

## The global trend of infertility: an original review and meta-analysis

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### ABSTRACT

**Background and aims:** Infertility is one of the most important conditions in reproductive system and there is no reliable estimates for global prevalence of infertility. Therefore, knowing the prevalence of infertility is important and can be effective in decision making.

**Methods:** We systematically reviewed all published papers in Medline database and Scopus (1988–2010). Univariate and multivariate approaches were applied to assess the causes of heterogeneity among the selected studies. Meta-regression was used to examine the relationship between the prevalence of infertility and the year of study. Data manipulation and statistical analyses were performed using Stata 11.1.

**Results:** The study population was not similar in all papers. Studies evaluated the prevalence of infertility in the general population, the total female population, women and couples. Some studies defined infertility as failure to conceive within 12 months of regular sexual life without contraception methods while other studies defined it as failure to conceive within 24 months of regular sexual life without contraception methods. Overall, 52 studies met our inclusion criteria and the pooled worldwide of infertility was obtained about 10%. The correlation between prevalence of secondary infertility and year of study was significant ( $P=0.039$ ).

**Conclusions:** Approximately 10% of the world's population suffers from infertility. Due to the negative impact of infertility on couples in various aspects of life, and the need for treatment and support programs, accurate estimate of infertility is essential worldwide.

**Keywords:** Meta-analysis, Meta-regression, Prevalence of infertility.

### INTRODUCTION

Infertility is one of the most important conditions in reproductive system.<sup>1, 2</sup> Infertility is defined as inability of a couple to access pregnancy after 12 months of regular, unprotected intercourse.<sup>3</sup>

Because of importance of women's health, many studies have been done to improve women's health.<sup>4-9</sup> There are no reliable estimates for global prevalence of infertility.<sup>10</sup> The incidence of female infertility is rising and varies from 10 to

20%.<sup>11</sup> In addition, infertilities, either primary or secondary, will occur for almost 15% of all women worldwide.<sup>12</sup> Female infertility occurs in about 37% of all infertile couples.<sup>13</sup> It ranged from 0.6% to 3.4% for the primary infertility and 8.7% to 32.6% for the secondary infertility.<sup>10</sup>

There are several adverse effects associated with infertility. Infertility has been suggested as a cause of instability in the lives of couples. A case-control study

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reported that the rate of remarriage is 3.5 times higher in infertile women.<sup>14</sup> The consequences of infertility are classified as societal repercussions, personal suffering, psychological disorders,<sup>15, 16</sup> and sexual dysfunctions.<sup>17</sup> Marital discord is also common in infertile couples, particularly when they are under stress for making medical decisions.<sup>15</sup> Clinical depression is also considerable in infertile women similar to women with heart disease or cancer.<sup>18</sup> Infertile women experience higher rates of psychological distress compared to fertile women.<sup>19</sup> However, infertility is indeed a clinical presentation rather than a disease.<sup>3</sup> Even couples undertaking in vitro fertility (IVF) have plenty of stress.<sup>20</sup>

A recent study has evaluated effects of infertility and its duration on female sexual functions. All primary infertile cases were categorized in three groups according to infertility duration: less than 2 years (Group I), 2-5 years (Group II), and 5 years or more (Group III). Sexual dysfunction was evaluated via Turkish version of female sexual function index. Comparison of fertile and infertile participants showed no significant difference between two groups in terms of scores of desire, arousal, lubrication, orgasm, sexual satisfaction, pain and total female sexual function index (FSFI) parameters. Although, all parameters and total FSFI scores were significantly different between the three groups, sexual satisfaction scores were almost similar.<sup>21</sup> In a case-control study, 119 infertile women were compared with 99 healthy females.<sup>22</sup> FSFI scores, frequency of sexual intercourse and masturbation and sex-life satisfaction were investigated. One fourth of healthy females (25%) were at risk of sexual dysfunction. The corresponding rate for infertile women was 40%. Infertile women had significantly lower scores in desire and arousal domains and significantly lower frequency of intercourse and masturbation, compared to the control group. Infertile patients reported a sex-life satisfaction score

