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Prevalence of Genital Tuberculosis among Infertile Women: A Systematic Review and Meta-analysis

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ABSTRACT

Genital tuberculosis is a kind of infectious diseases with a relatively high prevalence in developing countries. The aim of this study was to investigate the prevalence of genital tuberculosis among infertile women. A PubMed, Science Direct, Scopus, Google Scholar, SID, Magiran and Cochrane databases (from 1980 to the present, date of last search March 2016) was carried out using the search keywords tuberculosis, genital tuberculosis, female genital, genital tract, genital system, female infertility, endometrial tuberculosis, anti-tubercular therapy, bacteriological, tuberculin antigen, histological, infertility, fallopian tube diseases, prevalence, rate, percent in order to find the studies which have reported the prevalence of genital tuberculosis among infertile women. Data were extracted from retrieved studies and a meta-analysis was done. 23 studies were found. In these studies a total of 4361 infertile women have been studied. The prevalence of genital tuberculosis among infertile women with 95% confidence interval was 24.2% (18.5-29.99). The prevalence of genital tuberculosis among infertile women is high. It seems that exact planning and action for the prevention and treatment of genital tuberculosis can reduce the infertility prevalence and prevent the negative consequences of infertility

Keywords: Tuberculosis, Genital tuberculosis, Infertility, Women infertility

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INTRODUCTION

Tuberculosis is a common infectious disease around the world which usually caused by the bacterium Mycobacterium tuberculosis. Annually, millions of new cases of tuberculosis are detected around the world and millions of deaths due to tuberculosis infection are reported. [(1)] Genital tuberculosis is a kind of tuberculosis with different prevalence rate in different regions. In various reports, the prevalence of genital tuberculosis has been reported from less than 1% to over than 20% in different countries. [(1,2)] According to various epidemiological surveys, the cases of genital tuberculosis in the world have been increased from 22 million to 1.86 billion affected

people only between 1995 and 2005. [3] Genital tuberculosis is a main cause of infertility especially among women. In some countries, tuberculosis infection has been estimated as the leading cause of infertility. [1] Infertility which has been defined as the inability to achieve conceive after one year of regular and unprotected intercourse is a major concern of all countries due to its widespread negative consequences. [4] Reports indicate that this condition affects about 10 to 20 percent of couples of the reproductive age around the world. [4,5-9] Studies show that there is a one case of infertility in each 5 or 6 couples. [8] Also, the trend analysis says that the prevalence of infertility is increasing around the world at alarming rate. [4,6,10,11] Infertility rates vary widely between countries and even within countries. [5] Generally, infertility cases are divided into 2 categories named primary and secondary infertility. Primary infertility refers to the inability to give birth either because of not being able to become pregnant, or carry a child to live birth while secondary infertility refers to the inability to conceive or give birth when there was a previous pregnancy or live birth. [12,13]

Infertility causes are different. These causes include both male and female factors. According to studies, about 30% of infertilities are due to the male factors, 40 to 50% have the origin of female factors and 20 to 30 percent of cases are caused by either both male and female factors. [13] As noted earlier, researchers believe that genital tuberculosis is among the main causes of infertility. Given that availability of accurate information about the prevalence and causes of infertility is required for sound planning in order to prevent the couples' infertility, [12] in this secondary study we attempted to estimate the prevalence of genital tuberculosis among infertile women using the results of previous published studies.

MATERIALS AND METHODS

Search strategies:
An electronic databases' search including PubMed, Science Direct, Scopus, Google Scholar, Cochrane, SID and Magiran was done (date last searched March 2016). We searched free text search keywords tuberculosis, genital tuberculosis, female genital, genital tract, genital system, female infertility, endometrial tuberculosis, anti-tubercular therapy, bacteriological, tuberculin antigen, histological, infertility, fallopian tube diseases, prevalence, rate, percent with "Or" and "And" operations in the title and abstract of studies. Also, for finding of publications which may not be found through the databases' search and for increasing the sensitivity of study, a manual search of the reference list of the retrieved studies was done. No language restriction was placed but only articles which their publication date was from 1980 till now were included in the study. Search was conducted by 2 researchers independently and the third researcher checked the agreement of retrieved results with these 2 researchers.

