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Original Article

Associations of Hookah and Cigarette Smoking With In Vitro Fertilization Outcomes: A Cross-Sectional Study

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Abstract

Objective: The global prevalence of smoking among women of reproductive age is significant, and the impact of tobacco on assisted reproductive technologies requires evaluation. This study aimed to determine the association between cigarette or hookah smoking with in vitro fertilization (IVF) outcomes.

Materials and methods: In this cross-sectional study, we enrolled 200 women undergoing their first IVF cycle at Arash Infertility Center (Tehran, Iran). Ovarian response, oocyte maturity (Metaphase I (MI) and II (MII), embryo quality, and pregnancy outcomes were compared between cigarette smokers and non-smokers, as well as between hookah users and non-users.

Results: Among the 200 participants, cigarette smokers (n=100) had significantly fewer mature (MII) oocytes than non-smokers (6.72±2.90 vs. 8.63±6.20; P = 0.036). Hookah users (n=100) did not show a significant decrease in the number of MII oocytes compared to non-smokers (8.06±5.81 vs. 8.73±6.12; P = 0.512). There were no significant differences in MI oocytes, embryos obtained, embryo quality, or chemical and clinical pregnancy rates between cigarette smokers and non-smokers. Hookah users had more MI oocytes compared to non-users (7.88±5.63 vs. 6.05±4.44; P = 0.010). The chemical pregnancy rate was higher in the hookah-user group than in non-users (P = 0.036). Logistic regression analysis showed no link between cigarette smoking, hookah smoking, age, or BMI and pregnancy rates.

Conclusion: Cigarette smoking may impair oocyte maturation, while hookah use showed inconsistent associations with IVF outcomes. These findings should be interpreted cautiously due to the limited sample size and cross-sectional design.

Keywords: Cigarette Smoking; Water Pipe Smoking; Fertilization In Vitro

Introduction

Infertility affects many couples worldwide, and In-vitro fertilization (IVF) is the cornerstone of treatment. Despite recent advances, the live birth rate per cycle remains modest, and this issue highlights the need to identify modifiable factors affecting success, especially factors related to

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lifestyle. Smoking is one of the most common and potential exposures affecting success rate of infertility treatments.

Smoking is common among women of reproductive age, with current global estimates of use ranging from 15 to 17% (1, 2). In Iran, recent national data show that approximately 4.4% of women are current smokers (3). While the adverse effects of smoking on general fertility and pregnancy are well established, its specific effect in the context of IVF is less clear and findings are conflicting (4). Some studies report that female smoking is associated with reduced ovarian response, fewer retrieved oocytes, and lower fertilization and pregnancy rates (5-9).

Conversely, other studies have found no significant association between smoking and major IVF outcomes such as oocyte quality, embryo development, or clinical pregnancy rate (10-13).

In contrast to cigarettes, hookah (water pipe) smoking has been less studied in relation to reproductive health, despite its prevalence in many regions, especially in the Middle East. The limited evidence available on hookah and fertility focuses primarily on semen parameters in men, and there are almost no data on its effect on ovarian response, embryo quality, or pregnancy outcomes in women undergoing IVF (14).

Identifying factors affecting IVF outcomes and developing targeted protocols are crucial for improving success rates (15). While the adverse effects of cigarette smoking on fertility are well documented, its impact on in vitro fertilization remains inconsistent, and evidence regarding hookah use is scarce. Therefore, this study aimed to evaluate the associations of cigarette and hookah smoking with oocyte maturity, embryo quality, and pregnancy outcomes among women undergoing in vitro fertilization.

Materials and methods

This cross-sectional study examined the association between cigarette or hookah smoking with IVF outcomes among women undergoing IVF at Arash Infertility Center, Tehran University of Medical Sciences. Ethical approval was obtained (IR.TUMS.MEDICINE.REC.1401.223). All individuals participating in the study received comprehensive information regarding the objective of the study. All participants signed informed consent.

