Original Article

Association of Positive History of Pulmonary Tuberculosis with Female Infertility

Babak Eshrati, Ph.D.[1, 2, 3*], Koorosh Houlakooei, Ph.D.[2], Mohammad Kamali, Ph.D.[1], Jafar Hassanzadeh, Ph.D.[2], Mehrdad Borhani, Ph.D.[2], Fahimeh Kashfi, M.Sc.[1], Farshad Pourmalek, Ph.D.[2]

1. Epidemiology Department, Royan institute
2. School of Public Health, Tehran University of Medical Sciences
3. Arak University of Medical Sciences, Directed of Research

Abstract

Background: The etiology of infertility has direct influence on the plan and outcome of its management. In this paper we showed the effect of history of tuberculosis (TB) on female infertility among infertile couples admitted to Royan infertility management center.

Material and Methods: This case control study was performed on cases that were diagnosed with female infertility (308 women). Controls were women whose husbands were infertile due to some male factor (314 women). Those who had both female and male infertility were excluded from the study. The observed variables were BMI>25 kg/m^2, positive history of smoking, tuberculosis, sexually transmitted disease and pelvic inflammatory diseases.

Results: The age adjusted odds ratio of history of tuberculosis for female infertility was 6.21(95 CI: 1.31-29.56).The attributable risk in exposed group was about 1%.

Conclusion: According to our study, positive history of tuberculosis may be responsible for female infertility.

Keywords: Female Infertility, Tuberculosis, Attributable Risk, Case Control Study

Introduction

The prevalence of infertility is about 10-20% among couples (with some what equal prevalence among men and women).There are many factors that can affect female fertility. Some, such as tubal or age factor, are completely known and some are in debate (e.g. endometriosis, cervical or immunologic factors) (1).

There is little information about the prevalence and trend of infertility even in well-developed countries but there are some evidences showing that environmental and infectious factors are growing (2). There are various reasons for infertility in different social and geographical regions of the world. In a study performed by World Health Organization (WHO), the etiologies of female infertility were mentioned as follows: Tubal factors (36%), ovarian factors (33%), endometriosis (6%), and unknown causes (40%). Similar distribution of etiologies was identified in Latin America, Asia and Middle East (3).On the other hand it is important to note that the etiology of infertility has a direct effect on diagnosis and management of the disorder (4).

Female genital tuberculosis is a disease which may have no symptoms and may be discovered inadvertently during an infertility workup (5). Considering the fact that genital TB is difficult to be diagnosed , many patients may be diagnosed as genital tuberculosis in endemic areas (6-8). This may cause over diagnosis and inappropriate treatment of patients who have past history of tuberculosis.

In this paper we intend to show the association and effect of history of pulmonary tuberculosis (TB) on female infertility among infertile couples admitted to Royan infertility center.

Material and Methods

In this case-control study, women admitted to "Royan institute for the management of infertility" and diagnosed as pure infertile (whose husbands were normal in terms of fertility) were enrolled into our study. Controls were selected randomly among women who

were diagnosed as infertile only due to male factors (their husbands' disorder).

In this case we can assume that both cases and controls are from a single population (i.e. controls who were infertile due to male factors had attended the same center as cases if they had female infertility as well).Those infertile couples who were diagnosed as having both male and female infertility (mixed infertility) were excluded from the study. The diagnoses were based on the recorded documents for each patient available in the archive of the institute. Finally 308 case and 314 controls were eligible for the study. For all eligible cases and controls, weight, height, age, history of Tuberculosis, cigarette smoking, previous sexually transmitted disease, pelvic inflammatory disorders, and the result of the management procedures were gathered from existing records of the patients. We divided each case and control group into 2 different groups according to BMI less or more than 25 Kg/m^2 (12). This means we defined BMI as a dichotomous variable. Data analysis was performed using Stata (8) software (9) for calculating odds Ratio (OR) and its 95% confidence interval as well as logistic regression modeling for adjusted estimation of odds ratio.

In order to measure the effect of different exposures on female infertility we estimated attributable risk in exposed group and its confidence interval using the following formulas (10, 11):

Formula NO.1: $AR = P(E \backslash D)(1 - (1/OR)$

Formula NO 2:

$$Var(AR) = mn_0(n_1 m_0 m + nn_0 m_1)/n^3 m_0^3$$

In which the P (E\D) is the prevalence of exposure in diseased cases, n_1 and n_0 are the number of exposed and unexposed cases and m_1 and m_0 are the exposed and unexposed controls. In order to determine the difference of numeric variables between the 2 groups of cases and controls we used t test. All the P values less than 5% were considered as significant differences. The information gathered from both cases and controls were confidential and contained no names. Cases and controls entered the study after signing informed consent.

The ethical issues of the study were approved by ethical committee of Tehran University of medical sciences and health affairs.

