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Do Lifestyle and Physical Factors Influence Fertility Potential and Assisted Reproduction Outcomes in Infertile Men?

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Abstract

Background: The effects of lifestyle and physical factors on male fertility potential are controversial and these disagreements have increased public and research attention.
Objectives: This study was planned to evaluate the effects of modifiable lifestyle and physical factors on the semen quality and assisted reproductive outcomes.
Methods: This prospective study evaluated lifestyle and physical factors in 306 infertile men under an assisted reproductive program such as body mass index, age, abstinence time, tobacco smoking, varicocele treatment, physical activity, caffeine consumption, and the use of cell phones, as well as sperm chromatin integrity and condensation, semen parameters, and assisted reproductive outcomes between 2016 and 2018. Statistical analysis was performed using SPSS version 20 and CorrelationAttributeEval and Ranker modules of WEKA software were applied to evaluate the effect of each feature/factor of men on the biochemical pregnancy rate.
Results: A negative association was seen between the total sperm count and abstinence time (< 3 days, P = 0.02) and caffeine consumption (> 4 cups/d, P = 0.03). A decreased sperm concentration, normal morphology, motility, and chromatin normality were found in the categories of older age (> 35-years-old) and elevated BMI (> 30, P = 0.03). The poor embryo quality (grade D) and increased spontaneous abortion were found in men with high age, BMI, caffeine consumers, and smokers. The effects of smoking, age, and BMI weighed more than the effects of other parameters on biochemical pregnancy.
Conclusions: Factors such as aging, elevated BMI, smoking, and high consumption of caffeine via affecting sperm parameters and increasing DNA damage may affect assisted reproductive outcomes (e.g., poor embryo quality and high abortion).

Keywords: Physical Factor, Lifestyle, ART, Male Factor Infertility, Pregnancy

1. Background

About one-half of the reproductive abnormalities have been reported in the male partner, but a few risk factors have been studied and identified for male fertility potential (1). Many studies suggest that semen quality can be influenced by lifestyle and physical factors such as smoking, obesity/overweight, sexual activity, stress, physical activity, diet, especially alcohol and caffeine, age, using cell phones, and varicocele (2, 3).

For example, several studies have reported that there is an adverse relationship between obesity and normal semen quality (4, 5). A negative association was also found between advancing age in men and quality of ejaculates and chromatin disorders (2). On the other hand, some authors have reported that elevated body mass index (BMI) affects sperm quantity and quality (4); however, in another study, these results were rejected (6). Therefore, there are contradictory results about the lifestyle, physical factors, and male fertility potential.

Nevertheless, the presence of risk factors for fertility potential was suggested in some reviews (7, 8). Little information is available on whether lifestyle and physical factors in men are related to assisted reproductive outcomes such as the rate of fertilization, zygote and embryo quality, clinical pregnancy, and abortion rate.

2. Objectives

Therefore, this study was planned to find the risk parameters related to lifestyle and physical factors such as age, BMI, smoking, using cell phones, physical activity, abstinence time, caffeine consumption, and repaired varicocele, which were supposed to change the semen quality

and chromatin status of men admitting to an in vitro fertilization (IVF) clinic. In addition, the effect of these factors on assisted reproductive technique (ART) outcomes was studied.

3. Methods

3.1. Study Population

The study population consisted of 450 men under an in vitro fertilization-intracytoplasmic sperm injection (IVF-ICSI) program admitting to the Alzahra Educational and Remedial Center (IVF center) from May 2016 to May 2018. They were invited to take part in the study to evaluate the effects of lifestyle and physical factors on male reproductive health. Out of 450 men attending this infertility treatment center, informed consent was obtained from 306 of them to participate in the study. The men with diseases of diabetic, thyroid, and/or taking hormone medications were excluded from the study. The couples who had faced female factor infertility were also excluded.

3.2. Information About Lifestyle and Physical Factors

The information about lifestyle and physical factors was obtained using a detailed questionnaire.

• On the day of oocyte retrieval, the weight and height of the patients (both men and women) were accurately measured.

