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REVIEW ARTICLE

Prevalence of Primary Infertility in Iranian Men; A Systematic Review

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Abstract: **Introduction:** Primary infertility (PI) is one of the most common problems with an increasing incidence globally. Studies conducted in several parts of Iran have reported different a prevalence for this infertility type, so we investigated PI prevalence in the Iranian male population. **Method:** This study was performed using the keywords "primary", "infertility", "prevalence", "men", "male", and "Iran" in international databases, including MedLine, Scopus, Web of Science, ProQuest, as well as domestic databases, including scientific information database (SID) and Magiran. We included original articles estimating PI prevalence and the cause of infertility in the general population and infertile Iranian couples referred to infertility centers. PI prevalence in men was not reported in any included studies, so using weighting based on sample size, the average PI prevalence in the studied couples and any male factors ("male" factors plus "both" factors) was estimated. **Result:** Thirty-two studies were obtained in the initial search. Ultimately, seven studies (five studies on infertile couples and two studies on the general population) were selected. The weighted average prevalence of PI was 81.26% (81.1-81.43) in referred infertile couples and 5.76% (5.63-5.89) in the general population. The overall estimate of PI prevalence in these groups was 46.35% (46.15-46.54) and 1.93% (1.89-1.97), respectively. **Conclusion:** The PI prevalence in different parts of Iran has been reported in the mentioned population, there was no domestic study on PI prevalence in men, so further studies to validate our results are needed.

Keywords: Iran; Primary male infertility; Systematic review

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1. Introduction

Infertility is one of the most common problems in human societies, and many couples with this problem experience various personal and family challenges. In general, infertility is divided into two categories, including primary and secondary types (1, 2). The term primary infertility (PI) is used when a couple never conceive, and secondary infertility is the incapability to conceive in a couple who have at least one successful conception in the past (3). Current studies indicated that PI is the inability to conceive after one year of unprotected intercourse and in older ages (> 35 years) for even six months (4). Numerous studies have assessed the prevalence of infertility in different communities and have reported different results. Around the world, the rate of infertility prevalence is varied from 15-20% in different regions (5), and based on the epidemiological and demographic definitions of the World Health Organization (WHO), the prevalence rate of infertility ranges from 12.8-9.2%, respectively (6-8). Men have been found to be individually responsible for 20-30% of infertility cases, and almost 40–50% of all infertility cases are related to male factors (9, 10). Male infertil-

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ity can occur because of several male factors, such as failure in sperm motility, function, spermatogenesis, sexual activity, and endocrine system (11, 12). Moreover, infertility may be caused by both male and female factors. In addition to male factors, female factors, like tuboperitoneal and ovulation disorders, have a role (13, 14). According to one study, the rate of PI ranged from 1.5% to 2.6%, in which the male contribution to these rates of infertility based on WHO estimates ranged from 0.4-1.82% (15). Another study showed that in 2011, the prevalence of PI was 20.2% in Iran (16). This is while one of the latest published studies reported that PI prevalence in Iran was 8% (17). By reviewing various studies in Iran, male factors are responsible for half of the infertilities (18) whose treatment is complicated, and influencing factors, levels, and infertility patterns is different in various regions. The sources of this difference are the methodological differences or the use of different definitions of infertility.

It is expected that the rate of infertility would increase in future years by considering the development of human societies, changes in people's lifestyles, and personal habits (19). Since the rate of infertility is one of the appropriate indicators to plan for family health, and because of the need and importance of studies in this field, herein, we have reviewed the prevalence of male PI in Iran.

2. Methods

The present study is a systematic review of the prevalence of PI in men in Iran. The results of this study are based on studies conducted in Iran. We retrieved all epidemiological studies published in journals in the databases of Scopus, ProQuest Medline, Web of Science, and also national databases, including scientific information database (SID) and Magiran. The search was performed using valid keywords (infertility, primary infertility, prevalence, Iran, men, male) in Persian and English and their possible combinations.

2.1. Study selection and data extraction

First, two independent researchers that majored in the field of embryology and general medicine collected all studies related to infertility in Iran from inception to the end of 2020. Then, we prepared a list of abstracts. At this stage, all studies with the keyword "infertility" as well as study titles containing "infertility prevalence" were included in the initial list. We included original studies that reported the prevalence of PI and influencing factors in the general population and infertile Iranian couples referred to infertility centers. Other studies that did not have a full text or were about the prevalence of female infertility or only related to risk factors were excluded. Then, a checklist of information was created including the name of the first author, study title, year and place of study, sampling method, sample size, type of study, infertility measurement tool, the prevalence of PI, and the prevalence of four infertility factors ("male" factors, "female" factors, "both" factors and "unexplained" factors) and mean or age range of men included in the study. The researchers reviewed the final checklist, and finally, related studies were included.

