

Prevalence of Infertility in Iran: A Systematic Review And Meta-Analysis

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Purpose: In the present study, a systematic review and meta-analysis was conducted to determine the prevalence of infertility in Iran.

Materials and Methods: A search of studies was performed in June 2019 on Scopus, PubMed, Web of Science (WOS), Scientific Information Database (SID), Magiran, Irandoc and Google scholar using keywords related to infertility. The search for articles was limited to those published over the past 20 years in Persian and English languages. In this research, only population-based studies were included.

Results: The results of the analysis showed that the overall prevalence of infertility was 7.88%, 95% CI: 5.61-10.51. The prevalence of primary and secondary infertility after sensitivity analyses was 3.09%, 95% CI: 2.27-4.02 and 2.18%, 95% CI: 1.56-2.89, respectively. The slope of meta-regression line showed that the prevalence of primary ($P = .7$) and secondary infertility ($P = .4$) is rising with a slow slope in Iran.

Conclusion: It is emphasized that the results of this study are related to the areas where investigations have been conducted and that there is high heterogeneity in findings. Given that information is not available in all parts of Iran, a population-based study or the design and implementation of further research is suggested.

Keywords: infertility; Iran; prevalence; meta-analysis

INTRODUCTION

Globally, infertility is a prevalent problem among couples that affects over 186000000 people worldwide, and most of its social burden is on women^(1,2). Infertility is defined as the lack of pregnancy after twelve months of unprotected sex⁽³⁾. In a number of developing countries, as well as in Iran, childbearing is a social value for married women⁽⁴⁾. Therefore, couples who experience this critical condition are at risk of depression, anxiety, low self-esteem, dissatisfaction^(5,6), and reduced quality of life⁽⁷⁾, not to mention a further significant economic burden for the couple and the society⁽⁸⁾. Various studies have proposed several infertility risk factors including alcohol consumption, chronic diseases, overweight, smoking⁽⁹⁾, exposure to environmental toxins, coping with stress⁽¹⁰⁾, consumption of fried foods⁽¹²⁾, and higher age of marriage⁽¹²⁾. The evidence shows that 21-22% of Iranian women suffer from lifetime primary infertility⁽¹³⁾, while different infertility rates have been reported in various parts of the world. A study in Canada shows 11.5-15.7% prevalence of infertility⁽¹⁴⁾. In another study in China on women of fertility age, infertility rate has been reported at 25%⁽¹⁵⁾ while studies on the incidence rate of infertility in Nigeria and Britain have reported it at 15.7% and 12.5%, respectively^(16,17). In a meta-analysis study in Iran examining the pub-

lished studies of 2001-2011, the primary and secondary infertility rates have been reported as 5.2 and 3.2%, respectively. It has been reported that infertility has an incremental trend in Iran⁽¹⁸⁾ and a meta-analysis study has shown that approximately 10% of the world's population suffers from infertility⁽¹⁹⁾. Direkvand Moghadam (2015) et al. conducted a meta-analysis study about the trend of infertility in Iran, in which the search for articles was carried on up to 2011⁽²⁰⁾. Another systematic review and meta-analysis was performed on epidemiology and etiology of infertility in Iran in 25 recent years until 2012⁽²¹⁾. These studies include a large number of investigations about infertility in Iran. In this research, we aimed to include the population-based studies. Since meta-analysis is a quantitative, formal, and epidemiological research design used for the systematic evaluation of previous studies to reach a conclusion about a collection of research works,⁽²³⁾ it has been used in the current investigation to determine the prevalence of infertility in Iran based on population based studies.

MATERIALS AND METHODS

Search strategy and Data sources

This study is related to a project in Shahid Beheshti University of Medical Sciences. The PRISMA checklist was used a search of articles for the study was con-

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Table 1. Summary of studies reviewed in this study.

