study from Turkey on the effects of caffeine intake level on neonatal health. We found that there was a negative association between the level of caffeine consumption during all three trimesters on the birth weight, length, and the Apgar scores. These negative effects were also detected when the caffeine intake level was higher in the pre-conception period for the first time in the literature. More studies using standardized methods and a meta-analysis of these studies may help to discover the relationship between caffeine and pregnancy outcomes, neonatal and childhood health.

CONCLUSION

The level of caffeine intake among pregnant women is still at a high level all over the world. The main goal of reducing caffeine consumption is to achieve healthy offspring. In clinical practice, the nurses should give education about the harmful effect of caffeine on fetal and neonatal health to pregnant and should encourage them to avoid decreasing the caffeine consumption.

Ethics Committee Approval: The study was conducted in accordance with the Helsinki Declaration and approved by Karabuk University Human Studies Ethical Comitee with protocol number 2018/9-21.

Informed Consent: Informed consent was provided from all patients who wanted participated in the study.

Authorship Contributions: Idea/Concept: YK, VYT, Design: YT, VYT, Supervision: YK, VYT, Data Collection or Processing: ED, Analysis or Interpretation: ED, Literature Search: YK, VYT, Writing: YK, ED, Critical Review: VYT, MT, References And Fundings: -, Materials: -.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they have no relevant financial.

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