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The Relation Between Trichomonas Vaginalis and Female Infertility: A Meta-Analysis

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ABSTRACT

Background & Objective: The association of Trichomonas vaginalis (*T. vaginalis*) and infertility is controversial. There is a doubt regarding the relation between *T. vaginalis* infection and female infertility. This study is the first meta-analysis that investigated the association between *T. vaginalis* infection and risk of female infertility.

Materials & Methods: Web of Science, PubMed and Scopus were searched using appropriate keywords as major international electronic bibliographic databases up to January 2020. Q-test and I^2 statistic were used for evaluating heterogeneity between studies as well as Begg's and Egger's tests for exploring publication. Results were reported by pooled odds ratio (OR) estimate from individual studies by choosing random-effects model.

Results: In total, 650 articles were obtained by initial search until January 2020 with 9779 women. Results of the pooled OR estimates showed a significant association between *T. vaginalis* and infertility in adjusted studies (OR=1.95; 95% CI: 1.46, 2.43). Based on Begg's and Egger's tests, there was no evidence of publication bias (P=0.532 and P=0.896, respectively).

Conclusion: There was a significant association between *T. vaginalis* and female infertility. However, more evidence is necessary to prove the potential association of *T. vaginalis* with an increased risk of female infertility.

Keywords: Infertility, Meta-analysis, Trichomonas, Females

Introduction

Sexually transmitted diseases (STDs) are usually considered the leading cause of infertility worldwide. About 70% of all pelvic inflammatory disease (PID) lead to tubal damage **(1)**. The *Trichomonas vaginalis* (*T. vaginalis*) is one of STDs and has a worldwide distribution **(2)**. *T. vaginalis* is categorized as the leading non-viral STDs in the world **(3)**. This infection is one of the parasites considered as the major public health concern **(4)**. According to the reports of the world Health Organization (WHO), protozoa *T. vaginalis* involves more than a half of all STDs worldwide which are curable. The studies have reported that *T. vaginalis* is in relation with endometritis, salpingitis and PID **(5)**.

High prevalence of *T. vaginalis* in women, and its association with severe adversarial reproductive results has made this infection a major health challenge in the world **(6)**. El-Shazly *et al.* showed that the rate of *T. vaginalis* among infertile women is considerably higher than fertile women **(7)**. However, the relation between *T. vaginalis* and infertility is controversial. In some studies a trend exists between *T. vaginalis* and infertility risk (8-10) while others do not show such an association **(2, 11-13)**.

Up to now, no meta-analysis has been performed to investigate the association between *T. vaginalis* infection and the risk of infertility. Literature search showed an adequate reports regarding *T. vaginalis* infection and the risk of infertility worldwide. Therefore the present meta-analysis was designed to assess whether *T. vaginalis* can cause infertility in females.

Methods

We used Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as a guideline to conduct this study **(14)**.

Eligibility Criteria

The association between *T. vaginalis* and infertility in observational studies were included with no

restriction on age, primary or secondary infertility, race, country, year, and study language. In the present study we considered *T. vaginalis* as exposure and infertility as the outcome.

Search Methods

Scopus, PubMed and Web of Science were searched as the three major relevant international databases by relevant keywords to assess the association between of *T. vaginalis* and infertility from inception to January 2020. The keywords searched were (*trichomonas vaginalis, trichomonas vaginitis, trichomoniasis vaginalis or trichomoniasis vaginitis*) and *(infertile or infertility)*. The references of relevant articles were also searched manually.

Data Collection and Validity Assessment

Articles were determined and relevant data were extracted by two of the researchers independently (ZS and NH). Disagreements between them were fixed by negotiation to reach to a consensus. Two authors separately extracted variables of interest from each study which was included first author, the setting of the study, publication year and country, number of patients, age, diagnostic modality for *T. vaginalis*, infertility, odds ratio (OR).

Quality of the selected studies was assessed by the Newcastle Ottawa Statement Manual (NOS) instrument **(15)**. A set of items included in this measure. They were selection, comparability, exposure, and outcome. If a study obtained seven star-items or higher was considered as high-quality and the rest were considered low-quality investigations.