Inclusion criteria consisted of women undergoing their first IVF cycle with ovarian stimulation using the agonist and antagonist protocol. Exclusion criteria included individuals receiving donor eggs, ovarian hyperstimulation syndrome, and the presence of systemic diseases, including diabetes, hypertension, and autoimmune diseases.

Participants completed a questionnaire covering demographics, fertility history, and detailed smoking habits. Laboratory tests measured follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels. Outcomes included the number of MI and MII oocytes, embryos obtained, embryo quality, and pregnancy rates.

Smoking status was self-reported. Participants were classified as current cigarette smokers if they reported daily or occasional cigarette use within the past three months, and as hookah users if they smoked hookah at least once per week. Non-smokers were defined as women with no tobacco exposure during the past year. Covariates, including age, BMI, infertility duration, and baseline FSH, were controlled for using multivariable logistic regression models.

Embryo Grading and Quality Assessment:

Embryo quality was assessed on Day 3 of development using standardized morphological criteria (16). Blastomeres were evaluated for cell number, symmetry, and fragmentation by two blinded embryologists. Embryos were classified as:

Grade 1: lesser than 10% fragmentation, symmetrical.

Grade 2: Between 10 and 25% fragmentation.

Grade 3: Greater than 25% fragmentation or asymmetric blastomeres.

Embryos were scored as excellent quality (Grade 1), good quality (Grade 2), and poor quality (Grade 3).

Discrepancies (<5% of cases) were resolved by a third senior embryologist.

Subsequently, study's outcomes including the number of retrieved oocytes Metaphase I(MI) oocytes, the number of mature Metaphase II(MII) oocytes, number and quality of embryos (grade 1, 2, 3), and finally chemical pregnancy (positive pregnancy test 14 days after embryo transfer) and clinical pregnancy (observation of the gestational sac 6 weeks after transfer by Ultrasound) were compared between cigarette smoker and non-smoker groups, as well as between hookah users and non-users.

The sample size in this study was estimated to be 200 based on the study by Cinar et al. and considering the average number of metaphase II in the smoking group (8.7±6.9) and in the non-smoking group (12.4±9.3), taking into account a type I error rate of 5% and a power of 80% (6).

Table 1: Baseline characteristics of the participants in cigarette smokers, non-smokers, hookah users and non-users

Characteristics	Cigarette smoker (n=100)	Non-smoker (n=100)	p-value
Age (mean± SD)	34.2±5.8	35.3±5.3	0.355
BMI(mean± SD)	26.7±4.9	25.8±4.5	0.265
FSH(IU/ml) (mean± SD)	7.1±3.4	7.6±3.8	0.608
LH(IU/ml) (mean± SD)	5.9±4.3	6.1±4.2	0.362
	Hookah users (n=80)	**Non-users (n=120)**	**p-value**
Age (mean± SD)	32.2±5.4	35.3±5.3	0.001
BMI(mean± SD)	27.6±4.9	25.8±4.5	0.341
FSH (IU/ml) (mean± SD)	6.8±3.1	7.6±3.8	0.420
LH (IU/ml) (mean± SD)	11.5±14.3	6.1±4.2	0.080

Statistical analysis: Data were analysed using SPSS version 20. Qualitative variables were reported as frequencies and percentages, while quantitative variables were expressed as mean± standard deviation. The Kolmogorov-Smirnov test assessed normality. Group comparisons used the chi-square test for categorical variables and the Mann-Whitney test for continuous variables. Logistic regression evaluated associations between smoking and IVF outcomes, with significance set at $P< 0.05$.

Results

The study included 200 women. The mean age was 34.35 ± 5.8 years, with no significant difference between smokers and non-smokers (P = 0.355) (Table 1). Hookah users were younger than non-users (P = 0.001). Cigarette smokers had significantly fewer MII oocytes than non-smokers (6.72 ± 2.90 vs. 8.63±6.20; P = 0.036) (Table 2). Hookah users had more MI oocytes than non-users (P = 0.01). Additionally, chemical pregnancy rates were higher in hookah users compared to non-users (P = 0.03) (Table 3). However, the association between hookah use and chemical pregnancy was attenuated after adjustment for age and BMI in multivariable analysis. No significant differences were observed in embryo quality or clinical pregnancy rates between groups (Tables 2 and 3).