Author/ Year/ References	Location	Population	Infertility Rate			Overall	Urban	Rural	Quality Assessment		Outcome
			Current Primary	Life Time Primary	Secondary				Selection	Comparability	
Afroughi (2019) ⁽⁴⁹⁾	Kohgiluyeh Va Boyer- Ahmad	2284 couples, - aged upper than 15 yr	-	-	-	249 (10.9%)	152 (10%)	97 (12.7%)	*****	*	**
Mirzaei (2018) ⁽⁵⁰⁾	Yazd	2611 women aged 20-49 yr	81 (2.6%)	-	75 (2.1%)	135 (4.73%)	-	-	*****	*	***
Rostami Hormozgan Dovom (2014) ⁽⁵¹⁾	Golestan, Gazvin, Kermanshah,	888 women 18-45 yr.	57(6.4%)	238 (21.1%)	69 (7.8%)	-	-	-	*****	*	**
Hosseini (2012) ⁽⁵²⁾	Esfahan, Hormozgan, Kermanshah, Golestan	2296 women 18-49 yr.	72(3.2%)	599 (26.1%)	40 (1.7%)	-	-	-	*****	*	**
Esmailzadeh (2012) ⁽⁵³⁾	Babol	1140 women 20-45 yr.	47(4.3%)	132 (12.2%)	20 (1.9%)	-	-	-	*****	*	**
Akhondi (2013) ⁽⁵⁴⁾	National	17187 women aged 20-40	3472 (20.2%)	-	-	-	-	-	*****	*	**
Kazemijaliseh (2015) ⁽⁵⁵⁾	Tehran	1067 women 18-45 yr	-	185 (17.3%)	-	-	-	-	*****	*	***
Aflatoonian (2009) ⁽⁵⁶⁾	Yazd	5200 couples 18-65yr	170 (3.48%)	-	107 (2.04%)	277 (5.52%)	144 (6.8%)	133 (5.3%)	*****	*	**
Esmaelzadeh Mogadam ⁽⁵⁷⁾	Mazandaran	2953 couples	16(4%)	351 (11.9%)	38 (1.3%)	389 (13.2%)	14.4%	12.3%	****	*	*
Badr (2006) ⁽⁵⁸⁾	Tabriz	2623 couples whose wives were at their reproductive age	54 (2.05%)	-	34 (1.30%)	88 (3.35%)	-	-	*****	*	**
Vahidi (2009) ⁽⁵⁹⁾	National	10783 women 19-49yr.	368 (3.4%)	2685 (25.2%)	-	-	-	-	*****	*	**
Safarinejad (2006) ⁽⁶⁰⁾	National	11441 women 15-50 yr.	526 (4.6%)	-	389 (3.4%)	915 (8%)	-	-	*****	*	**
Nojomi (2002) ⁽⁶¹⁾	Tehran	1174 women 40-50 yr.	18 (1.5%)	98 (8.3%)	43 (3.7%)	141 (12%)	-	-	*****	*	**
Shafi (2016) ⁽⁶²⁾	Babol	1081 women 20-45 yr.	46 (4.25%)	168 (15.5%)	-	-	-	-	****	*	*

ducted in June 2019 by two independent investigators and the disagreement between the investigators was resolved by consensus. The authors limited the electronic search of papers to the last 20 years, which was done across the databases of Scopus, PubMed, Web of Science (WOS), Scientific Information Database (SID), Magiran, Irandoc and Google scholar. The search for articles was limited to Persian and English languages over 2000-2019. Also, a manual search was conducted among the references included in the articles. The search process and study selection was performed by two independent reviewers and any disagreement between the reviewers was solved by a third person.

Search strategy

The study used the following keywords: infertility, sub hypofertility, reduced fertility, sterility, prevalence, Iran, which were combined with 'OR' and 'AND' op-

erators.

Inclusion and exclusion Criteria

Inclusion criteria for the research were as follows: cross-sectional population-based or community based studies, married life >1 year and mentioned prevalence of primary (not becoming pregnant about one year after unprotected intercourse based on the WHO standard), or secondary (couples who were pregnant at least once before), or lifetime infertility or primary lifetime infertility (couple had experienced primary infertility in their life). Studies such as review, letter to editor, case report, case control, case series as well as those with irrelevant results were excluded.

Data Extraction

The main outcome in this study is the prevalence of overall, primary and secondary infertility. In this research, two researchers participated in data extraction

Table 2. The result of subgroup analysis.