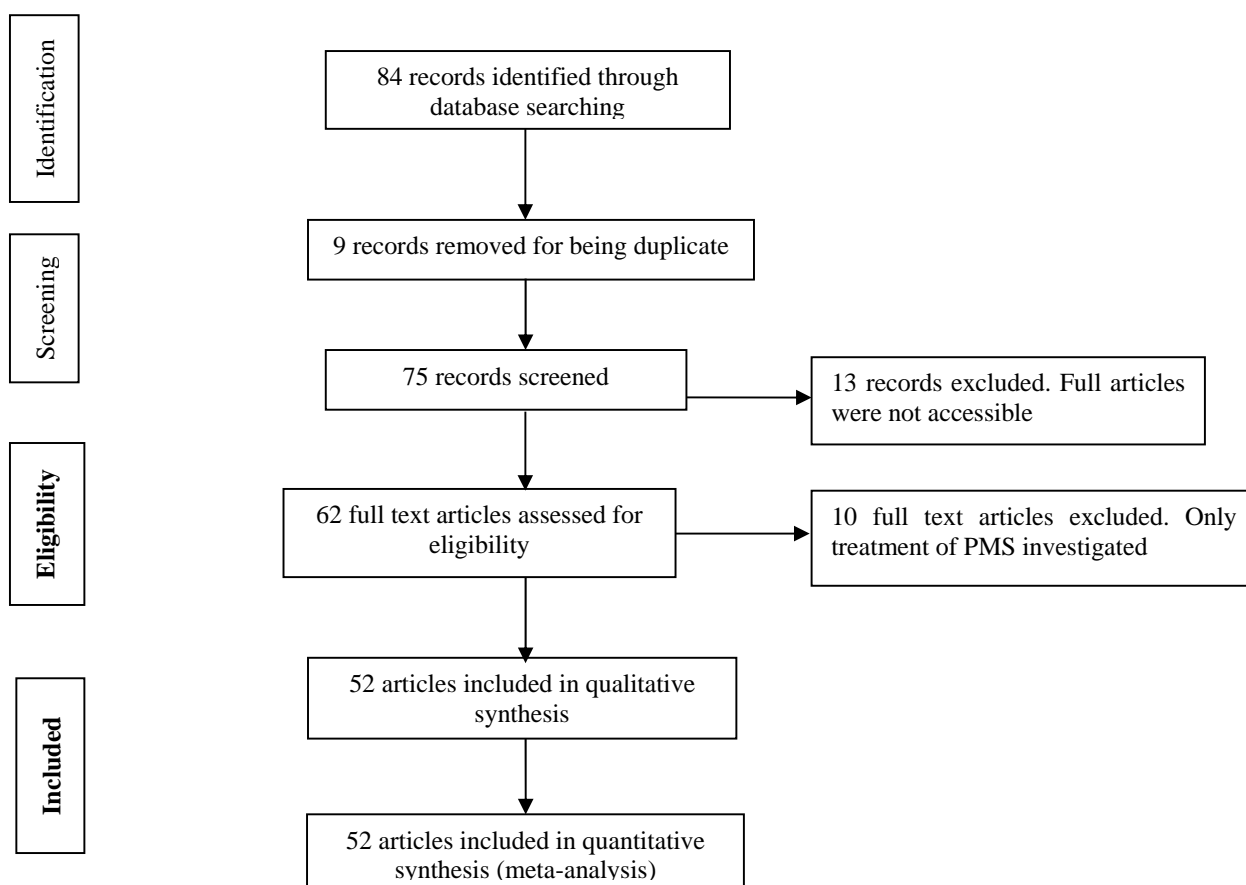
similar to that of the controls retrospectively before diagnosis, whereas their current sex-life satisfaction scores were significantly lower than control group.<sup>22</sup>

Trying to improve reproductive health is the most logical approach to reducing the infertility. Therefore, knowledge of the prevalence of infertility is important and it can be effective on the decision making.

## METHODS

This originally meta-analysis reviewed the global prevalence of infertility. We electronically searched the English-language medical literature published between 1988 and 2010 using the available databases including PubMed, Medline and Scopus. The protocol was designed using widely recommended methods and reported according to PRISMA.<sup>23</sup> Using the medical subject headings (MeSH), we searched "infertility", "epidemiology of infertility" and "prevalence of infertility" and all related subheadings.

