

Prevalence and Pattern of Infertility in Iran: A Systematic Review and Meta-Analysis Study

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Abstract

Context: Infertility is a complex reproductive issue worldwide. Knowledge about the prevalence of any health problems like infertility is the first step towards policymaking in order to make effective decisions.

Methods: An electronic systematic review was conducted in 2019 through search in PubMed, Scopus, Web of Science, Science Direct, and EMBASE data bases. Following the evaluation of the articles by the research team, 11 articles were accepted based on the inclusion criteria of the study. The information was analyzed utilizing Stata software version 11.

Results: The results of analysis on 58,746 participants showed that the prevalence of primary infertility was 5.0% (95% CI: 4.0, 6.0%; I2: 98.20%) and the prevalence of secondary infertility was 2.0% (95% CI: 1.0, 3.0%; I2: 98.48%). The prevalence of primary and secondary infertility by gender was higher in women (6% and 3%, respectively). The prevalence of primary infertility was more common in people under the age of 35.

Conclusions: In Iran, the pattern of infertility presents a higher prevalence of primary infertility, which is probably due to the differences in the pattern of sexual relations in Iran. The more prevalence is primary infertility and infertility in women under the age of 35, the more attention should policymakers pay to provide effective plans for reducing infertility in the future.

Keywords: Infertility, Prevalence, Meta Analysis, Systematic Review, Iran

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1. Context:

Infertility is a common health problem defined as a the failure in pregnancy after one year of regular unprotected sexual intercourse (1, 2). Infertile couples experience different problems, including sexual (sexual dysfunction), financial (costs of treatment), and psychological problems (depression, anxiety, stress, lower quality of life (QOL), stigma, social exclusion, feelings of failure) and other problems, such as domestic violence and being childless (3-7).

All around the world, 10% of population, 13 % of women, 10 % of men, and 15% of couples of reproductive ages suffer from infertility. The prevalence of primary infertility is about 12-15% (8-11) and this rate is increasing in the world. In a study by Sun and colleagues from 1990 to 2017, the prevalence of primary infertility was reported to have increased to 14.9% for female and

8.2% for male (9). In the United States, the prevalence of infertility was reported to be 15.5% (12). In another study on 53 countries, the prevalence of primary infertility was 0.6% -3.4% (13).

Certain studies have investigated the prevalence of infertility in Iran. In 2009, the prevalence of lifetime primary infertility and current primary infertility were 24.9 % and 3.4% , respectively (14). In 2013, the prevalence of primary infertility was reported to be 20.2% (15). In 2014, the prevalence of infertility, primary infertility, and secondary infertility were 13.2%, 5.2%, and 3.2%, respectively (16). The prevalence of primary infertility in 2019 was 20.2% for clinical definition, 12.8% for epidemiological definition, and 9.2% for demographic definitions (17). Such studies have estimated the prevalence of infertility in Iran to be higher than the global average.

The evidence shows that the prevalence of infertility

is disparate in different countries. It could be attributed to the definition of infertility, gender of population, the age of population, and other factors. Due to different results in estimating the prevalence of infertility, overestimation, and unclear prevalence of infertility based on region, age, and gender, we decided to conduct a systematic review. This systematic review can determine the prevalence of primary and secondary infertility and the pattern of incidence based on age and sex. Therefore, it can help policymakers to schedule a program for infertile people. In this research, we aimed to investigate whether the prevalence of infertility in Iran is higher than that of the global average.

2. Methods:

Study design

This study was done in conformance with the PRISMA-P statement and registered on PROSPERO (CRD42017073835). Based on the PICO process, the study population comprised all the articles in which the desired statistics were reported in couples, women, or men. The intervention was considered to be the prevalence of infertility and the results extracted from the article. Comparisons were made for infertility prevalence statistics between primary and secondary types, different ages, couples, women, or men. The outcomes were to obtain a pattern of infertility prevalence in Iran.

