Review Article

Prevalence of Genital Tuberculosis in Iran: A Systematic Review and Meta-analysis

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Abstract

Introduction: Genital tuberculosis is a rare condition with different prevalence in different areas. Genital tuberculosis may be asymptomatic or may be associated with atypical symptoms and imitators of other diseases; hence, it is quite essential to determine the prevalence of the disease in order to consider it as a differential diagnosis in patients with similar symptoms. Therefore, the present study was conducted to determine the prevalence of genital tuberculosis in Iran. **Methods:** From the beginning of databases, 2018, International {PubMed, Web of Science (WOS) and Google scholar} and National {Scientific Information Database (SID), Magiran} databases were searched for related observational studies that were conducted in Iran including only on Iranian Patients and published in English and Persian languages until 2018 June 30. The quality of the articles was evaluated using the Hoy D tool. **Results:** Out of 855 initial studies, 6 studies were included in systematic review and meta-analysis, respectively. The overall prevalence of genital tuberculosis in 11756 patients was 6.3% (95% CI: 3.4, 9.1; I^2=93.58%). **Conclusion:** The present systematic study and meta-analysis showed high prevalence of genital tuberculosis in the general population of Iran, providing further proof on the importance of the issue and the attention of the authorities to disease control. Targeted screening, especially for populations at risk, both those with tuberculosis and those in contact with them, especially in the presence of symptoms, seems to be of paramount importance.

Keywords: Tuberculosis; Genital tuberculosis; Female genital; Genital tract; Genital system; Female infertility; Endometrial tuberculosis; Anti-tubercular therapy; Bacteriological; Tuberculin antigen

Introduction

Tuberculosis is a common infectious disease that is often caused by the *Mycobacterium tuberculosis*. Millions of new cases of tuberculosis and millions of deaths caused by this disease are reported all around the world each year. Genital tuberculosis is a rare condition with different prevalence in different areas; however, the actual incidence rate is not clear due to several unidentified cases of this disease. [1] In various reports, the incidence of genital tuberculosis has been reported from less than 1% to more than 20% in different countries. [1,2] Tuberculosis occurs in lungs in more than two-thirds of cases; thus, it is extra-pulmonary in less than 1/3 of the cases. Extra-pulmonary tuberculosis develops in lymph nodes, genital ulcers and genitourinary tract, three areas which account for 10-15% of extra-pulmonary tuberculosis. [3] Genital tuberculosis is a chronic disease with nonspecific signs and symptoms of pelvic inflammatory disease that do not respond to commonly used medical treatments and can show symptoms of infertility, menstrual disorders, abdominal pain, pelvic pain and weight loss. It also develops by the obstruction of the fallopian tubes, hydro-salpinx, peripheral adhesions, and, rarely, enterotube fistula; [3-5] also, genital tuberculosis might present as a pelvic mass in medical examination. This disease is diagnosed by providing menstrual blood and Endometrium culture; however, tissue biopsy and sending a sample for pathological diagnosis might also facilitate the process. None of the available tests can detect all genital tuberculosis cases, and histopathological and culture methods still play an important role in the diagnosis. [6-8] Infertility, Asherman's syndrome, chronic pelvic pain, vaginal discharge and bleeding, postmenopausal bleeding, amenorrhea, and ascites, are the symptoms of tuberculosis in the reproductive system. Infertility and vaginal bleeding are the most important complaint of women before and after menopause. [9-12] The prevalence of female reproductive TBs is increasing, so female gynecologists are increasingly confronted with tuberculosis patients.

Literature Review

Genital tuberculosis may be asymptomatic or may be associated with atypical symptoms and imitators of other diseases; [4] hence, it is quite essential to determine the prevalence of the disease in order to consider it as a differential diagnosis in patients with similar symptoms. Therefore, the present study was conducted to determine the prevalence of genital tuberculosis in Iran.