Two researchers independently screened the titles of all recode citations, removed duplicate records and detected potentially relevant studies for inclusion. Abstracts from selected citations were then independently reviewed by two researchers for further relevance, with full text manuscripts retrieved if determined as appropriate. In case of disagreement, a third consultant acted as an intervener. 84 abstracts were selected. The following data were extracted from included studies: first author, study population, type of data collection, sampling methods, type of study and main findings. The eligible studies were those which reported "infertility", "epidemiology of infertility" and "prevalence of infertility". However, articles which included treatment of infertility were excluded. Out of 75 abstracts, 62 articles were categorized as potentially eligible for meta-analysis and systematic review. In the last stage, 52 full text articles were selected for review (Figure 1).



**Figure 1:** Results of the systematic search in literature

Data synthesis occurred through meta-analyses using the random effect model of Mantel-Haenszel, with available data presented in a Forest plot. Variance for each study was calculated using the binomial distribution formula. The presence of heterogeneity was determined by the chi-2 test with a significance level of  $<0.1$  combined with an  $I^2$  statistic for estimate of inconsistency within the meta-analyses. The  $I^2$  statistic estimates the percent of observed between-study variability due to heterogeneity rather than to chance and ranges from 0 to 100 percent (Values of 25%, 50% and 75% were considered as representing low, medium and high heterogeneity, respectively). For this review,

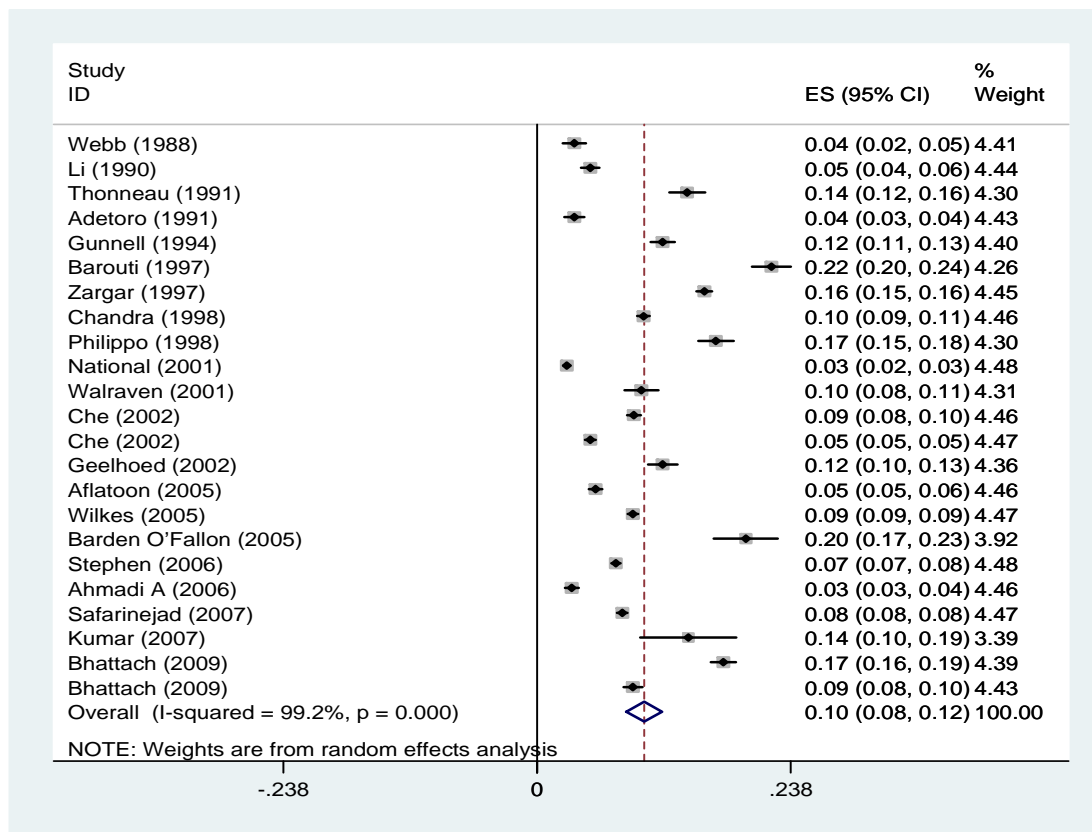
we determined that  $I^2$  values above 75% were indicative of significant heterogeneity warranting analysis with a random effect model as compared to the fixed effect model to adjust for the observed variability. This heterogeneity was further explored through subgroup analyses and meta-regression. A univariate and multivariate approach was employed to assess the causes of heterogeneity among the selected studies.

Meta-regression was used to examine the relationship between the prevalence of infertility and study's year and sample size. All analyses were conducted using Stata version 11.1 (Stata Corp LP, College Station, Texas).