Comparison of the outcomes of IVF between smoker and non-smoker groups indicated a significant reduced M2 oocyte in smokers compared to non-smokers (P = 0.036) (Table 2). In hookah users increased number of M1 oocyte, and chemical pregnancy compared to non-hookah user were reported (Table 3). There were no significant differences between both smokers and hookah users compared to individuals using none (Table 4). Logistic regression showed no association between smoking, age, or BMI and pregnancy rates (Table 5).

Based on the logistic regression conducted, the results indicate no association between cigarette smoking, hookah smoking, age and BMI with pregnancy rate (Table 5).

Discussion

Our results indicate that cigarette smoking was associated with a reduced number of mature (MII) oocytes, consistent with potential oxidative stress and follicular damage. In contrast, hookah use was associated with a higher number of immature (MI) oocytes and an increased rate of chemical pregnancy, although the latter finding may be influenced by confounding factors such as younger age among hookah users.

Table 2: Comparison of the outcomes of IVF between cigarette smoker and non-smoker groups

Outcome	Cigarette smokers (n=100)	Non-smokers (n=100)	p-value
M1 Oocytes (mean± SD)	6.72±2.90	6.78±5.20	0.930
M2 Oocytes (mean± SD)	6.72±2.90	8.63±6.20	0.036
Number of embryos (mean± SD)	2.04±0.56	1.93±0.57	0.123
Chemical pregnancy [n (%)]	1(11.1%)	8(88.9%)	0.880
Clinical pregnancy [n (%)]	6(13.6%)	38(86.4%)	0.265
Embryo quality A [n (%)]	29(28.2%)	14(13.6%)	0.426
Embryo quality A→B [n (%)]	62(63.1%)	80(77.7%)	0.153
Embryo quality B [n (%)]	9(8.7%)	6(8.7%)	0.287

N: number

Table 3: Comparison of the outcomes of IVF between hookah users and non-users groups

Outcome	Hookah users (n=80)	Non-users (n=120)	p-value
M1 Oocytes (mean± SD)	7.88±5.63	6.05±4.44	0.010
M2 Oocytes (mean± SD)	8.06±5.81	8.73±6.12	0.512
Number of embryos (mean± SD)	1.98±0.51	1.92±0.61	0.083
Chemical pregnancy [n (%)]	4(44.4%)	5(56.8%)	0.036
Clinical pregnancy [n (%)]	26(59.1%)	18(40.9%)	0.255
Embryo quality A [n (%)]	23(28.7%)	20(15.9%)	0.524
Embryo quality A→B [n (%)]	50(66.3%)	92(73%)	0.334
Embryo quality B [n (%)]	4(5%)	11(11.1%)	0.223

The higher chemical pregnancy rate in hookah users is unexpected and may reflect sampling bias or chance findings. Importantly, no detrimental effect on embryo quality or clinical pregnancy rates was observed for either form of smoking. Results of logistic regression performed indicated no association between cigarette smoking, hookah smoking, age, and BMI with pregnancy rate.

Previous studies have reported inconsistent effects of smoking on IVF outcomes (4, 17). In a study by Cinar et al. (4), the effect of cigarette smoking on IVF outcomes was assessed. Interestingly, while the smoker group had a significantly higher number of total and mature oocytes retrieved, no significant differences were detected between smokers and non-smokers in fertilization rate, oocyte quality index, pregnancy rate, or embryo development rate ($p > 0.05$). Additionally, cigarette smoking in males did not significantly affect IVF outcomes. Finally, similar to the results of our study, regression analysis in Cinar et al. study showed no significant differences in fertilization rates, clinical pregnancy rates, and embryo quality based on the smoking status of either the male or female participants.