Study selection:
Full texts or abstracts of all articles, documents and reports were retrieved through an advanced search. After removal of repeated cases from retrieved studies, the unrelated ones were identified and removed by reviewing the title, abstract and full text of all remaining articles and the related studies were selected which then were entered into the quality assessment process. It should be noted that to prevent bias caused by reprint (publication bias of transverse and longitudinal), the investigation of results for identification and removing of duplicate studies was done with researchers.

Quality assessment of the studies:
The quality assessment process of related studies was done using a valid quality assessment checklist (Moosazadeh et al., 2014) which has been prepared based on the STROBE (Strengthening the reporting of observational studies in epidemiology) checklist (Von Elm et al., 2007). This checklist contains questions related to different aspects of a study including the type of study, the study design, study population, sample size, samples matching method, objectives, inclusion and exclusion criteria, analyzing method and appropriate reporting of results based on the objectives in which for each question a score has been considered. We completed this checklist for each of related retrieved studies, separately and those studies which obtained at least 8 score were selected for including in meta-analysis.

Data Extraction:
The required data from studies which passed the quality assessment process successfully including the their title, name of first author, publication year, sample size (number of infertile women), the location of study, the type of study, the prevalence of genital TB among infertility cases were extracted.

Inclusion criteria:
All studies which obtained the minimum required score of quality assessment checklist and which had reported the sample size and the prevalence of genital TB in infertile women were included in the study.

Exclusion criteria:
Studies were excluded if the prevalence of genital TB among infertile women was not reported and if the sample size was not specified. Also, the abstracts of seminars without full text, case-reports and studies which didn't obtain the minimum required score of quality assessment checklist were excluded from study.

Data analysis:
Data analysis was done through Stata software version 11. The standard error of genital TB prevalence among infertile women in each study was calculated using binominal distribution formula. The index of heterogeneity between studies was determined using Cochran (Q) and I-squared tests. Random effect model was used to estimating the prevalence of genital TB due to the heterogeneity of studies. The point prevalence of the genital TB among infertile women was calculated using 95% confidence interval and forest plot in which, the size of square represents the weight of each study and its booth sides' lines represent 95% confidence interval.

RESULTS

Table1. Characteristics of primary studies which were included into the meta-analysis

No.	First Author	Publication year	Study area	Sample size (n., infertile women)	Genital tuberculosis (%)
1	Chhabra [16]	1986	India	150	14
2	Jindal [17]	2006	India	150	7.2
3	Namavar Jahromi [18]	2001	Iran	41	75.6
4	De-Vynck [19]	1990	South Africa	451	7.98
5	Al Eryani [20]	2015	Yemen	151	31.1
6	Eshrati [21]	2007	Iran	308	2.9
7	Jindal [22]	2012	India	443	38.1
8	Khanna [3]	2011	India	100	26
9	Kulshrestha [23]	2011	India	196	60.2
10	Mani [24]	2003	India	110	13.6
11	Marana [25]	1991	Italy	101	2.97
12	Nadgouda [26]	2010	India	170	10
13	Neelam [27]	2005	India	186	44.1
14	Oosthuizen [28]	1990	South Africa	109	21
15	Parikh [29]	1997	India	300	39
16	Patted [30]	2009	India	96	21
17	Punyashetty [31]	2012	India	230	3.9
18	Shaheen [32]	2006	Pakistan	534	2.43
19	Shahzad [33]	2012	Pakistan	150	20
20	Shanti Sri [34]	2013	India	100	12
21	Singh [35]	2008	India	70	48.5
22	Gupta [36]	2007	India	150	26.7
23	Rozati [37]	2006	India	65	49.2