## RESULTS

During the search of resources, a total of 84 articles were found. After exclusion of duplicate articles, 52 articles were selected for analysis (Figure 1). The articles were published between the years 1988–2010. Characteristics of studies are presented in Figure 2.

In most studies, the two-stage stratified sampling method was used. The cross-sectional study was the most common type. The overall global prevalence of infertility was presented in 23 articles. The pooled global infertility is 10% (95% CI: 8-12).

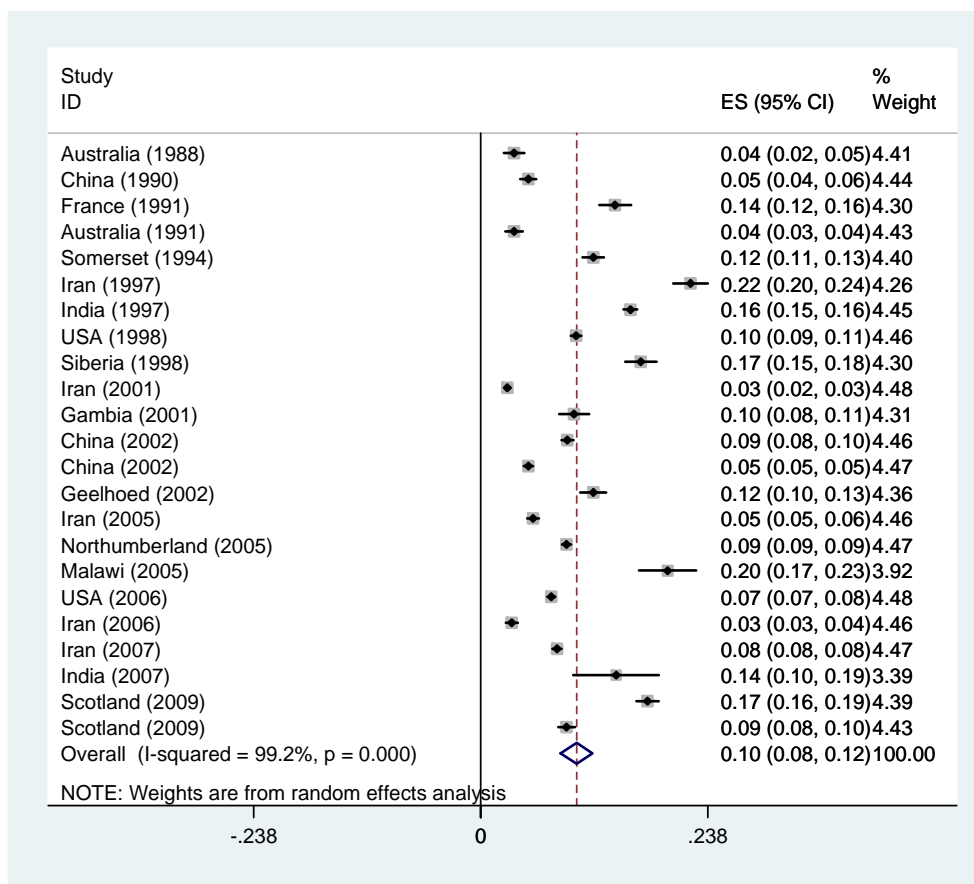


**Figure 2:** The global prevalence of infertility according to researcher, year and prevalence.

Squares represented effect estimate of studies with 95% confidence interval with size of squares proportional to the weight assigned to the study in the meta-analysis. The diamond represents the overall results and 95% confidence interval of the random effect of the meta-analysis.

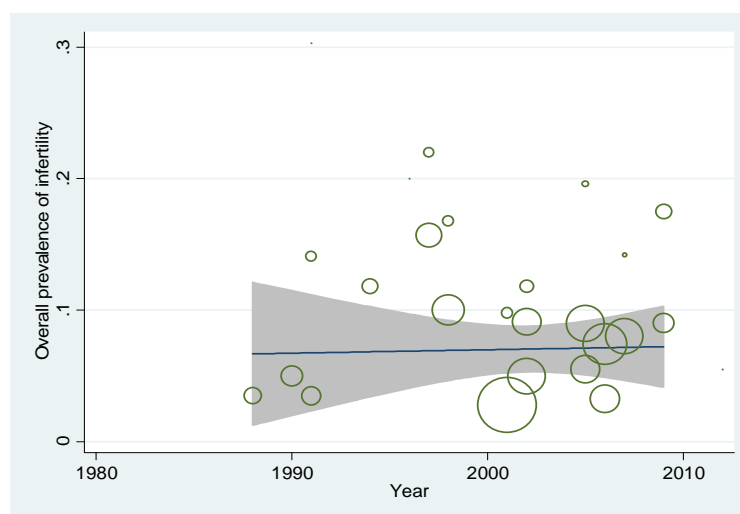
Figure 3 represents the prevalence of infertility according to the country where the research was conducted. Figure 4 presents the articles on the prevalence of infertility according to the continent. The highest

