Epidemiological Analysis on Related Factors of Male Infertility in Shandong, China

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ABSTRACT
Objectives: To explore factors affecting male infertility to provide evidence for the etiology, prevention intervention and reproductive health services for male infertility.
Methods: A total of 16,286 male patients from 2011 to 2016 in Reproductive Hospital Affiliated to Shandong University, China were selected. We conducted surveys on these cases and analyzed the influencing factors of male infertility using logistic regression models.
Results: Univariate logistic regression analysis results showed that there was a statistically significant difference in educational level, career distribution and smoking between the case group and the control group (p<0.05). After controlling confounding factors in the multivariate logistic regression model, suffering from mumps or varicocele or orchitis (OR=1.228, p<0.001) in the past and smoking (OR=1.159, p=0.010) was associated with male infertility.
Conclusion: Suffering from mumps or varicocele or orchitis in the past and smoking could increase the risk of male infertility. Measures should be taken to reduce the incidence of male infertility.
Keywords: Male infertility; Influencing factors; Multi-factor analysis

INTRODUCTION
Infertility is a term doctors use if a woman can not be pregnant due to her spouse after at least one year of trying when they did not take any contraceptive measures. About 15% of couples have infertility problems, and about 40% ~ 50% were caused by male factors. The incidence of male infertility is growing in recent years. Most studies demonstrated that the decline of semen quality was associated with the deterioration of the global environment, the growing incidence of male reproductive diseases, the change of lifestyle and bad living habits. Male infertility has lead to heavy mental pressure, and become one of the main reasons for social and family instability. Semen routine analysis is an important test for the clinical evaluation of male fertility [1-3]. "Chinese Medical Association Men’s Disease Diagnosis and Treatment Guide Series-Guidelines for the Diagnosis and Treatment of Male Infertility" reported that the overall quality of semen in Chinese men was decreasing at a rate of 1% per year. As a result, it was necessary to explore related factors of male infertility. In this study, we used 16286 cases who saw a doctor from 2011 to 2016 in Reproductive Hospital Affiliated to Shandong University, China to further evaluate factors associated with male infertility.

MATERIALS AND METHODS
Subjects
16286 cases who saw a doctor from 2011 to 2016 in Reproductive Hospital Affiliated to Shandong University, China were chosen as subjects of our study. We divided subjects into a case group and a control group. 10286 infertile males because of their own poor semen quality entered the case group. 6000 infertile males caused by female partners' factors were recruited in the control group.

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Inclusion criteria

The case group needs to meet all of the following conditions: 1. Men had normal erection and sexual function; 2. Male semen was abnormal, and the routine detection indicators (endocrine, fallopian tube angiography, B-ultrasound, ovulation monitoring) of female partners were normal; 3. Infertility caused by male factors.

The control group needs to meet all of the following conditions: 1. Males had normal erection and sexual function; 2. Male semen was abnormal, but at least one routine detection indicator (including endocrine, fallopian tube angiography, B-ultrasound, ovulation monitoring) of female partners was abnormal; 3. Infertility caused by female factors.

Exclusion criteria

The exclusion criteria included any one of the following: 1. Both male semen and female indicators were abnormal; 2. Men can’t get erect properly but their semen was normal; 3. Primary infertility patients without definite cause while all indicators of the husband and wife were normal.

Methods

Medical records of all subjects were obtained from the medical records room of Reproductive Hospital Affiliated to Shandong University, and the general characteristics and test results of the subjects were recorded by professionals. Basic conditions (family address, education, and occupation), living habits (smoking), past history (mumps, varicocele, testicles) of all subjects were obtained from the medical record management system of the Information Management Center of the Reproductive Hospital affiliated to Shandong University.

Statistical analysis

The database of this study was established by professionals using Microsoft Excel. Data were input into Excel in parallel random double entry. Data were analyzed by SPSS21.0. Differences were examined with an independent sample t-test or chi-square test with SPSS version 21.0 (SPSS, Chicago, IL). The binary logistic regression model was also conducted to explore related factors of male infertility after adjusting confounding factors. Bilateral p<0.05 was considered to be statistically significant.

RESULTS

Comparison of residential areas

In the case group, 6919 and 3367 subjects lived in urban and rural areas, respectively. There were 4022 and 1978 subjects living in urban and rural areas in the control group. There was no statistically significant difference between the case group and the control group (p>0.05) (Table 1).

| Living areas | The case group (N(%)) | The control group (N(%)) | χ² | p-value |
|--------------|-----------------------|--------------------------|----|---------|
| Urban group  | 6919 (67.3%)          | 4022 (67.0%)             | 0.093 | 0.760 |
| Rural group  | 3367 (32.7%)          | 1978 (33.0%)             |     |         |

Comparison of education

There were 4834 subjects with junior high school and below, 3188 subjects with senior high school, and 2264 subjects with college and above in the case group. In the control group, there were 3074 subjects with junior high school and below, 1920 subjects with senior high school, and 1006 subjects with college and above. The difference between the case group and the control group was statistically significant (p<0.05) (Table 2).

| Education | The case group (N(%)) | The control group (N(%)) | χ² | p-value |
|-----------|-----------------------|--------------------------|----|---------|
| Junior high school and below | 4834 (46.9%) | 3074 (51.2%) | 67.135 | 0.000 |
| Senior high school | 3188 (31.0%) | 1920 (32.0%) | | |
| College and above | 2264 (22.1%) | 1006 (16.8%) | | |