Results

According to the analysis of the existing data of eligible cases and controls (308 cases and 314 controls), the mean of ages of cases and controls were 28.52 (SE=0.36) and 27.77 (SE=0.315) years, respectively. Using t test and calculating the P values, no statistically significant difference was detected between the mean ages of the 2 groups (P=0.117). The maximum and minimum ages were 49 and 18 in cases and 44 and 16 in the control group, respectively. The mean BMI was 26.19 (SE=0.51) Kg/m^2 in cases and 24.88 (SE=0.49) Kg/m^2 in controls .Using t test the calculated P value was 0.065. A number of characteristics of cases and controls are compared in table 1 and possible diagnoses recorded in medical records of cases are shown in table 2.

In order to consider the simultaneous effect of different exposures on female infertility, we performed an analysis using logistic modeling. The results are shown in table 3.

Considering table 3 and calculated odds ratios, the attributable risk and its standard deviations for history of TB was 0.014±0.004.

Table 1: Distribution of cases and controls according to BMI

Characteristics	Cases (%)	Controls (%)	Odds Ratio (95% CI)	P value
History of Pelvic Inflammatory Disease	9 (2.9%)	3 (1%)	3.12 (0.84-11.64)	0.08
Smoking (Including Passive smoking)	32 (10.4%)	28 (8.9%)	1.18(0.70-2.02)	0.53
Irregular Menses	149 (48.4)	77 (24.5)	2.88 (2.05-4.06)	0.0001
History of Tuberculosis	9 (2.9%)	2 (0.6%)	4.70 (1.01-21.91)	0.03
History Of Sexually Transmitted Disease	3 (1%)	1 (0.3%)	3.08 (0.32-29.76)	0.37

Table 2: Different diagnoses of studied cases

Diagnosis	Number	Percent
Tubal factor	94	30.4
Age factor	9	2.8
Anovulation	108	35.1
Endometriosis	8	2.5
Luteal phase Deficiency	5	1.5
Recurrent Abortion	6	1.8
PCOD	8	2.5
Cervical factor	17	5.6
Uterine factor	6	2.1
Vaginismus	2	0.7
Premature ovarian Failure	12	4.0
Impotency	1	0.4
Chromosomal factor	1	0.4
Pelvic adhesion	1	0.4
Other causes	30	9.8

Table 3: Results of logistic regression model

Exposure	Odds Ratio (95% CI)	P value
History of Tuberculosis	6.21 (1.31-29.56)	0.02
Irregular Menses	3.42 (2.39-4.89)	0.0001
Age	1.04 (1.01-1.07)	0.004

Discussion

According to the results of this study the effect of tuberculosis on female infertility was calculated as 1% in the study population. However, this was in contrast to the 4 fold increase of odds of having history of TB in female infertile patients.

Case control studies are confronted with different biases. One of these is selection bias in which cases and controls are selected from different populations in a case control study (12).

We tried to reduce this bias by selecting the controls from the same population since both cases and controls are selected from the same clinic(13).

The matter of interviewer bias (the sort of bias caused by interviewer by completing the questionnaire with certain intentions) can be a drawback of case control studies(12), but we collected our data from medical records of "Royan infertility clinic" (for both cases and controls), which were completed before the diagnoses were made. So we can assume that, both cases and controls are asked with the same precision about the intended exposure.

According to previous studies, the different causes of female infertility are tubal factors (35%), endometriosis (6%), ovulation disorders (33%) and unknown causes (40%) (2). Results of our study also showed that in our group of patients the causes of infertility were quite the same.

Pelvic inflammatory disorders are one of the most prevalent causes of infertility. (14). In this regard it has been mentioned that about 11% of tuberculous pelvic inflammations can occur with no clinical symptom (15). In a study performed by Aka in Turkey, from a total of 57 women hospitalized due to pulmonary tuberculosis, 12.3% had genital TB simultaneously (16).

This may be due to hematogenous spread of the infection from the lungs to other organs. Unfortunately in our study genital TB was not confirmed at the time of recording. Therefore more detailed investigations using more accurate diagnostic tools are necessary.

According to our data tuberculosis could have been responsible for about 1 percent of female infertility in the studied population. Considering the effect of tuberculosis prevention on prevention of female infertility we didn't find any similar study in our country. In contrast to the results of many studies (17-20) there was no association between BMI and female infertility in our study. Calculating the power of our study for detection of such association we found the power to be low (32%). A larger sample size may have resulted in more accurate results. On the other hand in another study in "Royan institute" there was no significant association between polycystic ovarian disorder and BMI (21). Other studies have revealed that BMI is responsible for ovulatory disorders which results in infertility (22).

Conclusion

In our study about 38% of cases had disorders of ovulation. So it seems that for detection of any association between BMI and female infertility the specific cause of infertility must be considered in the study.

Irregular menstruation can be a result of other causes of infertility including tuberculosis (6, 23).

However in our study we couldn't exactly prove the etiology of irregular menstruation in the patients using their medical records.

Acknowledgement

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