Assessing Heterogeneity Among Studies and Publication Bias

The heterogeneity among studies was assessed by Q-test and I^2 test **(16)**. Also we used Funnel plot as the graphical scale and the Begg's and Egger's tests **(17)** to determine possible publication bias, and the random effect model was used to estimate the relation between *T. vaginalis* and infertility **(18)**. For controlling risk factors of infertility (smoking, age, race, contraceptive use and number of pregnancies), meta-analysis was performed by two ways including crude and adjusted form. Data was analyzed by Stata 14 at 0.05 significant level.

Results

A total of 650 studies were collected for the study up to January 2020 and 105 duplicate articles in the mentioned databases were excluded. In continue by evaluating the titles, 511 studies were dropped. In the second assessment, 25 were excluded based on studying the full article. Finally, 9 studies included in the final analysis (Figure 1). Of these nine selected studies, six were case-control **(1, 2, 7, 8, 10, 12)** and three were cross-sectional **(9, 19, 20)**. There was no cohort study in this meta-analysis.

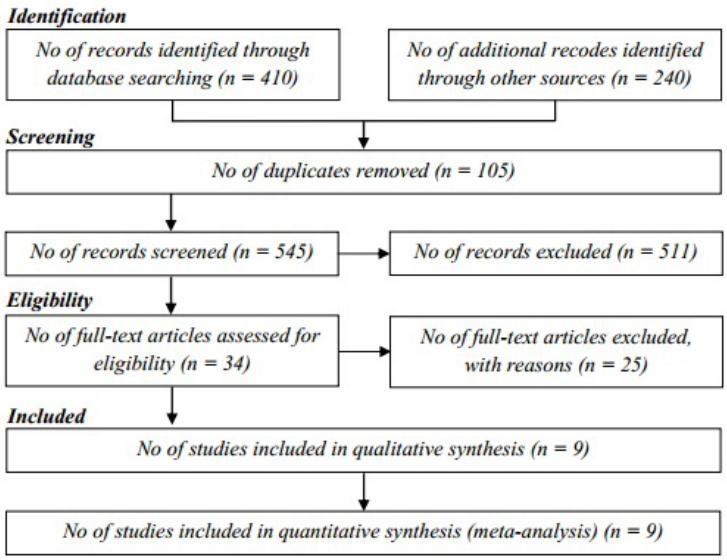

Figure 1. Flow diagram of choosing the relevant studies

Effects of Exposure

In this study, the relation between *T. vaginalis* and risk of female infertility was assessed in Figure 2. Results of the adjusted OR estimates indicating a significant relation between the *T. vaginalis* and the risk of infertility (OR=1.95; 95% CI: 1.46, 2.43). However results of the crude estimate was not significant (OR=0.55; 95% CI: 0.10, 1.00). The results in adjusted and crude studies were homogenous.

Subgroup analysis was performed based on design of the studies. Results of the OR estimates showed a significant association between *T. vaginalis* and infertility in case-control studies (OR=1.50; 95% CI: 1.08, 1.93) while in cross-sectional studies, the

observed association was not significant (OR=1.79; 95% CI: - 0.15, 3.74).

Publication Bias

Based on the Begg's and Egger's tests, there was no evidence of publication bias (*P*=0.532 and *P*=0.896, respectively) and studies were nearly symmetrical (Figure 3).

Quality of the Studies

According to the NOS scale, of included studies seven studies were high- quality and two low-quality.

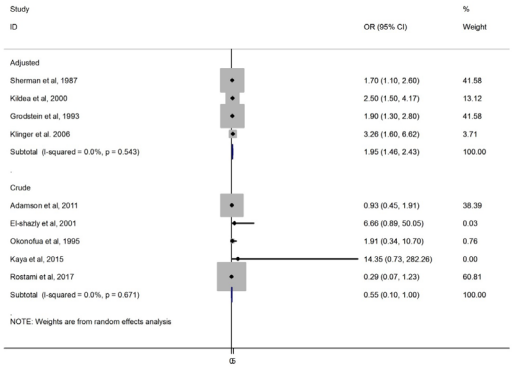

Figure 2. Forest plot of the association between trichomonas vaginalis and infertility