number of articles on the infertility was conducted in Asia. The lowest number of articles on the prevalence of infertility was reported in Australia and Africa.



**Figure 3:** The prevalence of infertility according to the country.

Squares represented effect estimate of studies with 95% confidence interval with size of squares proportional to the weight assigned to the study in the meta-analysis. The diamond represents the overall results and 95% confidence interval of the random effect of the meta-analysis.

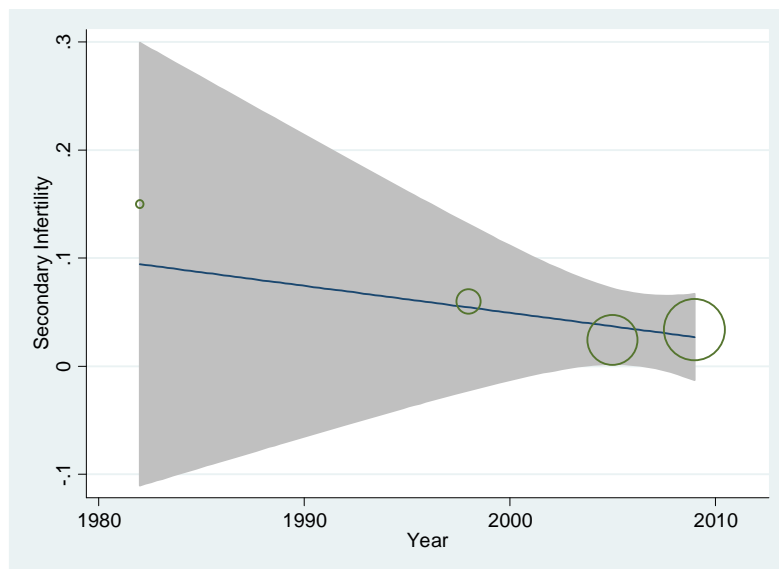


**Figure 5:** Meta-regression plot of the overall prevalence of infertility based on the year of study.

Figure 4. The prevalence of infertility according to the continent and year. Squares represented effect estimate of studies with 95% confidence interval with size of squares proportional to the weight assigned to the study in the meta-analysis. The diamond represents the overall results and 95% confidence interval of the random effect of the meta-analysis.

However, meta-regression scatter plot showed an increasing trend in the prevalence of infertility during 1988-2010, but the correlation between overall prevalence of infertility and year of study was not significant ( $P= 0.602$ ) (Figure 5).

The correlation between prevalence of secondary infertility and the year of study was significant. ( $P= 0.039$ ) (Figure 6).



**Figure 6:** Meta-regression plot of the prevalence of secondary infertility based on the year of study.

The study population was not similar in all studies. Studies evaluated the prevalence of infertility in the general population, the total female population, married women and married couples. Based on these results, the total female population was the highest study population.

Some studies have mentioned of infertility as failure to achieve a pregnancy

within 12 months of regular sexual life without contraception methods. While other studies are considered infertility as failure to achieve pregnancy after 24 months of regular sexual life without contraception methods. Most of the studies were cross-sectional studies. In some studies don't provide for the study type.