Occupational distribution

In the case group, there were 2674 workers, 4011 farmers, 824 drivers, and 1000 medical staff. In the control group, there were 1622 workers, 2636 farmers, 666 drivers, and 76 medical staff. There was a statistically significant difference between the case group and the control group (p<0.001) (Table 3).

| Occupation | The case group (N(%) | The control group (N(%) | χ² | p-value |
|------------|----------------------|-------------------------|----|---------|
| Workers    | 2674 (26.0%)         | 1622 (27.0%)            | 630.87 | <0.001 |
| Farmers    | 4011 (39.0%)         | 2636 (44.0%)            | | |
| Drivers    | 824 (8.0%)           | 666 (11.1%)             | | |
| Medical staff | 1000 (9.7%)  | 76 (1.3%)               | | |
| Others     | 1777 (17.3%)         | 1000 (16.7%)            | | |

Smoking

There were 8126 smokers in the case group and 4088 smokers in the control group. The proportion of smokers in the case group was higher than that in the control group and the difference was statistically significant (p<0.001) (Table 4).
Table 4: Comparison of smoking between the case group and the control group.

| Smoking | The case group (N(%)) | The control group (N(%)) | χ² | p-value |
|---------|-----------------------|--------------------------|-----|---------|
| Yes     | 8126 (79.0%)          | 4088 (68.1%)             | 238.663 | 0.000 |
| No      | 2160 (21.0%)          | 1912 (31.9%)             |     |         |

Multivariate analysis

After adjusting for education, living place, occupation, past history, smoking and so on in the multivariate logistic regression model, past history and smoking were related to male infertility (Table 5).

Table 5: Results of multivariate analysis.

| Variable | OR (95% CI) | p-value |
|----------|-------------|---------|
| Occupation | 1.141 (0.551-0.363) | 0.722 |
| Smoking   | 1.159 (1.036-1.296) | 0.010 |
| Past history | 1.228 (1.095-1.376) | 0.000 |
| Living place | 1.326 (0.692-2.541) | 0.395 |
| Education  | 1.131 (0.559-2.288) | 0.732 |

DISCUSSION

With varying degrees of difference in different regions, the incidence of male infertility is increasing globally. Male infertility is not an independent disease, but a result of multiple factors, such as work intensity, exposure to noise, mental stress, occupation, and annual per capita income all influenced the endocrine and reproductive processes in different ways. Although there was no statistical significance between the case group and the control group, the incidence rate of male infertility in the case group living in cities was significantly higher than that in the rural areas. It is speculated that the reasons may be the increasing haze and work pressure in cities.

The low level of education directly led to the rate of medical treatment. In the case group, only 368 people had gone to the hospital for examination. The rate of the visit was only 43.2%, which attracted our attention. Because some diseases, such as orchitis could be cured if found early. As a result, it is necessary to improve the educational level of the whole people and strengthen the publicity of reproductive health knowledge.

There was a statistically significant difference in smoking between the case group and the control group, which was consistent with the results of Ai-Bader [6]. Due to long-term smoking, harmful substances in cigarettes accumulated in the body, resulting in a decrease in the number of sperm, which is one of the possible factors causing male infertility. As it is reported that smoking can reduce the quality of semen, impair male reproductive function, affect male gonads and hormones, and even influence the maturation and proliferation of germ cells [7].

People who were welders, drivers and bakers had a high incidence of infertility [8-11]. The average temperature of the scrotum in male drivers during driving was 2.2°C higher than that during walking. This was mainly due to the heat radiation caused by engine operation. The soft seat and long sitting position may cause the driver’s groin temperature to rise. This may interfere with the temperature regulation function of the scrotum, causing the temperature of the scrotum to rise, thereby damaging the spermatogenic epithelium and causing spermatogenic disorders [12]. Long-term pesticides, especially those exposed to heavy metals, pesticides, paints, chemical raw materials, low levels of production and medical care and lack of self-care awareness, ultimately affecting the spermatogenesis of men [13-15]. Therefore, male fertility was closely related to occupational factors, and we must strengthen occupational protection.

Past history and smoking were risk factors of male infertility. Regardless of the abnormality of the reproductive system such as testis and epididymis, the case group was more serious than the control group, which was an important factor influencing male infertility. We found that 5,965 subjects had varicose veins, which is consistent with the result of Foresta [16]. The prevalence of orchitis in this study was 13.9%, which was lower than other studies (40%), probably because some patients were reluctant to expose their medical history [17,18].

In the case group, subjects with spermatic vein varicocele illness accounted for 57.9%. Venous spermatic varicocele seriously affects the blood supply to the testes, which in turn affects the spermatogenic function of the testes. But most patients can restore fertility if they are treated promptly or with medication. In the case group, mumps patients accounted for 22.9%, while mumps affected the testicular spermatogenic function. Once mumps is found, it should be treated promptly, and prevention is the key.

CONCLUSION

Socioeconomic status, culture, smoking, and history of related diseases (mumps, spermatic vein varicose, orchitis, etc.) also had some influence, the most severe effects on sperm were spermatogenic
SUGGESTIONS AND COUNTERMEASURES

In summary, government, medical service, and other relevant departments should formulate effective measures such as improving the medical insurance system and reducing the economic burden of patients to reduce the incidence of male infertility. Besides, strengthen the self-cognition of male infertile patients and strengthen patients. Comprehensive measures should be taken to strengthen the self-cognition of male infertile patients, and society should care for and pay attention to male infertility.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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