In the initial search of electronic databases, a total of 25679 studies were found from them 23337 studies were removed after limiting the search. From remaining 2342 studies, 1356 ones were removed because of the overlapping of searched databases. By reviewing of titles and abstracts of 986 studies 833 studies were identified as unrelated. The remaining 153 studies were selected to investigating the full text after that 128 studies were removed from study due to their irrelevancy. The remaining 25 studies and 3 ones which were found in manual search were entered to be assessed based on the quality assessment checklist and inclusion and exclusion criteria from them 5 studies were removed and 23 studies found to be appropriate for our meta-analysis (Fig.1). The publication year of these 23 studies was from 1986 (Chhabra, et al., India) to 2015 (Al Eryani et al., Yemen). Also, in 18 cases the type of study has been reported from them 6 were retrospective, 10 were prospective and 2 were cross-sectional. Sampling method has been specified in 21 studies from which consensus sampling method has been used in 18 studies and the remaining 3 studies' method was random sampling. According to the country of study, from 23 included studies, 15 have been done in India, 2 in Iran, one in Italy, 2 in Pakistan, 2 in South Africa and one in Yemen. In 23 studies which were eligible to include in meta-analysis, genital TB prevalence has been investigated

among a total of 4361 infertile women which varies between 2.43% in Shaheen et al. (2006, Pakistan) with 534 samples to 75.6% in Namvar-Jahromi et al. (2001, Iran) with 41 samples.

The meta-analysis results showed that the heterogeneity between studies is high (I-sqaured: 97.9%, Q=1041.01, P-value<0.001). Therefore, the random effect model was used to estimating of prevalence. Based on this model, the prevalence of genital TB among infertile women with 95% confidence interval was calculated as 24.2% (18.5-29.99%). Also, the year of study was investigated using meta-regression as the suspected variable of heterogeneity which results showed that the effect of this variable is not statistically significant (B=0.4, P_{value}=0.489).