Sub Group Analyze	Primary Prevalence				Overall Prevalence				Secondary Prevalence			
	NO Of Studies	Prevalence (95% CI)	I ²	P	NO Of Studies	Prevalence (95% CI)	I ²	P	NO Of Studies	Prevalence (95% CI)	I ²	P
Time course												
2000-2010	5	2.39 (1.38-3.66)	97.72	<0.001	2	7.6 (6.88-8.36)	0	<0.001	4	3.15 (1.48-5.42)	95.29	<0.001
2010-2019	6	4.04 (3.08-5.12)	80.67	<0.001	5	7.93 (5.12-11.28)	98.51	<0.001	5	2.22 (1.36-3.29)	95.36	<0.001
Location												
Urban	-	-	-	-	3	9(4.9-14.18)	98.51	<0.001	-	-	-	-
Rural	-	-	-	-	3	6.92 (3.16-11.97)	98.7	<0.001	-	-	-	-

phases. After the article search, a preliminary assessment of the title or abstract of all articles was done and those that had reported the prevalence of total, primary, primary lifetime or secondary infertility were included in the next level of assessment. In the next stage, the researchers extracted a list of required information, including the prevalence of infertility, the place and time of the study, and the causes of infertility.

The two researchers were provided a checklist of information required for systematic evaluation, including the name of the researcher, title of the article, year and place of the study, sample number and collection method, study type, measurement tool, infertility, the overall prevalence of infertility, as well as the primary and secondary prevalence of infertility. In overall all items related to PICOS such as participants, comparisons, outcomes, and study design were extracted.

Risk of bias and quality assessment

A valid and reliable tool, namely Newcastle-Ottawa Quality Assessment Scale Adapted for Cross Sectional Studies, was used for quality assessment of the relevant studies. According to this tool, studies with a score of

five stars or more were included into the current study. Furthermore, this scale examined the methodology of the studies such as representativeness of the sample, sample size, non-respondents, ascertainment of the exposure comparability, assessment of the outcome, statistical test measurement criteria⁽²³⁾. **Table 1** shows the results of bias risk and quality assessment.

Statistical Analysis

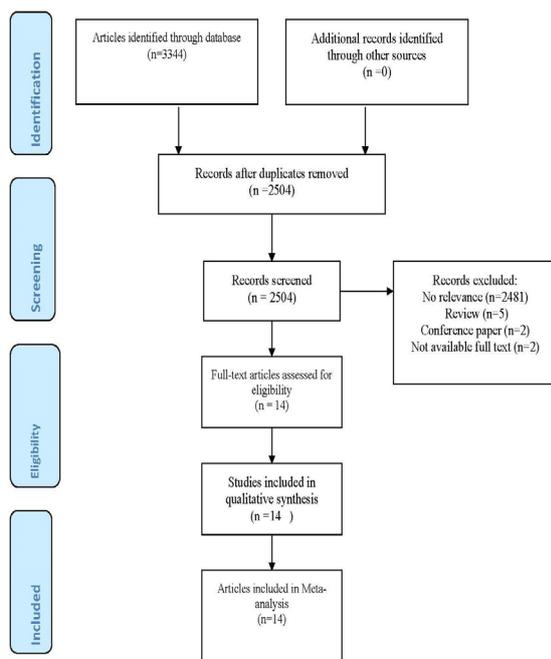
Effect size in this study was the prevalence of infertility, the variance of which (with 95% confidence interval) was calculated using the binomial distribution. The effect size of individual studies is calculated by weighting each one of them by its inverse variance, and a confidence interval (CI) is thus obtained⁽²⁴⁾. Each study was weighted inversely proportional to its variance. To calculate the variance of each research, a binomial distribution was used. The Q statistics and I2 index with α significance level of <10% were used to investigate heterogeneity. In this research, the random-effects model is considered when there is heterogeneity among the studies (I2 > 50%)⁽²⁵⁾. The authors used the Begg's and Egger's test to check publication bias⁽²⁶⁾. In our investigation, Metaprop command in STATA was used to stabilize the variances⁽²⁷⁾. Meta-regression, sensitivity analysis and sub group analysis were employed to evaluate the potential source of heterogeneity and possible source of bias. For unmeasured confounding factors, the sensitivity analyses were used for estimation of the true effect of sizes⁽²⁸⁾ and STATA software (version 11.2) was our tool for data analysis.