• The baseline questionnaire contained questions about exercise phrased as follows:

Doing regular exercise, the duration of exercise (in number of years), the number of exercise hours per week, and the most frequent type of exercise. Therefore, physical activities were categorized based on the intensity of activities as follows: Yes or no.

• The type of caffeine consumed during lifetime included tea, coffee, milk chocolate, and dark chocolate. The caffeine consumption was categorized as 0 cup/d, ≤ 1 cup/d, 2 - 3 cups/d, and $>$ 4 cups/d (9).

• The use of cell phones was categorized based on the duration of using this equipment ($\geq$ 1 h/d or no).

• Cigarette smokers were divided into two groups of consumers and non-smokers.

• We also specifically studied the effect of varicocele treatment in men with either subclinical or grade 1 varicocele on the semen quality.

• The semen quality was evaluated in relation to abstinence duration ($<$ 3, and $>$ 3 days of abstinence), too.

3.3. Semen Analysis

The evaluation of semen parameters was done according to the World Health Organization (WHO) criteria (10). The analyzed parameters were volume, concentration, morphology, motility, pH, liquefaction time, and agglutination rate.

The assessment of the sperm chromatin status was done using toluidine blue (Sigma, Germany) and aniline blue (Sigma, Germany) stains. Toluidine blue stain is used to assay chromatin integrity that binds to the sites of the damaged DNA structure. The aniline blue staining was performed to detect the internal structural defects of sperm samples that bind to histones. 300 sperms were analyzed in each slide under a light microscope.

3.4. ART Procedures

Controlled ovarian hyperstimulation was done based on the protocol of long luteal suppression. The retrieved follicles were prepared to inject based on the ICSI procedures using an inverted microscope (Olympus IX70, Tokyo, Japan). Injected oocytes were cultured into G1^{PLUS} (Vitrolife, Sweden) and incubated in a humidified atmosphere with 5% CO_2 at 37°C.

The evaluation of oocyte fertilization was done at 16 - 18 hours after microinjection in the presence of two pronuclei. The grading of two-pronuclear zygotes was done according to the Scott et al. scoring system (11). The evaluation of embryo grade was done based on their morphology at 48 - 72 hours after injection (12).

Suitable embryos were transferred as intrauterine at 48 - 72 hours after ICSI. Increasing serum beta-HCG and the observation of intrauterine sac with a heart function were considered as biochemical and clinical pregnancy at two and four weeks after embryo transfer (ET), respectively. Abortion was also determined as pregnancy loss spontaneously after the observation of pregnancy by ultrasound.

3.5. Statistical Analysis

Statistical analysis was performed using SPSS version 20 (IBM, Armonk, NY, USA). The effects of lifestyle and physical parameters on semen parameters, chromatin status, and ART outcomes were analyzed using binary and multinomial logistic regression. $P < 0.05$ was considered statistically significant.

To evaluate the effect of each feature/factor of men on the chemical pregnancy rate, CorrelationAttributeEval and Ranker modules of WEKA software were used.

4. Results

4.1. Study Population

306 couples attending an infertility clinic to be treated under IVF-ICSI cycles took part in the study. The mean age of the women participating in the study was 31 $\pm$ 5.2 years and there was no statistical difference in their age and BMI (21.7 $\pm$ 3.8).

4.2. Lifestyle and Physical Factors Among Study Participants

The results showed that 28.1% of the study participants were lower than 25 years old. Most of them were 26 - 35 years old (34.3%) and higher than 35 years old (37.5%). The overweight (BMI: 25 - 29.9 kg/m^2) was observed in 50.6% of the participants, whereas 18.6% were obese (BMI: > 30 kg/m^2) and 30.7% had normal weight (BMI: 18 - 24.9 kg/m^2). 58.4% of the men used the cell phones more than one hour per day and had physical activity more than once per week (51.6%). In addition, abstinence before the semen analysis was higher than three days in most of the studied men (61.4%).