Registration and eligibility criteria

Consistent with Cochrane's book, the methods selected for this systematic review have been applied for systematic reviews by using preferred reporting items for systematic reviews and meta-analyses

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(PRISMA). [13] In the present study, observational researches were entered. On the other hand, case series, case reports, and letters to editors were excluded. The statistical population was all Iranian extrapulmonary TB patients. In the present study, the information sources related to the prevalence of genital tuberculosis were investigated. The minimum sample size was considered to be 25 participants.

Searching strategies and databases

The review of references and resources was done using the Medical Subject Headings (Mesh) and keywords related to the source of information on the incidence of genital tuberculosis. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Migiran) and journals were searched; unlimited searching, in terms of both setting and language, was done from 1995 to June 30, 2018. PRESS standard and the Health Sciences Librarian were used for designing the strategy.

MEDLINE application was used to search other databases. In addition, PROSPERO was used to provide a systematic search that was completed recently. To search for headlines and abstracts, Boolean (and, or, not), mesh, coordinate {truncation} * and related words were used; following keywords were used to provide a comprehensive context: tuberculosis, genital tuberculosis, female genital, genital tract, genital system, female infertility, endometrial tuberculosis, anti-tubercular therapy, bacteriological, tuberculin antigen, histological, infertility, fallopian tube diseases, and prevalence rate and percent.

