

A case-control study of the factors affecting male infertility

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Background/aim: Infertility is defined as the inability to conceive after at least 1 year of unprotected intercourse. In about one third of infertile couples, a male factor is the primary problem. Thus, the present study aimed to determine the most common risk factors for male infertility in Iranian men.

Materials and methods: This case-control study included 268 men attending an infertility clinic in Shiraz, Iran. In this study, 161 fertile men were compared with 108 infertile ones regarding risk factors such as smoking habits, drug consumption, hernia, varicocele, job, and BMI. The data were analyzed using logistic regression analysis and t-test.

Results: The mean age of the fertile and infertile participants was 37.5 ± 7 and 36.3 ± 10 , respectively. Our findings demonstrated a statistically significant relationship between male infertility and hernia, varicocele, taking ranitidine, job, and BMI. With an increase of 1 cigarette per day, there was a 1% decrease in the motility of the sperm. Moreover, with an increase of 1 year of cigarette smoking, 800,000 sperm are lost.

Conclusion: The results revealed varicocele and hernia as the most common risk factors in men attending the infertility clinics in Shiraz. In addition, strenuous work could cause testicular injury.

Key words: Male infertility, varicocele, cigarette smoking, case-control, risk factor

1. Introduction

Infertility is defined as the inability to conceive after at least 1 year of unprotected intercourse. In about one third of infertile couples, a male factor is the primary problem (1). Infertility is a common condition, affecting 15% of couples trying to conceive. Infertility evaluation includes an assessment of both the female and the male partner to discern the factors contributing to their difficulty in conceiving. A more detailed investigation is performed as dictated by individual factors (2).

Infertility causes personal and social problems for couples and it is noteworthy that, even today, recognizable causes of male infertility are present in only 40% of cases (3). Treatment of male infertility is difficult, especially in many developing countries (4). In developing countries, patterns of infertility are quite different from those in developed countries. Moreover, the incidence of preventable infertility is much higher in developing countries, and Iran is no exception (5).

A study conducted by the WHO has shown that 43% of women and 30.7% of men suffer from secondary infertility

and that there is a preventable cause of infertility in both (6).

In men, infertility risk factors, such as male accessory gland infection, mumps orchitis, varicocele, and cryptorchidism, are well documented. Many researchers have also shown the effects of environmental factors, such as toxic materials, pesticides, and radiation, on male infertility and demonstrated that toxic materials and pesticides could cause a decrease in sperm concentration (7,8). Moreover, oxidative stress has been recognized as one of the main causes of male infertility and impaired sperm (9).

Furthermore, smoking can be associated with male infertility; it can affect the motility and morphology of the sperm, and one study showed that oxidative stress in smokers was significantly higher than in nonsmokers (10). Treatment of infertility is expensive for the families and identifying the risk factors can be of great help to prevent infertility in many cases. Considering the fact that a limited number of studies have been conducted on the causes of infertility in men in Iran, the present

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study aimed to determine the most common risk factors for male infertility in men attending infertility clinics in Shiraz, Iran.

2. Materials and methods

The current case-control study was carried out in an infertility clinic in Shiraz, Iran, in 2011. This center provides infertility services for men from Shiraz as well as from other cities. The study sample consisted of 108 infertile men who had primary or secondary infertility and those who had been receiving treatment for more than 1 year. The control group included 161 fertile men randomly selected from among the clients of family planning clinics who had no history of infertility and had at least 1 child. The sample size in this study was determined based on the following formula:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

The infertility history, examination, and laboratory investigation used were those described in detail in each subject's record in the clinic. It should be noted that this study was approved by the Research Vice-chancellor of Shiraz University of Medical Sciences, Shiraz, Iran. In addition, written informed consent for taking part in the study was obtained from the patients in Zeinabiyeh hospital.

In this study, a structured questionnaire was designed in order to obtain information about the demographic characteristics, medical and reproductive health history, drug consumption, cigarette smoking, and varicocele and hernia diseases. Semen analysis was performed in the same laboratory. The study subjects were classified as smokers and nonsmokers. The smokers were also categorized according to duration of smoking. In addition, the consumed medications were classified as heart, blood pressure, diabetes, stomach, and tranquilizer drugs. Each subject's weight and height were also measured and recorded in the questionnaire.

The statistical analyses were performed using SPSS (version 17). The comparisons between the two groups were made using the odds ratios for characteristics such as smoking, varicocele, hernia, job, and drug consumption. In addition, t-test and analysis of variance (ANOVA) were used for continuous independent variables, such as weight and height. In order to determine the most significant factors, multivariate logistic regression tests were performed.

3. Results

The general characteristics of the infertile and fertile study subjects are presented in Table 1.

The study results revealed no statistically significant difference between the 2 groups regarding age, height, or duration of marriage. However, a statistically significant difference was found between the 2 groups regarding marriage age and weight.

The most commonly detected abnormality was decrease in sperm, which was found in 90 cases (83.3%). The results are shown in Table 2. The criteria of this table were identified by the World Health Organization (11).

In this study, the means of the sperm count, motility, and abnormal shape were 20×10^6 , 22.4%, and 62%, respectively.

Primary and secondary infertility were observed in 85.2% and 14.8% of subjects, respectively. In addition, in 27.8% of cases, both partners were infertile, among whom 50% had lack of ovulation and inactive ovaries, 24% had ovarian cysts, and the rest had problems such as salpingitis and fibroma.