A study by Fuentes et al. (17) assessed the impact of a recent history of cigarette smoking in both partners on ART outcomes. The recent history of smoking in female individuals was significantly linked to a reduced retrieved ovum, and, similar to the results of our study, no harmful impact of recent history of female smoking on implantation rates was detected. However, the recent history of male smoking significantly reduced live birth rates.

The evidence regarding the impact of hookah smoking on human fertility or reproductive outcomes is limited. In a cross-sectional study by Albeitawi et al. effect of hookah smoking on semen parameters in male individuals undergoing seminal fluid analysis at IVF laboratories was assessed. A total of 104 male individuals aged 25 to 45, with no history of smoking cigarettes and without chronic medical conditions, were included. Among them, 54 were hookah smokers, and 50 were non-smokers. Semen parameters were compared between the two groups. The hookah smokers showed non-significantly lower semen volume, normal morphology, and progressive motility than non-smokers, suggesting that hookah smoking does not have a significant effect on semen parameters (14).

Our results indicated that cigarette smoking did not have a statistically significant negative effect on IVF outcomes. Since smoking among Iranian women is relatively uncommon, larger studies including more female smokers are needed to better assess smoking's effects on infertility and IVF success.

Previous research has suggested that cigarette smoke can affect female reproductive organs (18, 19). However, confirming the direct effects of cigarette smoke on gamete and embryo development is difficult to study in vivo due to ethical and legal constraints.

Table 4: Comparison of IVF outcomes between tobacco users (cigarette and hookah) and non-users

Outcome	Cigarette & hookah users (n=75)	non-users (n=125)	P-value
M1 Oocytes (mean± SD)	7.14±1.57	6.00±4.54	0.152
M2 Oocytes (mean± SD)	7.14±1.57	6.45±9.21	0.452
Number of embryos (mean± SD)	2.00±0.01	1.90±0.60	0.631
Embryo quality A [n (%)]	23(30.7%)	20(15.9%)	0.524
Embryo quality A→B [n (%)]	48(64%)	92(73%)	0.232
Embryo quality B [n (%)]	4(5%)	11(11.1%)	0.413

Table 5: The association of cigarette smoking, age, BMI, and hookah smoking with pregnancy rate

Pregnancy rate	OR	CI 95%	P-value
Cigarette smoking	1.02	0.38-0.37	0.362
Age	1.05	0.41-3.42	0.683
BMI	1.07	0.77-5.53	0.154
Hookah smoking	1.5	0.48-4.99	0.472

OR: Odds Ratio; CI: Confidence interval

In contrast, IVF procedures provide an opportunity to observe fertilization and embryo development, allowing us to assess how smoking might impact these processes and pregnancy. In our study, we did not find significant negative effects of cigarette smoking on IVF outcomes. It is important to note that during IVF, embryos are cultured in media free of cigarette smoke products. Thus, studying cigarette smoking through IVF may not fully represent the true in vivo environment. Additionally, since IVF results are similar in smokers and non-smokers, IVF may offer an advantage for infertile patients who smoke by avoiding the harmful effects of cigarette smoke on sperm quality and movement (20, 21), as well as on fallopian tube function and the uterus. (22, 23) Nonetheless, further research is required to better understand the influence of smoking on reproductive health in both men and women.

This study had several limitations. Participants reported their smoking habits without any biochemical checks. The number of smokers in the sample was small, which affected the strength of the results. Potential confounders such as socioeconomic status, passive smoke exposure, and detailed causes of infertility were not adjusted for. Additionally, the cross-sectional design prevents establishing temporal or causal relationships. The follow-up period was short, so larger studies with longer follow-up are recommended.

Conclusion

Cigarette smoking may lower oocyte maturity in women undergoing IVF, while hookah smoking showed inconsistent associations with reproductive outcomes. Larger, prospective studies with biochemical confirmation of smoking status and comprehensive adjustment for confounders are needed to clarify these findings and their clinical consequences.

Conflict of Interests

Authors declare no conflict of interests.

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