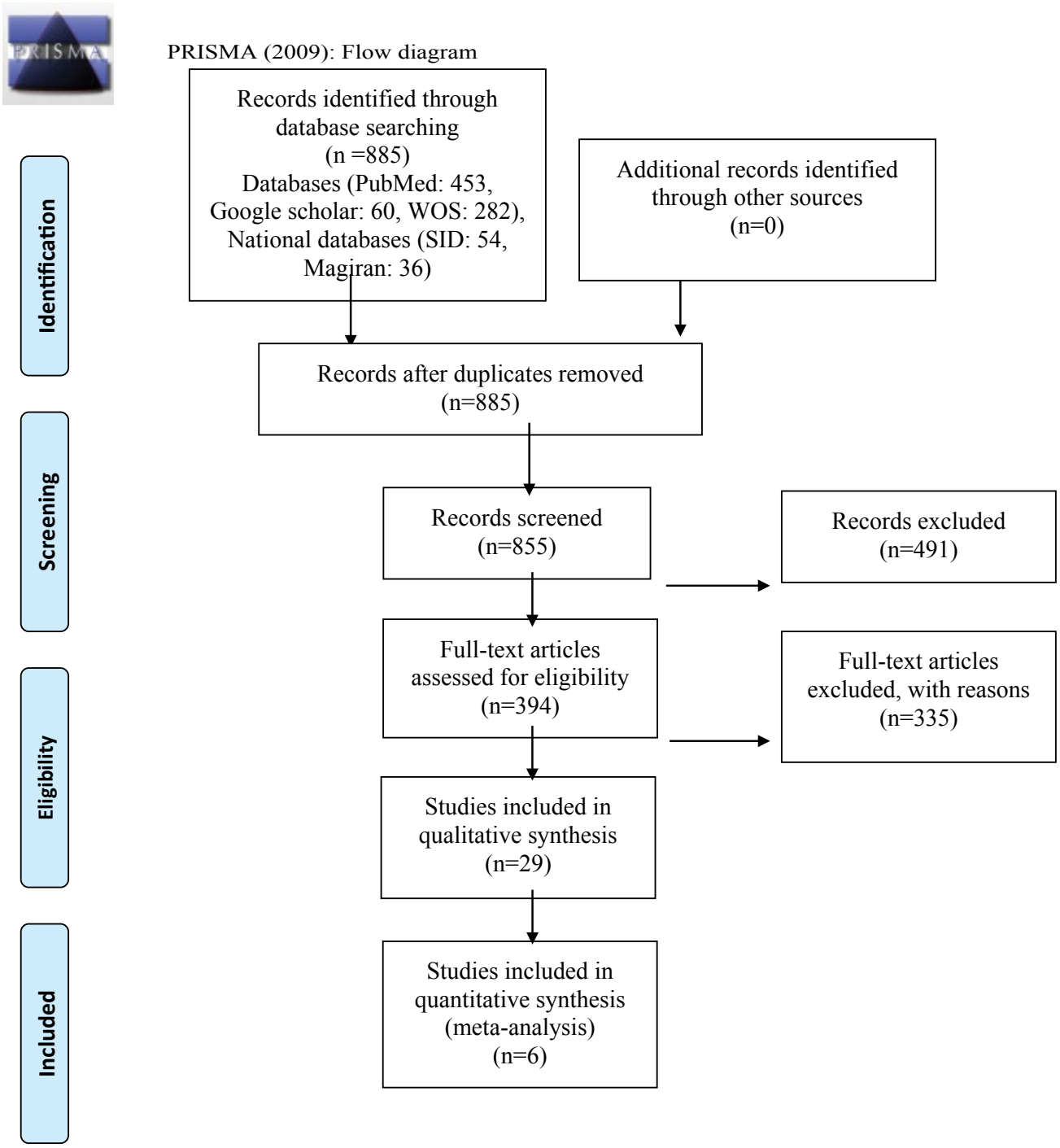

Figure 1: Flow diagram.