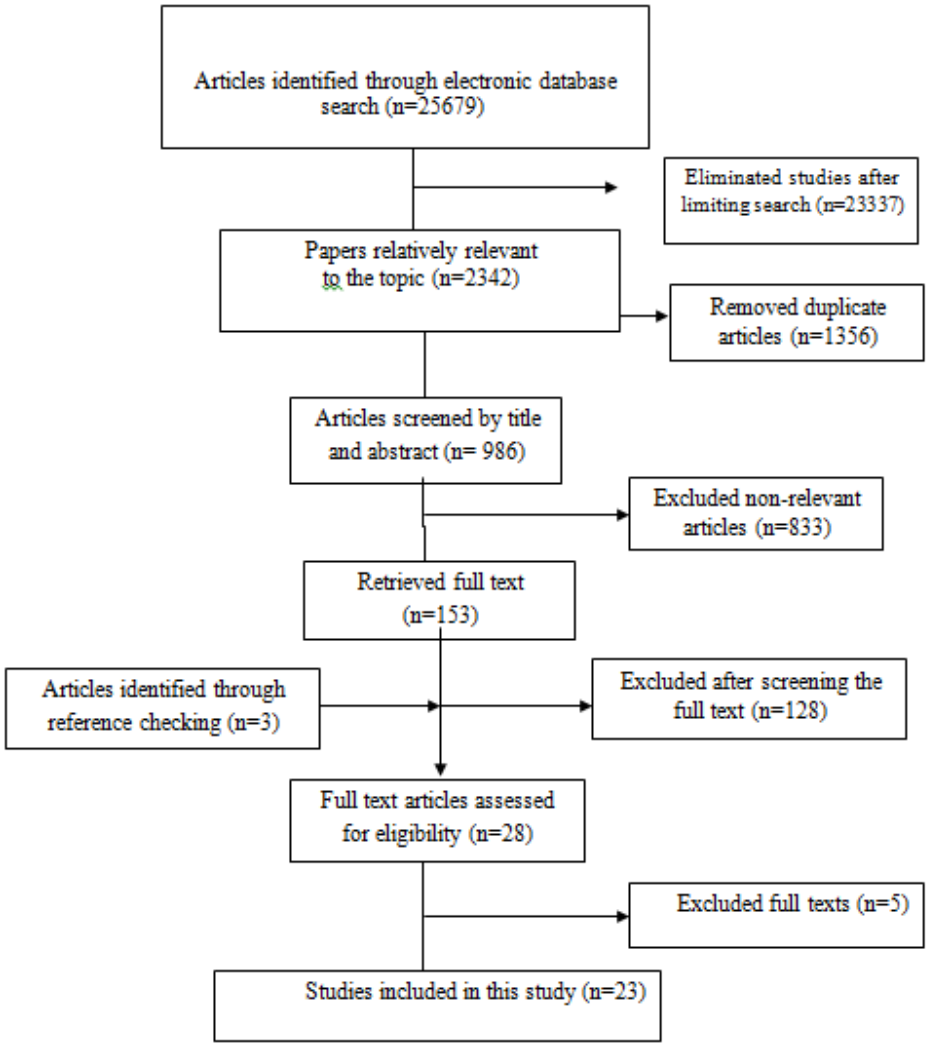

Figure1. Literature search and review flowchart for selection of primary studies

DISCUSSION

Tuberculosis remains as the most important cause of mortality from infectious diseases. Annually, millions of people around the world die due to tuberculosis. More than 90% of TB deaths occur in developing countries. Genital tuberculosis is a kind of tuberculosis even though in recent years its incidence in developed countries has decreased steadily but it remains as one of the most challenging health problems in developing countries. [38]

Several studies have shown that genital tuberculosis is closely associated with infertility. The actual prevalence of genital tuberculosis and followed infertility is unclear, but in areas where TB is common, it is the leading cause of

infertility in women. In general, many researchers have shown that infertility is the most common complication of genital tuberculosis. [39]