RESULTS

This research was based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist. In this study, 14 population-based studies were entered into the final analysis phase (**Table 1**). The number of participants in this study was 62728 and **Figure 1** shows the process of article selection.

We used sensitivity analysis for obtaining reliable results and in order to ensure the stability of the results the sensitivity analysis have been used.

The results of the analysis showed that the overall prevalence of infertility in seven studies was 7.88%, 95% CI: 5.61-10.51%, $Q = 323.63$, $p < .001$. The current primary infertility prevalence rate in 12 studies was 4%, 95% CI: 1.4-7.85%, but after sensitivity analyses, the primary infertility prevalence rate in 11 studies was 3.09%, 95% CI: 2.27-4.02%, $Q = 245.14$, $p < .001$. The secondary infertility prevalence rate in nine studies was 2.59%, 95% CI 1.82-3.49%, but after sensitivity analy-

**Figure 1.** Flowchart of article selection.

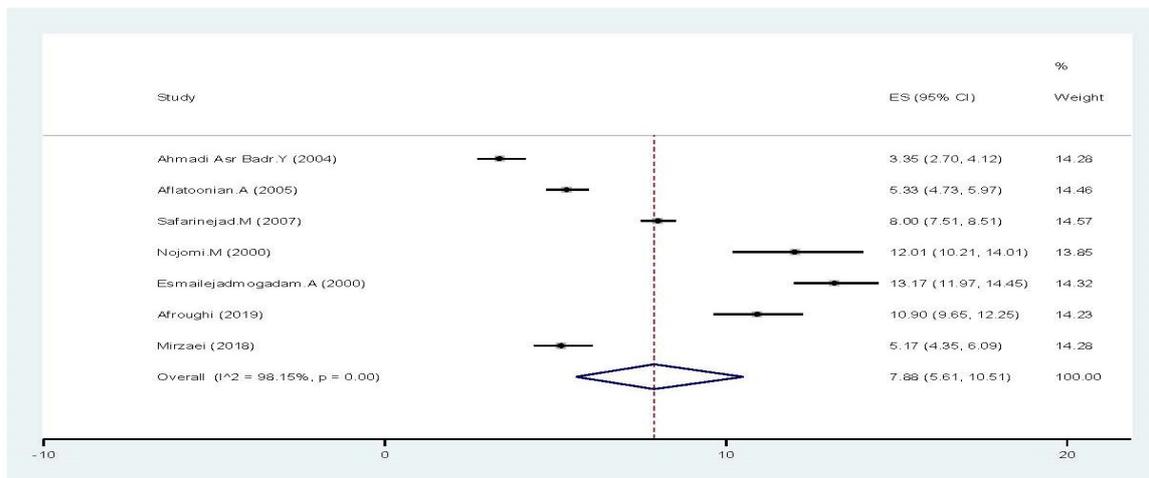


Figure 2. Prevalence of overall infertility by researcher, year, prevalence and 95% confidence interval in Iran. Each line segment indicates a confidence interval of 95%. The diamond mark shows the in all regions.

ses, the secondary infertility prevalence rate in 8 studies was 2.18%, 95% CI: 1.56-2.89%, $Q = 150.92, p < .001$. Also, the primary lifetime prevalence in eight studies was 13.96% 95% CI: 7.94-21.34%, $Q = 1329.38, p < .001$. **Figures 2-4** shows the prevalence of overall infertility, current primary infertility, and secondary infertility. According to the results of Begg's test ($p = .484$) and Egger's test ($p = .466$), there was no publication biases in this study, and because of heterogeneity, the random effect model was used (**Figure 5**).