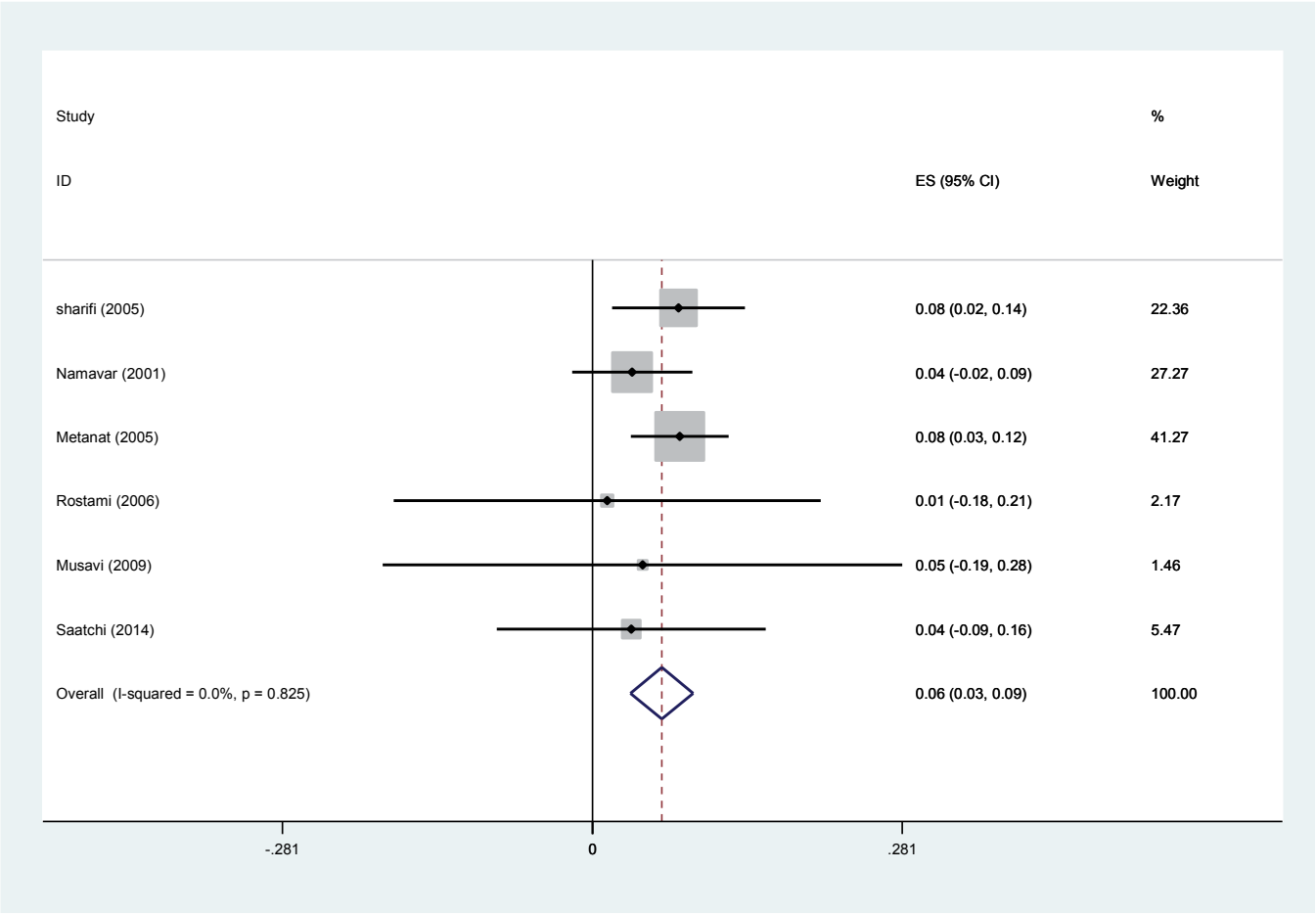

Figure 2: The incidence of genital tuberculosis and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line estimates the % value and the length of the lines showing the 95% confidence interval in each study.

Table 1: Characteristics of final included studies about prevalence of genital tuberculosis in Iran.

Author	Year	City	N	Type of study	Prevalence	Bias
Saatchi et al. [22]	2014	Hamadan	250	Cross sectional	0.035	Moderate
Musavi et al. [23]	2009	Kashan	66	Retrospective	0.0454	Low
Rostami et al. [24]	2006	Esfehan	89	Cross sectional	0.0133	Low
Metanat et al. [25]	2005	Zahedan	1798	Retrospective	0.0791	Low
Namavar et al. [26]	2001	Fars (Shiraz)	1245	Retrospective	0.036	Low
Sharifi et al. [27]	2005	Zahedan	973	Cross sectional	0.078	Low

Table 2: Prevalence of genital tuberculosis.

Study	Year	ES	95% Confidence Interval		Weight
			Up	Low	
Sharifi	2005	0.078	0.018	0.138	22.36
Namavar	2001	0.036	-0.018	0.090	27.27
Metanat	2005	0.079	0.035	0.123	41.27
Rostami	2006	0.013	-0.18	0.207	2.17
Musavi	2009	0.045	-0.19	0.281	1.46
Saatchi	2014	0.035	-0.087	0.157	5.47
Overall random pooled ES	-------	0.063	0.034	0.091	100

Research selection and data extraction

According to the research protocol, two researchers observed the titles and abstracts separately according to the eligibility criteria; in the next step, after the removal of repeated studies, the full text of the paper was studied based on the eligibility criteria and the required information was extracted. Consensus method was used to solve the disagreements between two researchers. The extracted data included the general information (corresponding author, year and place), characteristics of the research (research design, sample size, location, study period, and risk of bias), and characteristics of participants.

Quality control

To assess the quality of the methodology and bias risk, each observation study was evaluated using a tool developed by Hoy et al. [14] This 10-item

scale evaluated the quality of the study in two dimensions, including external credentials (items 1 to 4 target populations, sampling frame, sampling method, and minimum indirect neglect) and internal validity (items 5 up to 9 covering methods for data collection, case definition, study tools, and data collection mode and item 10 covering assessing relevant assumptions or analyzes). The risk of abuse was assessed by two researchers separately and possible disparity of ideas was resolved by consensus.

Aggregation of data

All eligible studies were included within the systematic review. The heterogeneity of primary studies was assessed by performing I^2 tests. Subgroup analysis was conducted to determine the heterogeneity based on the participants in the study, gender, and age. Meta-analysis was performed using the STAT 14 statistical software.