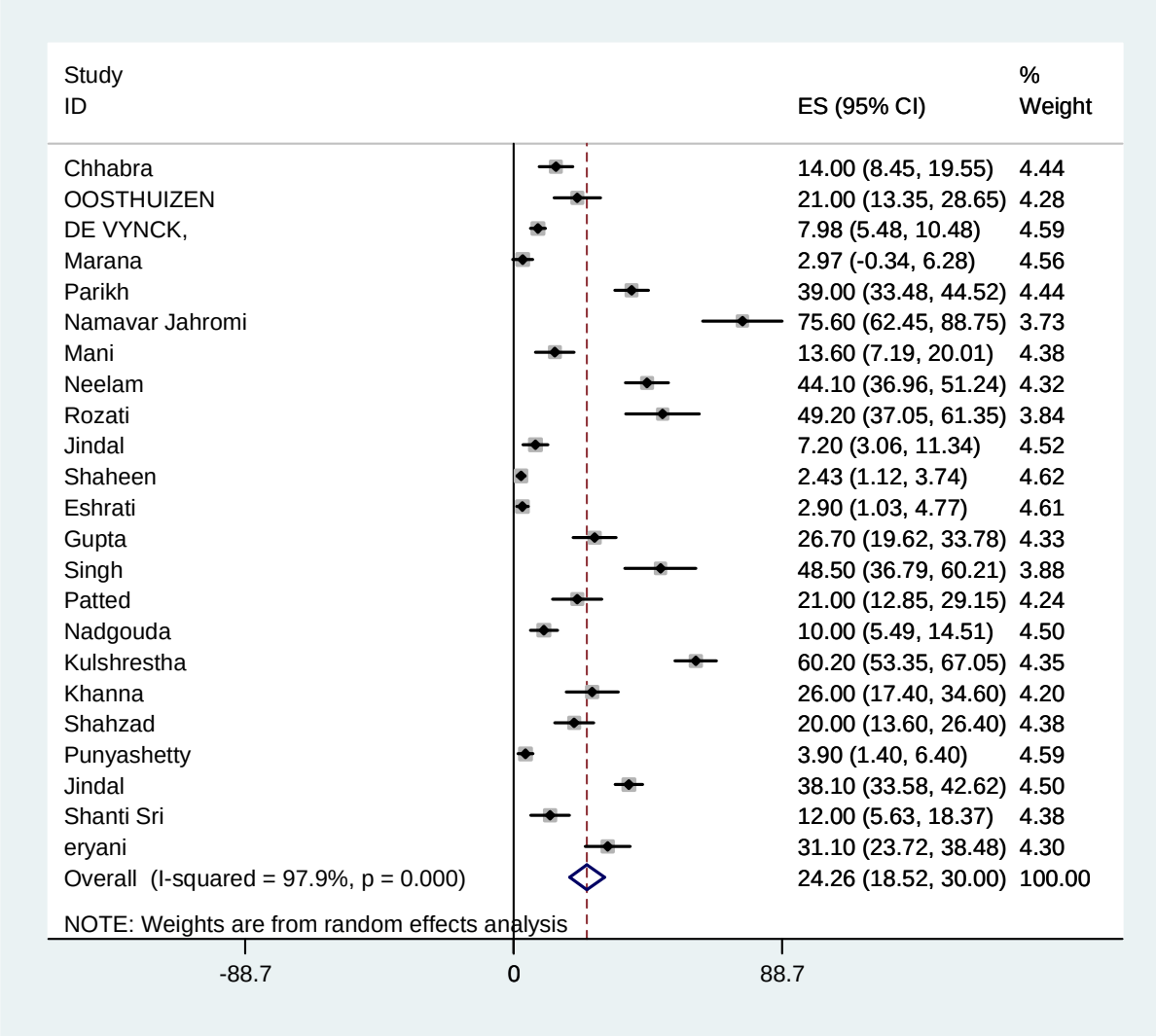

Fig 2. Genital TB prevalence among the infertile women in primary studies included in the meta-analysis and the total estimation

Considering the close relationship between genital tuberculosis and infertility, in recent decades some studies have been done to investigate the prevalence of genital tuberculosis among infertile women. Based on our knowledge till now the meta-analysis of these studies has not been published. Therefore, this study was aimed to analyze the findings of published studies on the prevalence rate of tuberculosis in infertile women. For this purpose, an extensive search was carried out in different databases; studies were retrieved and their quality was assessed using a valid quality assessment checklist. Finally, 23 studies were found to be eligible for including in the meta-analysis. The majority of these studies (15 from 23) have been conducted in India.

Also, all of these studies with the exception of one study have been done in developing countries. As previously mentioned, in recent years the prevalence of genital tuberculosis in developed countries has declined to somewhat. Maybe that's why most studies on the prevalence of tuberculosis in women with infertility have been carried out in developing countries because genital tuberculosis prevalence rate in these countries is still high.

Our findings show that the prevalence of genital tuberculosis in infertile women in the studies included in this meta-analysis ranged from about 2 to 75 percent. However, most studies have reported that a high percentage of studied infertile women were diagnosed to have genital tuberculosis. Our meta-analysis showed that the overall prevalence of genital tuberculosis in infertile women is 24.2% (18.5 -29.99%). Therefore it can be concluded that genital tuberculosis is probably one of the main causes of infertility. This finding is important from 2 aspects. First, as noted earlier genital tuberculosis, itself is one of the major public health problems in developing countries with a high burden of morbidity and mortality. Second, it seems that genital tuberculosis is one of the main causes of infertility. Infertility is also one of the major concerns in the most of countries. Despite the recent advancements of assisted reproductive technology, the prevalence of infertility has increased in recent decades and millions of young couples are suffering from this condition around the world. [38-41] Therefore, the relatively high prevalence of genital tuberculosis in developing countries is worrying both in terms of its morbidity and mortality and its adverse effect on fertility ability which also has widespread negative consequences. Our meta-analysis findings performed the relatively high prevalence of genital tuberculosis in infertile women. Therefore, it seems that the prevention and treatment of genital tuberculosis should be one of the main priorities of health systems, especially in developing countries.

CONCLUSION

Genital tuberculosis is one of the major concerns of health systems, especially in developing countries. Due to the confirmation of relatively high prevalence of genital tuberculosis among infertile women it seems that exact planning and action for the prevention and treatment of genital tuberculosis can reduce the infertility prevalence and prevent the negative consequences of infertility in addition to the reduction of tuberculosis mortality.

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