Search strategy and data sources

An electronic systematic review search was conducted using PubMed, Scopus, Web of Science, Science Direct, and EMBASE. Two members of the research team independently searched all databases with the same keywords employing MeSH terms and non-MeSH terms. The keywords included infertility, sub fertility, infecundity, Iran, prevalence, sterility occurrence, and frequency and their Persian equivalents. The searches were restricted from 2000 until the end of 2019.

The articles were extracted from the relevant sites using the specified queries. Two members of the research team selected the studies. In case of disagreement, the third researcher reviewed them. After searching all the possible sources, for the quality control of the selected

articles, a standard checklist was utilized according to the Cochrane guide. Their quality was evaluated by two researchers in terms of methodology and their information was entered into the checklist.

The evaluation criteria of the articles were: the number of samples examined, research method, data collection sources, infertility type, reproductive age range, how to complete the data collection, and the inclusion and exclusion criteria.

Inclusion criteria

All the peer-reviewed, descriptive, cross-sectional, and case-control studies in English and Persian estimating the prevalence of infertility in the study population.

All the studies that provide information on the number of infertility cases in the study population.

Exclusion criteria

The review studies, case reports, letters to the editor, and abstracts of articles without the full text and the cases in which the infertility ratio could not be estimated.

Evaluation of quality

After determining the relevant studies in terms of inclusion and exclusion criteria, a checklist (Newcastle Ottawa scale) was used to evaluate the quality of articles for cross-sectional studies (43). These checklists perform a quality assessment based on three dimensions: 1) how to choose, 2) comparability, and 3) outcome/exposure. Finally, the articles with a score equal to or greater than 7 were evaluated as having good quality.

Statics analysis

The data were analyzed with Stata software version 14. The infertility ratio with the associated confidence interval was used to express the effect size. The heterogeneity index was determined to be between the initial studies using Cochran (Q) and I² tests. I² over 70 indicated the presence of significant heterogeneity. According to the heterogeneity value of the model, a random or fixed effect was calculated to estimate the infertility ratio in the Metaprop function. The effect of

the role of each initial study in the overall estimation was examined via sensitivity analysis. Additional analyses, such as meta-regression and subgroup, based on gender (18) and the mean age ($35 \geq$ or < 35), were performed to find suspected variables of heterogeneity. Diffusion bias was also checked with the Begg test.

3. Results

2888 studies were extracted from the reviewed sites. After removing duplicates and unrelated studies, 11 full text studies remained. Figure 1 depicts the flowchart of the study.

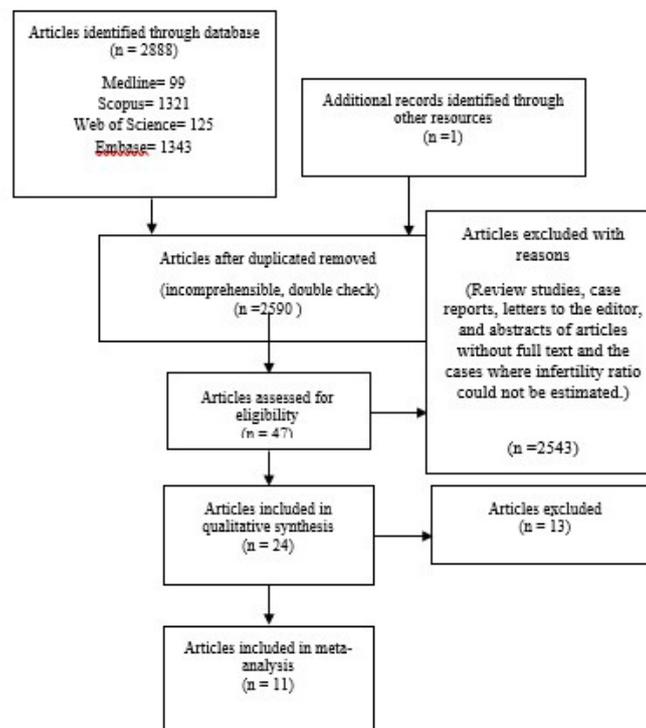


Figure1: The figure shows the process of the studies.