65.3% of the studied men were non-smokers and repaired varicocele was reported by 31.6% of the participants. Most of the participants had non-everyday caffeine drinking (49.6%).

4.3. The Effects of Lifestyle and Physical Factors on Semen Quality

Younger age (< 25 years) was negatively associated with abnormal morphology (< 4%: P = 0.03 and 4% - 14%: P = 0.001) and the percentage of sperm head abnormalities (< 30%; P = 0.000 and 30% - 35%; P = 0.03) compared to the men higher than 35-years-old. The age of 25 - 35 years also showed declined head abnormalities of lower than 30% (P = 0.001). Age (< 25 years) was also negatively associated with lower motility (< 32%; P = 0.000), whereas it was positively related to the decrease in the percentage of spillage (P = 0.017).

The overweight participants had declined sperm concentration (P = 0.05) and semen volume (P = 0.001). The obesity was negatively associated with motile sperm cells (P = 0.000).

Tobacco smoking was negatively related to normal sperm morphology (P = 0.000). Repaired varicocele was negatively associated with declined sperm concentration (P = 0.05) and motile sperm cells (P = 0.000).

The abstinence time of lower than three days was negatively related to the total sperm count (P = 0.02) compared to the abstinence time of more than three days. Everyday coffee drinking decreased the risk of total sperm count of lower than 60 million (P = 0.03) compared to higher consumption of caffeine ($\geq$ 4 cups/d) (data not shown).

4.4. The Effects of Lifestyle and Physical Factors on Chromatin Structure

Younger age (< 25 years) was significantly associated with a decrease in abnormal chromatin condensation (8.16%, P = 0.003). In addition, the men with normal weight (BMI: 18.5 - 24.9) showed a significant association with a decrease in damaged chromatin rate (P = 0.017). The results showed that smoking habits were positively associated with increased damaged chromatin (P = 0.000) in comparison with non-smoker men (data not shown).

4.5. The Effects of Lifestyle and Physical Factors on Reproductive Outcomes

A positive association was found between men with age of lower than 25 years and good quality of embryos (grade A: P = 0.001 and grade B: P = 0.000) compared to other groups. The negative effects of lifestyle and physical factors were obviously observed on pregnancy and abortion rates (Table 1). As a result, the pregnancy rate significantly increased in men with age of lower than 25 years in comparison with other groups (P = 0.02). In addition, the percentage of abortion decreased in these groups significantly (P = 0.002). A negative association was also observed between being normal weight and abortion rate (P = 0.000).

The results showed smoking men had a lower percentage of zygotes with high quality (Z1 degree: P = 0.001 and Z2 degree: P = 0.005) compared to nonsmokers. Smoking habit among the study participants was positively associated with abortion rate (P = 0.000). Moreover, a positive association was found between caffeine consumption ($\leq$ 1 cup/d) and grades of A and B quality of embryo (P = 0.03 and P = 0.02, respectively) compared to consuming more than 4 cups/d. However, a negative association was found between caffeine consumption (0 and $\leq$ 1 cup/d) and abortion rate (P = 0.000 and P = 0.001, respectively) (Table 1).

4.6. Factors Ranking

Another important experiment is to measure the effect of each feature/factor on male fertility potential. In this way, CorrelationAttributeEval and Ranker modules of WEKA software were used. Table 2 shows the effects of different features/factors. The effect of smoking and age weighed more than the effect of other parameters on chemical pregnancy.

5. Discussion

This study was conducted to evaluate the semen quality and ART outcomes (such as fertilization rate, zygote and

Table 1. The Effect of Physical Factors and Lifestyle on IVF-ET Outcomes[a]