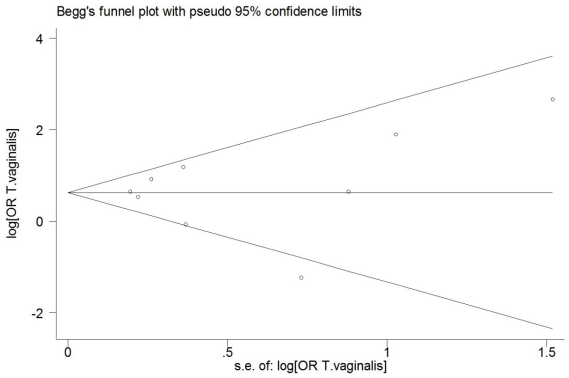

Figure 3. Funnel plot of the association between trichomonas vaginalis and infertility

Table 1. Characteristics of the included studies to the meta-analysis

1st author, year	Country	Design	Sample	Diagnosis method	age	Estimate	Adjustment	Quality
Sherman *et al.*, 1987	USA	Case-control	1312	Medical records	20-39	OR	Adjusted	High
Grodstein *et al.*, 1993	USA	Case-control	3833	Not reported	No data	OR	Adjusted	High
Okonofua *et al.*, 1995	Nigeria	Case-control	178	Under microscope	27.8	OR	Crude	Low
Kildea *et al.*, 2000	Australia	Cross-sectional	342	Medical records	30.4	OR	Adjusted	High
El-shazly *et al.*, 2001	Egypt	Case-control	280		No data	OR	Crude	High
Adamson *et al.*, 2011	India	Case-control	1923	Culture	25.9	OR	Crude	Low
Kaya *et al.*, 2015	Turkey	Case-control	51	CPLM	31.1	OR	Crude	High
Rostami, 2017	Iran	Cross-sectional	420	Culture	33.74	OR	Crude	High
Klinger, 2006	Tanzania	Cross-sectional	1440	M-PCR	20-44	OR	Adjusted	High

OR: Odds Ratio, author: Author

Table 2. The subgroup analysis according the study design

Subgroups	Studies		
	No. of studies	OR (95% CI)	I^2
Case-control studies	6	1.50(1.08, 1.93)	0.0%
Cross-sectional studies	3	1.45(-0.15, 3.74)	84.4%

OR: Odds Ratio, CI: confidence interval

Discussion

To our knowledge, this was the first meta-analysis in the world to assess the association of *T. vaginalis* and infertility in females. Based on this evidences, *T. vaginalis* in females is a risk factor for infertility. There was no cohort study in this meta-analysis. In subgroup analysis, there was a significant association between *T. vaginalis* and infertility in case-control studies.

Many microorganisms including bacteria, parasites, viruses and yeasts can be involved in female reproductive and lead to infertility **(21)**. *T. vaginalis* is identified in nearly 3.15% of asymptomatic admitted women in infertility clinics **(21)**. Some studies have shown that tubal infertility is nearly twofold as high in women who showed a history of *T. vaginalis* compared to women without infection **(8, 10)**.

T. vaginalis in females might play a main role in preterm labor, and low birth weight in pregnancy. *T. vaginalis* is also is in relation with cervical intraepithelial neoplastic and atypical pelvic inflammatory disease and these complications can lead to infertility in women **(21)**.

T. vaginalis can decrease the complement elements and elevate the IgA level in serum prolactin and vaginal discharge **(22)**. According to these results, screening and treatment of *T. vaginalis* seems necessary to control STDs and female infertility.

In the current study, there were some limitations. (a) In some studies only the unadjusted OR were reported. However for controlling known risk factors of infertility we used the adjusted form in this meta-analysis. However, this might introduce information bias and limitation in our results. (b) Some studies did not distinguish primary and secondary infertility and cause of infertility (tubal, ovulation, etc). Therefore, we could not perform subgroup analysis for them. Despite these limitations, the findings show that *T. vaginalis* is a risk factor for female infertility in adjusted studies with 9779 participants.

Conclusion

T. vaginalis is a risk factor for female infertility in adjusted studies with 9779 participants. More studies are needed to assess the potential association of *T. vaginalis* with an increased risk of female infertility.

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Conflict of Interest

The authors declare no conflict of interest.

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