The overall estimation of primary infertility ratio after deleting the study conducted by Badr and co-workers (26) was 5.1% (95% CI: 3.7, 6.3) and after deleting the study conducted by Mohammad Mohammad Beigi and colleagues (24) was 4% (95% CI: 2.8, 5.1%) (the lowest and highest values of the total estimated size, respectively). Regarding the overall estimation of secondary infertility, the highest rate was obtained after the omission of the study by Akhondi and

Meta-analysis findings

In 11 studies, 58,746 subjects (ranging from 380 to 17187 in each study) were evaluated. Seven infertility cases were reported in women, two in couples, and two in men. The studies were published between 2002 and 2019 (Table 1; 14, 15, 18-28).

The overall estimated infertility ratio in 11 studies was estimated to be 5.0% based on the random effect model (95% CI: 4.0, 6.0%; I²: 98.20%). Regarding the overall estimation of secondary infertility, a combination of nine studies reporting a secondary infertility ratio of 2.0% (95% CI: 1.0, 3.0%; I²: 98.48%) was estimated (Figure 2: A-B).

co-workers (2.2%, 95% CI: 1.1, 3.2%) and the lowest one was obtained following the omission of the study by Safarinejad and colleagues (1.5%, 95% CI: 0.0, 2.0%) (Figure 3: AB; 15, 19).

The overall estimation of the proportion of primary infertility by gender was 6% (95% CI: 4.0, 8.0%) in women, 3% (95% CI: 2.0, 3.0%) in couples, and 2% (95% CI: 2.0, 3.0%) in men (seven studies in women, two studies in couple, and two studies in men).

Table 1: Characteristics of the studies included in the meta-analysis

Author/References	Year	Population	Number of Primary infertilities	Number of Secondary infertilities	Duration of marriage (year)	Sex	Quality number	Range of population age
Hosseini and colleagues	2012	2296	48	-	-	Male	7	25-60
Hosseini and colleagues	2013	2400	72	4	-	Male	7	18-49
Sadegh Moghadam and colleagues	2008	380	25	20	7.43±1.7	Female	7	15-49
Mohammad Beigi and colleagues	2002	902	130	36	17.69±3.23	Female	7	15-49
Sedaghat and co-workers	2003	1987	144	28	-	Female	9	25-45
Vahidi and colleagues	2009	11370	385	-	-	Female	9	19-49
Safarinejad and co-workers	2007	11441	915	389	17.4 ± 8.6	Female	9	15-50
Akhondi and colleagues	2019	17187	456	36	-	Female	8	20-40
Hosseini and co-workers	2012	2400	72	40	-	Female	9	18-49
Badr and colleagues	2006	3183	65	39	-	Couple	7	15-49
Aflatoonian and colleagues	2009	5200	170	107	12.88 ± 13.05	Couple	8	16-95

The prevalence of primary infertility in people under the age of 35 was higher than that in people over the age of 35 (5% (95% CI: 4.0, 7.0%) and 4% (95% CI: 2.0, 6.0%), respectively).