	Fertilization Rate %	Zygote Degree, %				Embryo Quality, %				Biochemical Pregnancy Rate N/ET (%)	Abortion Rate N/Beta+ (%)
		Z1	Z2	Z3	Z4	A	B	C	D		
Age, y											
< 25	58.7	29.1	46.4	14.2	10.2	28.8	39.0[b]	19.9	12.2	18/35[c] (51.4)	3/18[c] (16.6)
26 - 35	67	32.5	41.3	16.1	10	29.1	40.3[c]	20.7	9.82	40/99 (40.4)	10/40 (25)
> 35	63.1	28.1	36.9	19.2	15.7	12.4	38.3	24.1	25	36/101 (35.64)	13/36 (36.1)
BMI, kg m^{-2}											
18.5 - 24.9	67.19	28.65	32.6	25.96	12.79	32.45	37.6	12.9[c]	16.99	26/79 (32.91)	7/26[b] (26.92)
25 - 29.9	61.5	27.6	30.9	24.3	17.1	30.2	29.8	21.9	17.9	37/107 (34.5)	10/37 (27)
> 30	67.4	21	27.3	36.2	15.4	18.1	25.1	38.7	17.9	13/39 (33.33)	4/13 (30.7)
Tobacco smoking											
Yes	64.5	14.2[b]	21.8[d]	32.2	31.8	24.6[d]	20[d]	31.7	23.5	18/64 (28.12)	8/18[b] (44.4)
No	65	29.6	34.7	19.6	16	39.1	34.1	18	8.66	58/166 (34.9)	5/58 (8.62)
Repaired varicocele											
Yes	62.3	28.6	36	24.2	11	26.8	32.3	22.1	18.6	20/58 (34.48)	6/20 (30)
No	65.9	31.5	38.5	21.1	8.86	36.3	37.1	14.5	11.9	55/171 (32.1)	19/55 (34.5)
Using cell phones, ≥ 1 h/d											
Yes	66	29.6	32.7	22.8	14.7	28.4	34.1	20.4	16.9	50/142 (35.2)	15/50 (30)
No	62.45	30.08	34.18	20.51	15.23	31.18	34.16	23.81	10.85	26/88 (29.54)	7/26 (26.92)
Physical activity, ≥ once/wk											
Yes	62.7	34.91[d]	37.12[d]	13.76	14.21	30.01	32.92	19.36	17.71	39/120 (32.5)	12/39 (28.2)
No	66.8	24.65	26.06	19.32	29.97	23.45	24.9	23.02	28.63	38/109 (34.86)	11/38 (28.94)
Abstinence time, d											
< 3	64.82	30.09	34.87	21.46	13.58	31.99	32.4[b]	22.06	13.52	36/97 (37.11)	9/36 (25)
> 3	65.15	26.78	29.76	28.13	15.33	27.5	31.16	26.83	14.51	37/118 (31.35)	14/37 (37.83)
Caffeine consumption, cup/d											
0	65.2	35.7	38	19.5	6.68	35.1	36.3	14.1	14.3	44/137 (32.1)	7/44[b] (15.9)
≤ 1	60.9	33.3	37.9	21	7.73	35.1[c]	39.2[c]	19.07	6.62	10/30 (33.3)	2/10[b] (20)
2 - 3	62	33.9	37.8	22.4	5.73	30.4	34.2	24.9	10.2	8/30 (26.66)	3/8 (37.5)
≥ 4	67.1	31.9	34.7	23	10.2	28.1	29.2	26.6	15.9	14/45 (31.11)	6/14 (42.8)

Abbreviations: BMI, body mass index; ET, embryo transfer; N, number.
[a]There were significant relationships between lifestyle factors and fertilization rate, zygote and embryo quality and abortion rate.
[b]P value < 0.001.
[c]P value < 0.05.
[d]P value < 0.01.

embryo quality, and pregnancy and abortion rates) in relation to different lifestyle and physical factors in infertile men. We observed several findings in this study: (i) The semen quality changed with lifestyle and physical factors such as age, BMI, varicocele treatment, tobacco smoking, abstinence time, and caffeine consumption, (ii) the lifestyle and physical factors affected the DNA integrity and condensation, and (iii) the lifestyle and physical factors

Table 2. The Effect of Different Features on Male Fertility Potential[a]

Feature	Effect (Biochemical Pregnancy Prediction)
Tobacco smoking	0.0795
Age	0.0554
BMI	0.0526
Caffeine consumption	0.0406
Ejaculation abstinence	0.0315
Physical activity	0.0271
Cell phones	0.0149
Repaired varicocele	0.0119

[a]The effects of smoking, age, and BMI weighed more than the effects of other parameters on biochemical pregnancy.

lead to changes in the ART outcomes (embryo quality and spontaneously miscarriage rate, in particular).