Subgroup analysis and Meta-regression:

In this study meta-regression, investigating the association between prevalence of current primary, overall and secondary infertility was investigated based on publication date of studies (**Figure 6**). The positive slope of meta-regression line showed that the prevalence of primary ($p = .7$) and secondary infertility ($p = .4$) in Iran was rising with a slow slope based on year and that the overall prevalence had a downward trend ($p =$

.7), which was not significant. **Table 2** shows the result of subgroup analysis. Our study showed that over the period of (2000-2010) to (2010-2019), the prevalence of current primary infertility increased from 2.39% to 4.04%, the overall prevalence slowly increased from 7.6 % to 7.93%, and secondary prevalence decreased from 3.15% to 2.22%. The prevalence of infertility in urban areas in the three reported studies was 9%, 95% CI: 4.9%-14.18%, $Q = 134.58, p < .001$ and in rural areas, it was 6.92%, 95% CI: 3.16-11.97%, $Q = 154.27, p < .001$.

DISCUSSION

This review study on 62728 persons in Iran indicated that the overall prevalence of infertility was 7.88%, the current primary and secondary infertility prevalence was 3.09% and 2.18%, respectively and the lifetime primary infertility was 13.96%.

For accurate estimation of infertility, we measured the

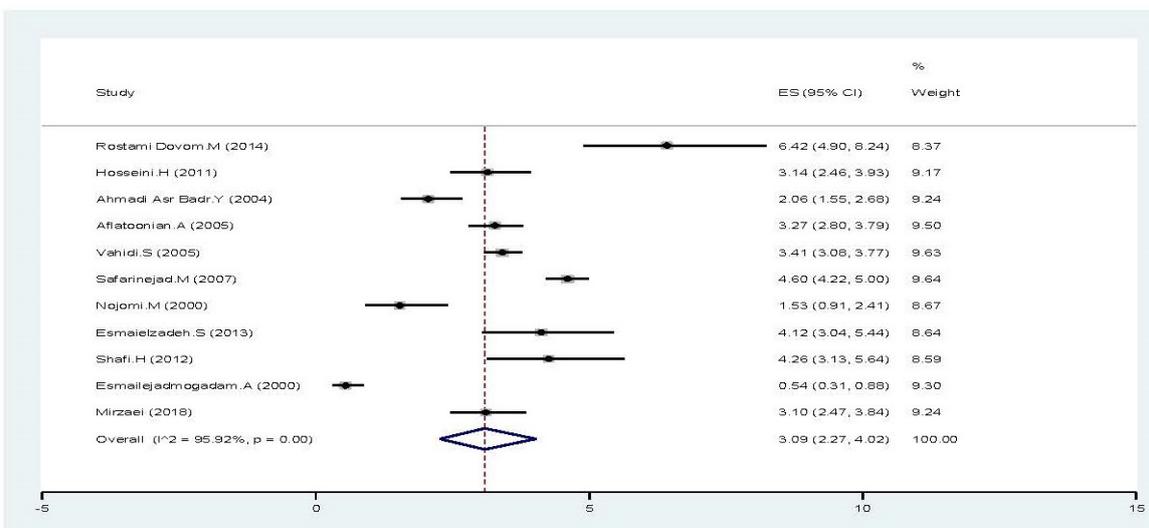


Figure 3. Prevalence of current primary infertility by researcher, year, prevalence and 95% confidence Interval in Iran. Each line segment indicates a confidence interval of 95%.The diamond mark shows the in all regions.