The mean duration of infertility treatment was 7.5 years. Furthermore, 64.8% of the subjects had been referred to the clinic in the first year, 14.8% in the second year, and the rest had referred to the clinic after 2 years. The relationships between infertility and factors such as cigarette smoking, BMI, job, varicocele, and drug consumption are shown in Table 3.

The history of cigarette smoking was similar in the 2 groups. Moreover, all the other variables showed statistically significant associations with infertility.

Table 1. General characteristics of the infertile men compared with the fertile ones.

Characteristics	Infertile men (n: 108) mean ± SD	Fertile men (n: 161) mean ± SD	Statistical significance
Age	36.3 ± 10	37.5 ± 7	P > 0.05
Height	173 ± 7	174 ± 6	P > 0.05
Weight	71 ± 11	77 ± 15	P < 0.05
Marriage age	26 ± 6	28 ± 5	P < 0.05
Duration of marriage	10 ± 8	10 ± 6	P > 0.05

Table 2. Characteristic of sperm in infertile men.

Semen analysis	Number	Percentage
Azoospermia ¹	33	30.6
Oligospermia ²	57	52.7
Decrease in motility ³	63	84
Abnormal shape ⁴	62	82.7

1. Total absence of sperm in the semen
2. Sperm concentration of $<15 \times 10^6/\text{mL}$ or total count $<39 \times 10^6/\text{mL}$
3. $<40\%$ motility
4. $<4\%$ normal morphology of sperm

Duration of smoking had no effects on the motility and morphology of the sperm. However, with an increase of 1 cigarette per day, there was a 1% decrease in the motility of the sperm. Furthermore, varicocele and hernia were respectively 2.4 and 1.6 times more in the manual workers compared to the subjects with office jobs.

All the subjects were questioned about their history of diseases. None of the study participants had a history of cryptorchidism or radiotherapy, only 1 had a history of chemotherapy, and 1 had orchitis. In the case group, 39 subjects (36%) had a history of varicocele, among which 76.9% underwent varicocele surgery and 33% had no sperm (azoospermia). In the control group, on the other hand, 1.2% of the subjects had a history of varicocele surgery.

4. Discussion

The male factor is the cause of infertility in about 50% of infertile couples and is considered a condition difficult to treat. The risk factors for male infertility differ from one country to another; therefore, it is important that any developing country determines the most influential factors

in its population (4). The level and patterns of infertility are also significantly different among various countries and regions (12).

In this study, the effect of risk factors for male infertility was evaluated in men attending an infertility clinic in Shiraz. Most of the infertile subjects were manual workers who performed strenuous physical activities. Overall, laborers seem to be more at risk of infertility, which could be due to the strenuous physical work and testicular damage and its effect on the quality of sperm. This group of workers suffered from hernia and varicocele.

Among the case group subjects who had a history of hernia, 63.6% underwent surgery and 57% had no sperm (azoospermia). Animal models have shown the substantial effects of hernia repair on the structures in the spermatic cord, which is more pronounced in mesh repairs. Future clinical studies, preferably on bilateral patients, are necessary to investigate the clinical relevance of the effects of inguinal hernia and hernia surgery on male fertility (13).

The results of the logistic regression analysis showed that varicocele had a stronger effect compared to the other factors. Comparisons between infertile and fertile men also showed that varicocele, which can be treated by simple surgery, and hernia played an important role in infertility.

The present study also assessed the association between using ranitidine and infertility and revealed a significant relationship between them. This study showed that the difference between average weight and BMI was statistically significant in both fertile and infertile groups. The average weight of the infertile men was 6 kg less than that of the fertile ones. This might be due to the fact that in this study a greater percentage of the infertile men were manual workers, whose weight is usually lower than others. The number of cigarette smokers in the 2 groups was not statistically significant and this result had been reported in some other studies as well (4,14,15). Furthermore, in other studies investigating the effects of smoking on semen

Table 3. Cross tabulation between the possible risk factors and male infertility.

Factors	Infertile men (n: 108)	Fertile men (n: 161)	Statistical significant
Varicocele	39 (36%)	2 (1.2%)	OR = 4
Ranitidine consumption	16 (14.8%)	9 (5.6%)	OR = 2.9
Hernia	11 (10.2%)	2 (1.2%)	OR = 2.5
Job (manual worker/office worker)	67 (62%) (manual worker)	94 (58%) (office worker)	OR = 2.3
Smoking	35 (34.4%)	38 (23.6%)	OR = 1.5
BMI	23.6	25.3	t = 3.5 P < 0.05

OR = Odds Ratio

parameters, the concentration, motility, and normal sperm forms were significantly higher among the smokers in comparison to the nonsmokers (16–18).

Furthermore, a study conducted in Iran (Babol) showed that female infertility could be affected by men's smoking. That study also showed that infertility was more prevalent among the women with high BMI (19).

Varicocele is recognized as the leading cause of male infertility because it can impair spermatogenesis through several distinct pathophysiological mechanisms. Moreover, current evidence supports oxidative stress as a key element in the pathophysiology of varicocele-related infertility, although these mechanisms have not yet been fully described (20).

In this study, varicocele and hernia were respectively 1.6 and 2.4 times more in the manual workers compared to the subjects with office jobs. Varicocele was the most prevalent cause of infertility among the men attending the infertility clinics in Shiraz. The relationship between

varicocele and male infertility has been shown in another study as well (21).

The study findings revealed no significant relationship between mumps and male infertility, which might be the result of ignorance and forgetting mumps in childhood. Nevertheless, some other studies have shown a relationship between mumps and male infertility (4). In conclusion, history of hernia, varicocele, manual labor, and smoking can be considered risk factors for male infertility.

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