Results

Selecting eligible papers and researches

In the initial search on various databases, a total of 855 articles were reviewed, 491 of which turned out to be repetitive during screening process of title and abstract. 335 articles were removed due to unrelated title; out of the remaining 29 articles, 6 articles met the inclusion criteria. Of the 23 articles that were removed, 4 were reviews, 5 were letters to editors, 3 had no complete text, and 11 had low quality and could not be considered in the research [Figure 1]. [15-27]

Characteristics of the researches and papers

The final research was conducted on 4421 participants; with an age range of 15 and 80 years old; a cross-sectional design was used in all studies. Research was conducted in only 5 provinces out of 31 provinces of Iran. Of the 6 studies, 2 were from Sistan and Baluchestan, [25,27] one from Isfahan, [24] one from Hamedan, [22] one from Shiraz, [26] and one from Kashan; [23] the majority of papers were conducted on outpatient cases (n= 5) through random sampling (n=5). Required data was collected through interview (n=6) and had a low bias risk (n=5) [Tables 1 and 2].

Meta-analysis prevalence of genital tuberculosis

Based on the results of random effects model, the incidence of genital tuberculosis in 11756 Iranian patients was 6.3% (95% confidence interval [CI]: 3.4, 9.1, I^2=98.82) [Figure 2].

Discussion

Genital tuberculosis is often asymptomatic and is diagnosed accidentally during infertility referrals. In general, the most common marker of pelvic tuberculosis is infertility, which accounts for about 40 to 70% of the main complaints of patients. [15,16] This specific type of tuberculosis remains one of the most challenging health problems in developing countries despite significant decrease of prevalence in developed countries, it. [17] Various studies have shown that there is a close relationship between genital tuberculosis and infertility. The actual incidence of genital tuberculosis and infertility is unclear, but in areas where tuberculosis is high, it is the main cause of infertility in women. In general, many researchers have shown that infertility is the most common complication of patients with genital tuberculosis. [18]

In a study in South Africa, Margolis et al. estimated the incidence of genital tuberculosis to be 6.15%, which is relatively close to what the present study showed. [19] Shahzad, in a study conducted on infertile women in Pakistan, estimated the incidence of genital tuberculosis to be 20%, which is higher than what the present study showed; this difference can be attributed to the difference in the studied population. [20] Also, in a study in India, the incidence of genital tuberculosis turned out to be 4.5%. [21] The results of the present study, in which 6 studies conducted on 4421 patients was analyzed, showed that the overall prevalence of genital tuberculosis in Iran was 6.3%, which was obtained from a comprehensive review of existing evidence (Iran is a country in the Middle East with a population of more than 80 million people); the age of participants ranged from 15 to 80. The spread of genital tuberculosis was very different and heterogeneous in different provinces. Genital tuberculosis is nowadays a challenging disease in all countries, especially in developing countries. The prevalence of genital tuberculosis in Iran was 6.3%, which turned out to be higher than India (4.5%) and lower than other countries, such as Pakistan (20%). [20-27] The findings of the present paper did not reveal any significant publication bias, because it was minimized by doing extensive research through a variety of databases.

Limitations

One of the limitations of the present study is the small number of studies conducted on the prevalence of genital tuberculosis in Iran. However, as long as the present researchers can claim, the present principled revision and statistical analysis has been the first attempt to evaluate the prevalence of genital tuberculosis among the entire Iranian population. Another limitation of this study is the inclusion of only 5 provinces out of 31 provinces of Iran, a fact which makes it difficult to generalize the results. Although investigators kept cautious of writers, institutes, journals and other related information, two independent reviewers supervised the selection of related papers and the third reviewer solved all the and possible disagreements.

Strengths

The researchers can claim that this study is the first systematic review conducted to determine the prevalence of genital tuberculosis in Iran. The present study was conducted on the basis of a systematic review plan and all databases were searched. Population-based studies were also applied to the final research. The method used to evaluate the prevalence of genital tuberculosis was PCR, which led to more efficient implementation of meta-analysis review.

Conclusion

The present systematic study and meta-analysis showed a 6.3% prevalence of genital tuberculosis in the general population of Iran, providing further proof on the importance of the issue and the attention of the authorities to disease control. Targeted screening, especially for populations at risk, both those with tuberculosis and those in contact with them, especially in the presence of symptoms, seems to be of paramount importance. Given the fact that the present study was conducted only in a few provinces, more comprehensive studies are recommended based on the anthropological weight of all provinces.

Conflict of Interest

The authors disclose that they have no conflicts of interest.

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