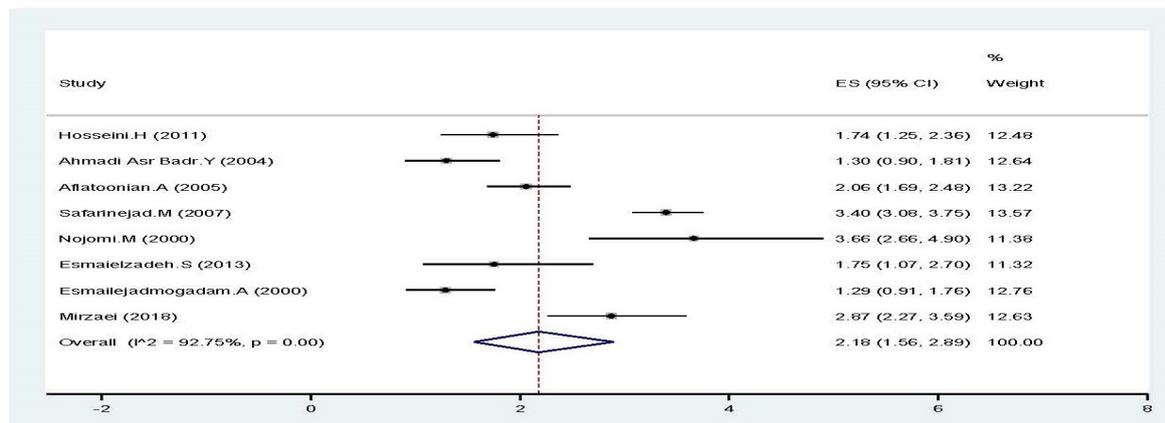


Figure 4. Prevalence of secondary infertility by researcher, year, prevalence and 95% confidence interval in Iran, each line segment is indicative of a confidence interval of 95%. The diamond mark shows all the regions.

prevalence of infertility only based on population-based studies. There is little difference between our findings and previous studies. Estimation of the prevalence of infertility is confronted with several practical difficulties⁽²⁹⁾ and there is inconsistency between infertility definitions in different studies⁽²⁹⁾. Parsanezhad et al. conducted a systematic review and meta- analysis on epidemiology and etiology of infertility in Iran over the recent 25 years until 2012, the results of which showed that the average rate of infertility in Iran is 10.9%⁽²¹⁾. In a systematic review study in 2013 wherein the trend of infertility prevalence in Iran was reported from nine investigations, the prevalence of overall infertility was reported as 13.2%, average primary infertility was 5.2%, and secondary infertility was 3.2%⁽³⁰⁾. Compared with the two previous reviews, our research included 14 studies. It seems that diverse study populations and newly published studies in the past six years result in different findings in this research. In different regions of world, studies report different prevalence rates. In an investigation in Saudi Arabia, the overall prevalence of infertility was 18.93%⁽³¹⁾. Zhang et al reported an incremental trend of infertility in Beijing⁽³²⁾. In a study in Colombo, the prevalence rate of primary infertility was 40.5 among 1000 women in their reproductive age, and the prevalence of secondary infertility was 160 among

1000 women at the same age⁽³³⁾. In another research in India, the primary infertility prevalence rate was 12.6%⁽³⁴⁾. A study in a Gambian population showed the prevalence rate of infertility as 14.3%, of which 33.9% had primary infertility and 59.1% had secondary infertility⁽³⁵⁾.

The result of our study showed that in the time course of 2000 to 2019, the prevalence of current primary infertility increased from 2.39% to 4.04%, the overall