## DISCUSSION

This study evaluated the prevalence of infertility in different parts of the world. Several studies provide different definitions for infertility. In some studies, infertility is considered as reproductive failure after two years of unprotected intercourse and in

others, infertility is considered as reproductive failure after one year of unprotected intercourse.<sup>24</sup>

In the present meta-analysis the pooled global infertility was obtained 10% (95% CI: 8-12). Several studies have reported a

wide range of infertility in different countries.<sup>25, 26</sup> In a study conducted in the United States (1982), the infertility in women aged 15- 44 years was obtained 13.9%.<sup>27</sup>

In Adamson et al study, 897 women aged 15-30 years participated and the prevalence of primary infertility was reported 12.6%.<sup>28</sup> Bhattacharya et al in 2009 studied 4466 women aged 31-50 years. Based on the results, 7% of the study participants had secondary infertility.<sup>29</sup>

In the present study, the prevalence of infertility evaluated based on the country research conducted. Three general studies measured infertility in Iran.<sup>30-32</sup> The primary infertility was evaluated in women aged 20-49 years in Tehran and the highest prevalence of primary infertility was obtained about 22%.<sup>30</sup> In Aflatoonian's study in 2005, 5200 couples aged 15-44 years participated. In this study, 5% of all participants suffered from infertility.<sup>31</sup> In another study, Safarinejad et al evaluated 12, 285 women aged 15- 50 years and found out that 8% of the study population experienced infertility.<sup>32</sup>

It is well known that the different definition of infertility is the cause of different prevalence.<sup>33</sup>

Meta-regression scatter plot showed an increasing trend in the prevalence of infertility during 1988-2010 but not significant. However, the correlation between prevalence of secondary infertility and year of study was significant. Another study has shown increased prevalence of infertility in recent years.<sup>34</sup>

The infertility rates have increased because of increasing the marriage age in many communities. Thus, fertility decline is expected in older women.<sup>35</sup>

## CONCLUSION

Approximately 10% of the world's population suffers from infertility. Due to the negative impact of infertility on couples in various aspects of life, and the need for

treatment and support programs, accurate estimate of infertility is essential across the world.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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## REFERENCES

1. Wiwanitkit, V. Difference in physiogenomics between male and female infertility. *Andrologia*. 2008; 40(3): 158-60.
2. Direkvand Moghadam A, Delpisheh A, Khosravi A. Epidemiology of female infertility; A review of literature. *Biosci Biotechnol Res Asia*. 2013; 10(2): 559-67.
3. Aflatoonian A, Baghianimoghadam B, Partovi P, Abdoli A, Hemmati P, Tabibnejad N, et al. A new classification for female infertility. *Clin Exp Obstet Gynecol*. 2010; 38(4): 379-81.
4. Direkvand-Moghadam A, Rezaeian M. Increased intravenous hydration of nulliparas in labor. *Int J Gynaecol Obstet*. 2012; 118(3): 213-15.
5. Direkvand-Moghadam A, Khosravi A. Effect of acupressure on post-operative nausea and vomiting in cesarean section: a randomised controlled trial. *J Clin Diagn Res*. 2013; 7(10): 2247-9.
6. Direkvand-Moghadam A, Khosravi A. Evaluating Shirazi (*Thymus vulgaris*) on menstrual pain using verbal multidimensional scoring system (VMS). *Afr J Pharm Pharmacol*. 2012. 6(39): 2761-2766.