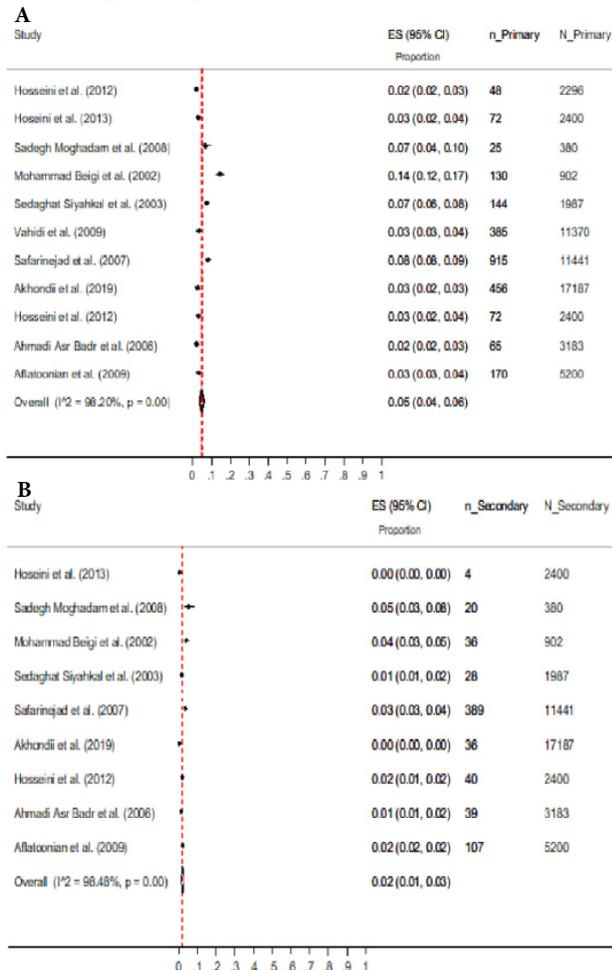


Figure 2: The figure shows the estimation of infertility ratio based on the random effect model: primary infertility (A), and secondary infertility (B).

The overall estimation of the proportion of secondary infertility by gender was 3% (95% CI: 1.0, 4.0%) in women, 2% (95% CI: 1.0, 2.0%) in couples, and 0.0% (95% CI: 0.0, 0.0%) in men (six studies in women, two studies in couples, and one study in men).

The prevalence of secondary infertility was similar to that of age; under the age of 35, it was 2 % (95% CI=1.0-3.0 %) and over the age of 35, it was 2% (95% CI=2.0-2.0%).

Meta-regression indicated that the association between the overall primary infertility ratio and the quality of the articles was not significant (B= -0.001, P=0.90). Meanwhile, the association between the overall primary infertility ratio and the publication date of articles was significant (B=-0.00, P=0.03), which showed a decrease in the prevalence of infertility over time (Figure 4).

Meta-regression implied an insignificant association among the overall secondary infertility ratio, the quality of included articles (B=-0.00, P=0.91), and the publication date of articles (B=-0.001, P=0.13).

Begg test revealed no publication bias in the included primary infertility articles (z=1.56, P=0.11) and secondary infertility articles (z= 0.83, P=0.40).