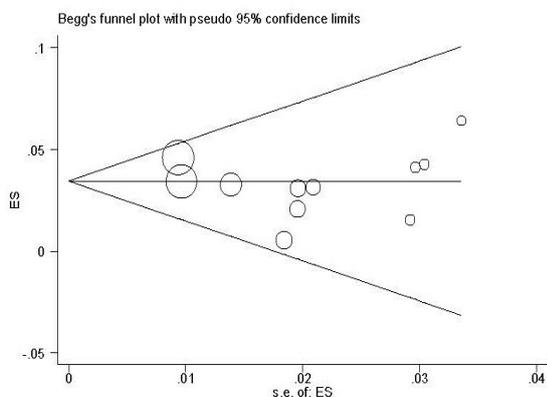


Figure 5. Funnel plot for checking publication bias

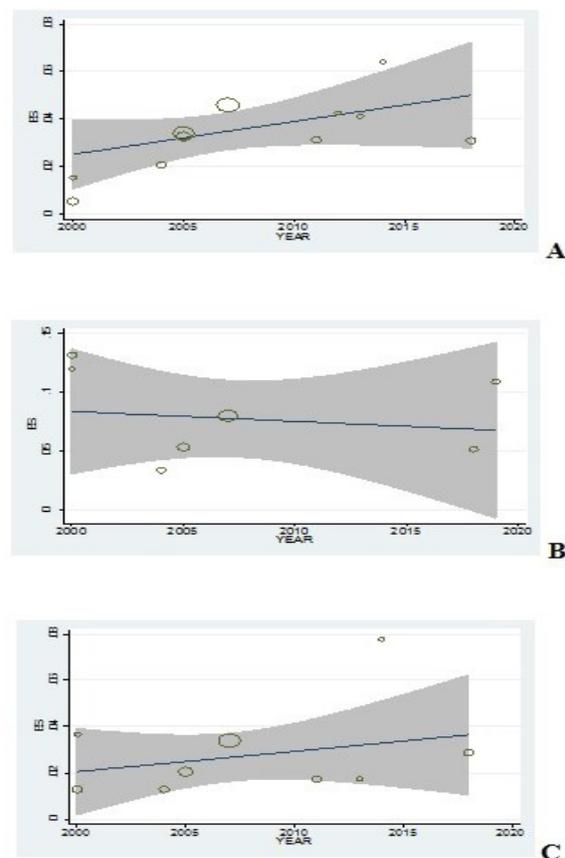


Figure 6. Meta-regression diagram: investigating association between prevalence of current primary (A) overall (B) and secondary (C) infertility, based on publication year of studies.

prevalence slowly increased from 7.6 % to 7.93%, and secondary prevalence decreased from 3.15% to 2.22%. In a 2007 study, it has been reported that approximately 72.4 million infertile people exist globally, of which 40.5 million people were in search of treatment⁽³⁶⁾. But according to the global estimation of infertility in 195 countries, the infertility and disability-adjusted life years related to the infertility had an increasing trend from 1990 to 2017⁽³⁷⁾. A study in Africa has reported that despite the reduced prevalence of primary infertility, the prevalence of secondary infertility is on the rise⁽³⁸⁾. An investigation in Turkey has shown that the prevalence trend of infertility has declined from 1993-2013⁽³⁹⁾. Global trends in infertility showed that the level of primary infertility was decreased in South Asia from 1990 to 2010⁽⁴⁰⁾. The best age for marriage of Iranian women is 20-27, which has the lowest prevalence rate of infertility⁽¹³⁾. Social change in communities, increased marriage age and delayed pregnancy in today's couples play an important role in infertility⁽⁴¹⁾. Factors such as the marriage age, environmental pollution, smoking and alcohol consumption, and lifestyle are involved in infertility⁽⁴²⁾. Therefore, change of lifestyle, control of chronic diseases, as well as fast and timely treatment of sexually transmitted diseases can increase the chance of fertility in women⁽⁴³⁾. Also, training strategies to increase awareness of couples in the field of reproductive health can be effective in the prevention of infertility⁽⁴⁴⁾.

Our finding showed that the prevalence of infertility in urban areas in three reported studies was 9%, 95% CI: 4.9%-14.18% and in rural areas of the three reported studies, it was 6.92%, 95% CI: 3.16-11.97%. According to evidence, urban fertility starts to drop earlier than rural fertility in developing countries, and it seems that rural-to-urban migration and higher rate of childbearing among them tends can lead this decreasing trend⁽⁴⁵⁾. Cultural and socio-economic factors, health care performance, and environmental factors can have an effect on the prevalence of infertility in each region⁽⁴⁶⁾. Prevalence and types of etiology of infertility are different in each geographic location⁽⁴⁷⁾. There is limited information about the prevalence of infertility in developing countries⁽⁴⁹⁾. Some evidence suggests that the social, economic, and psychological burden of infertility might be higher among infertile men and women in developing countries⁽⁴⁹⁾.

A reason for relatively high rate of infertility in Iran is that it is too late for many of these women to become pregnant. Also, statistics in urban and rural areas are changing due to the dominant culture of the region. One of the weak points of this study was its high heterogeneity. Another limitation of the study was that there were no relevant researches from different parts of the country that may affect the prevalence rate of infertility in Iran, which precludes the generalization of our finding to all regions of Iran. The strength of our study is that only population-based studies were included in it.

CONCLUSIONS

It is emphasized that the results of this study are related to the areas where studies have been conducted. Given that information is not available in all parts of Iran, a population-based investigation or the design and implementation of further studies are suggested.

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CONFLICT ON INTEREST

The authors declare that they have no competing interests.

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