In this study, a significant association was found between BMI and some semen parameters (i.e., sperm concentration and motility). A decrease in sperm concentration, as well as motility, was also revealed in men with overweight (high weight) compared to men with ideal weight (BMI: 18.5 - 24.9 kg/m^2). High BMI was also associated with significantly increased damaged chromatin.

Our results, in accordance with those of other studies, indicate a positive association between male infertility and excessive body weight. For example, Jensen et al. observed that low or high BMI and reduced semen quality were correlated with each other (5). This study also showed that high BMI increased endocrine changes in reproductive hormones (5). Hammoud et al. reported that elevated BMI decreased sperm concentration and progressive motility (4). In another study, a comparable difference was reported neither between elevated BMI and semen parameters nor between BMI and chromatin integrity and condensation. On the other hand, chromatin integrity was affected by aging (2). In this study, embryo quality decreased in men with elevated BMI (> 30 kg/m^2). In addition, the abortion rate increased in these patients. It can be inferred that elevated BMI may influence the semen quality and chromatin integrity so that its effect can be seen at the embryonic development stages.

However, a negative relationship was also found between aging and some semen parameters (sperm concentration, normal morphology, head defects, spillage, and abnormal chromatin condensation). Moreover, an increase in age leads to a decrease in sperm motility. It is in accordance with other studies, reporting an association between decreased motility and chromatin disorders and aging in men (2). The effect of aging was observed on the male fertility potential so that the embryo quality and pregnancy rate declined in older men (> 35-years-old) compared to younger men (< 25-years-old). In addition, the abortion rate increased in these participants.

In this study, no association was found between smoking habit and sperm parameters while the evaluation of the effects of smoking on male fertility showed that sperm morphology and chromatin integrity decreased in the men with smoking behavior. These results are in agreement with those of previous studies that smoking has a reverse relationship with sperm parameters (8). The declined zygote and embryo quality and therefore, increased the abortion rate were observed in couples with smoking men.

A negative association was observed between the total sperm count and lifestyle factors such as abstinence time (< 3 days) and caffeine consumption. Increasing caffeine consumption (more than 1 cup/d) led to decreased embryo quality and increased abortion rate. A study has reported that total testosterone and total/free estradiol increased and decreased, respectively, in men consuming caffeine (13). Therefore, hormonal changes arising from lifestyle can affect the spermatogenesis process and influence the male fertility potential (14).

In this study, the effects of varicocele treatment were investigated through the following questions: (1) Does sperm DNA damage decrease after varicocele treatment? (2) Are semen parameters improved after varicocele treatment? And (3) are assisted reproductive outcomes are improve after varicocele treatment? The results showed that chromatin damage and ART outcomes were improved, but the sperm concentration and motility were declined in these men.

5.1. Conclusion

Overall, data from this study indicated the significant effects of modifiable man lifestyle and physical factors (age, BMI, smoking habit, and caffeine consumption) on IVF-ET outcomes: Embryo quality, pregnancy rate, and abortion rate.

Conflicting results were obtained from this study attempting to answer the question of whether or not the effects of lifestyle and physical factors are observed on assisted reproductive outcomes including fertilization rate, zygote and embryo quality, pregnancy rate, and spontaneously miscarriage rate. In conclusion, it can be said that factors such as age, BMI, smoking habit, and high consumption of caffeine can decrease the success of ART outcomes.

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Footnotes

Authors' Contribution: All authors participated in the design of the study, interpretation, and analysis of the data and reviewing of the manuscript; Fatemeh Ghasemian and Mohammad Hadi Bahadori conducted the experiments and wrote the manuscript and Shahin Esmaeilnezhad supplied critical reagents.

Conflict of Interests: The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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