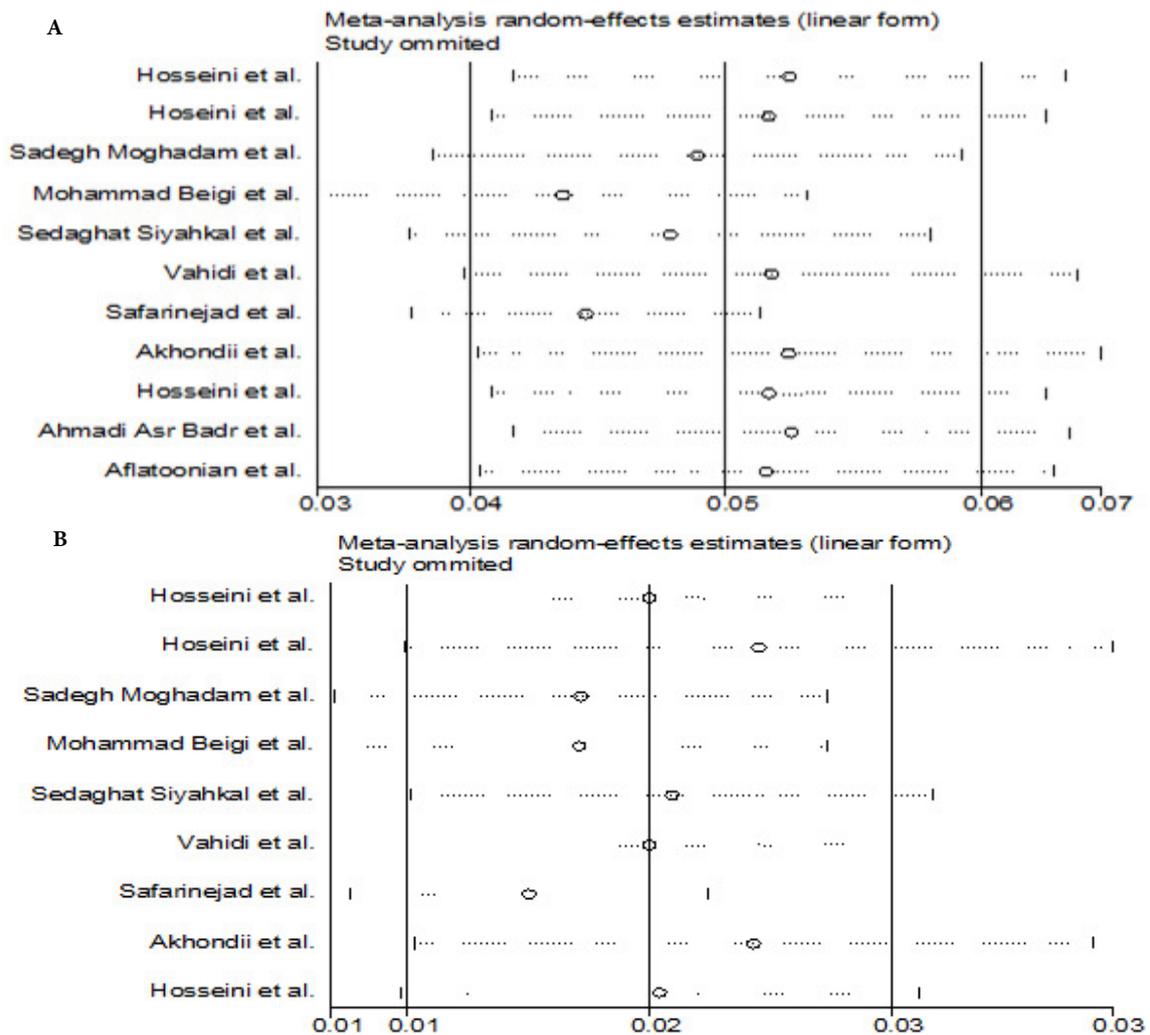


Figure 3: The figure shows the sensitivity analysis for determination the effect of each study on overall estimation of infertility ratio: (A) primary infertility, and (B): secondary infertility.

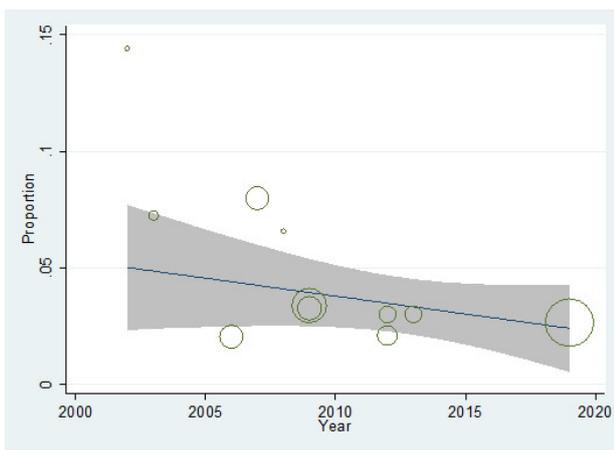


Figure 4: The figure shows the meta-regression analysis for estimation of the overall primary infertility.

4. Discussion

In our meta-analysis study on 58,746 cases, the prevalence of primary infertility and secondary infertility were 5% and 2%, respectively. Our finding was in line with that of Direkvand Moghadam and other

colleagues (2013); their study was conducted on 13 articles and 55658 people. They reported a prevalence of 13.2% of infertility cases for the overall infertility, 5.2% for primary infertility, and 3.2% for secondary infertility (27). In the meta-analysis by Parsanezhad and co-workers (2013), the prevalence of primary infertility, secondary infertility, and current infertility were 10.9%, 2.7%, and 3.3%, respectively (28).

The prevalence of primary infertility in their studies was higher than that in this study, which may be due to the use of lifetime primary infertility in their report whereas herein we used current primary infertility.