7. Direkvand Moghadam A, Jaafarpour M, Khani A, Comparison effect of oral propranolol and oxytocin versus oxytocin only on induction of labour in nulliparous women (a double blind randomized trial). *J Clin Diagn Res.* 2013; 7(11): 2567-9.
8. Direkvand Moghadam A, Ghazanfari Z, Sayehmiri K. Predictive factors for pelvic organ prolapse in Iranian women's: An ordinal logistic approach. *J Clin Diagn Res.* 2014; 8(1): 96-9.
9. Direkvand-Moghadam A, Sayehmiri K, Delpisheh A. Epidemiology of premenstrual syndrome, a systematic review and meta-analysis study. *J Clin Diagn Res.* 2014; 8(2): 106-9.
10. Mascarenhas MN, Cheung H, Mathers CD, Stevens GA. Measuring infertility in populations: constructing a standard definition for use with demographic and reproductive health surveys. *Popul Health Metr.* 2012; 10(1): 1-11.
11. Romero R, Romero G, Abortes I, Medina G. Risk factors associated to female infertility. *Ginecol Obstet Mex.* 2008; 76(12): 717-21.
12. Kumar D. Prevalence of female infertility and its socio-economic factors in tribal communities of Central India. *Rural Remote Health.* 2007; 7(2): 456-59.
13. Unuane D, Tournaye H, Velkeniers B, Poppe K. Endocrine disorders & female infertility. *Best Pract Res Clin Endocrinol Metab.* 2011; 25(6): 861-73.
14. Jumayev I, Harun-Or-Rashid M, Rustamov O, Zakirova N, Kasuya H, Sakamoto J. Social correlates of female infertility in Uzbekistan. *Nagoya J Med Sci.* 2012; 74(3-4): 273-83.
15. Volgsten H, Skoog Svanberg A, Ekselius L, Lundkvist Ö, Sundström Poromaa I. Risk factors for psychiatric disorders in infertile women and men undergoing in vitro fertilization treatment. *Fertil Steril.* 2010; 93(4): 1088-96.
16. Volgsten H, Svanberg AS, Ekselius L, Lundkvist Ö, Poromaa IS. Prevalence of psychiatric disorders in infertile women and men undergoing in vitro fertilization treatment. *Hum Reprod.* 2008; 23(9): 2056-63.
17. Drosdzol A, Skrzypulec V. Evaluation of marital and sexual interactions of Polish infertile couples. *J Sex Med.* 2009; 6(12): 3335-46.
18. Domar AD, Zuttermeister PC, Friedman R. The psychological impact of infertility: a comparison with patients with other medical conditions. *J Psychosom Obstet Gynaecol.* 1993; 14 Suppl: 45-52.
19. Omoaregba JO, James BO, Lawani AO, Morakinyo O. Psychosocial characteristics of female infertility in a tertiary health institution in Nigeria. *Ann Afr Med.* 2011; 10(1): 19-24.
20. Beutel M, Kupfer J, Kirchmeyer P, Kehde S, Köhn FM, Schroeder-Printzen I, et al. Treatment-related stresses and depression in couples undergoing assisted reproductive treatment by IVF or ICSI. *Andrologia.* 1999; 31(1): 27-35.
21. Iris A, Kirmizi DA, Taner CE. Effects of infertility and infertility duration on female sexual functions. *Archives of gynecology and obstetrics.* 2013; 287(4): 809-12.
22. Millheiser LS, Helmer AE, Quintero RB, Westphal LM, Milki AA, Lathi RB. Is infertility a risk factor for female sexual dysfunction? A case-control study. *Fertil Steril.* 2010; 94(6): 2022-5.
23. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009; 151(4): 264-9.
24. Gunnell DJ, Ewings P. Infertility prevalence, needs assessment and purchasing. *J Public Health Med.* 1994; 16(1): 29-35.
25. Che Y, Cleland J. Infertility in Shanghai: prevalence, treatment seeking and impact. *J Obstet Gynaecol.* 2002; 22(6): 643-8.



26. Vayena E, Rowe PJ, Peterson HB. Assisted reproductive technology in developing countries: why should we care? *Fertil Steril.* 2002; 78(1): 13-5.
27. Mosher WD. Infertility trends among U.S. couples: 1965-1976. *Fam Plann Perspect.* 1982; 14(1): 22-7.
28. Adamson PC, Krupp K, Freeman AH, Klausner JD, Reingold AL, Madhivanan P. Prevalence & correlates of primary infertility among young women in Mysore, India. *Indian J Med Res.* 2011; 134(4): 440-6.
29. Bhattacharya S, Porter M, Amalraj E, Templeton A, Hamilton M, Lee AJ, et al. The epidemiology of infertility in the North East of Scotland. *Hum Reprod.* 2009; 24(12): 3096-107.
30. Barouti E, Ramezani Tehrani F, Heydari Seradj M, Khalajabadi Farahani F, Mohammad K. Primary infertility in Tehran based on marriage age. *Hakim.* 1999; 15(2): 88-93.
31. Aflatoonian A, Seyedhassani SM, Tabibnejad N. The epidemiological and etiological aspects of infertility in Yazd province of Iran. *Iran J Reprod Med.* 2009; 7(3): 117-122.
32. Safarinejad M.R. Infertility among couples in a population-based study in Iran: prevalence and associated risk factors. *Int J Androl.* 2008; 31(3): 303-14.
33. Vahidi S, Ardalan A, Mohammad K. Prevalence of primary infertility in the Islamic Republic of Iran in 2004-2005. *Asia Pac J Public Health.* 2009; 21(3): 287-93.
34. Oliva A, Spira A, Multigner L. Contribution of environmental factors to the risk of male infertility. *Hum Reprod.* 2001; 16(8): 1768-76.
35. Naghavi M. Demographic and health survey in Iran. Tehran: Ministry of Health pub; 2002.

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