In a study by Naz and colleagues (2020) on 62728 cases, the prevalence of lifetime primary infertility, current primary infertility, and current secondary infertility were reported to be 13.96% , 3.09%, and 2.18%, respectively (29). Their systematic review indicated a different prevalence of primary and secondary infertility from the present study.

It could be on account of inclusion of couples and females in the study of Naz and colleagues (29) whereas

our study included couples, females, and males. Hence, this difference could be attributed to the prevalence of male infertility.

Impact of region

50% of couples that experienced infertility were observed in sub-Saharan Africa and South-Asia (30). In countries of South-Asia, the prevalence of infertility has been reported to be 15.5% in China (31), 13.6% in northern China (32), and 7.6% in India (33); for example, in a study by Mascarenhas (2012), the prevalence of infertility, the data from Demographic and Health Surveys (DHS) of 53 countries were analyzed. The results showed that the prevalence of primary infertility and secondary infertility were respectively 0.6%-3.4% and 8.7%-32.6% (13).

Comparison of primary and secondary infertility between Iran and other countries demonstrated that the pattern of infertility in Iran is different from that in other Asian countries.

This result indicates that the rate of primary infertility is similar to the trend of other countries while the rate of secondary infertility is lower. Different patterns of secondary infertility in Iran compared to that in other countries is probably due to the differences in the pattern of sexual relations. In other countries, the number of sexual partners increases with age, yet in Iran, this is usually constant.

Hence, the sexually transmitted diseases are less frequent compared to those in other countries (34).

Impact of gender

In the present study, 11 articles were reviewed in order to estimate the prevalence of infertility (seven studies in women, two studies in couples, and two studies in men).

The overall estimation of the proportion of primary infertility by gender was reported to be 6% (95% CI: 4.0, 8.0%) in women, 3% (95% CI: 2.0, 3.0%) in couples, and 2% (95% CI: 2.0, 3.0%) in men. Therefore, the prevalence of infertility was higher among women.

Previous studies have shown a higher prevalence of infertility in women than that in men. Datta and co-workers (2016) studied 15162 women and men in Britain and reported 12.5% of prevalence of infertility in women and 10.1 % of that in men (35).

Impact of age

The prevalence of primary infertility in people under the age of 35 was higher than that in people over the age of 35 (5% versus 4%).

Similar findings have been reported by certain studies; for example, Mascarenhas and colleagues showed that the prevalence of primary infertility was 2.7 % in women aged 20 to 24 years, 2.0 % in women aged 25-29 years, and 1.6% to 1.7% in women aged 30 to 44 years.

This study indicated that the prevalence of primary infertility was higher in women under the age of 30 (36).

Our finding revealed that the prevalence of secondary infertility was similar with age; accordingly, it was 2 % (95% CI=2.0-2.0%) for women under the age of 35 (95% CI=1.0-3.0 %) and over the age of 35.

In contrast, Mascarenhas and colleagues reported that the prevalence of secondary infertility was 2.6 % in women aged 20 to 24 years and 27.1 % in women aged 40-44 years. Therefore, the age pattern showed that with the increase in age in women, the prevalence of secondary infertility increased (36).

5. Conclusion

The findings of the current meta-analysis regarding the pattern of infertility in Iran showed that primary infertility has increased recently, which is probably due to the differences in the pattern of sexual relations. However, this needs further efficient education.

The higher is the prevalence of primary infertility and infertility in women under the age of 35 and younger people, the more we need policymakers to pay attention to this issue in their plans on reducing infertility in the future. Ultimately, the prevalence of infertility in Iran is not higher than the global average. Recommendations: There are limited studies on the prevalence of infertility in Iranian men; thus, it could be suggested that this issue be considered for future studies.

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Ethical approval:

The Ethics Committee of Shiraz University of Medical Sciences (SUMS) approved the study with the code of IR.SUMS.REC.1398.1134.

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Conflict of interests

The authors declared that they have no conflicts of interest.

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