2.2. Statistical analyses

Finally, because of the lack of reports the prevalence of PI in men in any of the included studies, using weighting based on sample size, the average prevalence of infertility in the studied couples was estimated, and regarding the total weighted average prevalence of infertility due to any male factor ("male" factors plus "both" factors), the prevalence of male PI was estimated in both the general population and the infertile patients referred to infertility treatment centers. The Weighted average was based on sample size, which means each included prevalence got a coefficient based on its sample size, so if the prevalence values were the results of studies with higher sample sizes, they could have a greater impact on the final average. Since we did not find any reported prevalence of PI in men, we decided to estimate it from the prevalence of PI in the couples. We wanted to know the approximate share of men in the reported prevalence of PI in the couples (the overall prevalence of PI), so we estimated the prevalence of PI in men by multiplying the overall share of men in infertility (i.e., the sum of male factor and both factor) in the overall prevalence of PI. All calculations were done by SPSS software, version 22.

3. Results

In the initial search, 209 studies were found using available keywords after removing duplicated studies. 132 studies were reviewed, of which 32 studies with related titles were included in the checklist. The final qualitative evaluation of studies was done using a researcher-made checklist. In total, only seven studies were finally approved (five studies on infertile couples and two studies on the general population). The flow diagram for searching and selecting studies is shown in Figure 1. The weighted average prevalence of PI was 81.26% (CI 95%: 81.1-81.43) in infertile couples referred to infertility treatment centers and 5.76% (CI 95%: 5.63-5.89) in the general population.

The overall estimate of the prevalence of PI regarding any male factors ("male" factors plus "both" factors) in couples referred to infertility centers and the general population was estimated to be 46.35% (CI 95%: 46.15-46.54) and 1.93% (CI 95%: 1.89-1.97), respectively. The summary of studies about infertile couples is shown in table 1 and figure 2, and studies about the general population are summarized in table 2.

As shown in table 1, which is classified based on the time of

publication, we observed a decreased trend in the prevalence of PI in infertile couples from 90.1% in 2007 to 64.3% in 2018.

4. Discussion

PI may be responsible for a dramatic infertility rate in men who refer to therapeutic centers (20). Fortunately, an accurate assessment of the prevalence of infertility using epidemiological studies can be useful to plan appropriate strategies for the prevention, treatment, and management of infertility and its socio-economic consequences (21). Hence, in the present review, we studied the prevalence of PI in men in Iranian populations for the first time. In a study on infertile couples referred to Royan Infertility Treatment Center during 1995-2001, the PI rate in 2492 couples was more than 90%; in which the rate of the male factors causing infertility was 50.5%, and the contribution of female factors was 28.6% (22). In another research, a cross-sectional study was performed on 405 infertile patients referred to Royan Institute, Tehran, during 2014-2015. PI rate of couples was 70.9%, while the male and female factors causing infertility were 36% and 21.7%, respectively (23).

In a study on 579 infertile couples referred to Besat Hospital located in Sanandaj City, between 2014 and 2015, among 579 cases, 372 (64.3%) showed PI, and the prevalence of male infertility and female factor was 30% and 52%, respectively (24). We observed a decreased trend in PI prevalence in infertile couples and male PI during 2001-2015. It seems that the increased use of Assisted Reproductive Technology (ART) after 2005 may be the cause of the decreased prevalence of infertility. In spite of this, In the only study by Saremi and colleagues in 2017, which was conducted on 764 infertile Iranian men referred to the infertility clinic of Sarem Women's Hospital (Tehran, Iran) from April 2006 to March 2012, male PI was found in 593 (77.6%) patients (25). These reported differences in the infertility of couples and men may be related to the recruitment process of the study population, infertility definitions, and the method of estimation. Moreover, it should be noted that these percentages are related to people who have been referred to this center because of infertility and were not a random sample of the general population. Furthermore, advances in the diagnosis, treatment, and prevention of infertility have led to considerable changes in the worldwide prevalence of infertility in the past decades. Globally, the prevalence of PI is estimated to be 1.5-2.6%; however, this prevalence in our study was dramatically higher than this result. In the current investigation, the major limitation was that we did not find any reported prevalence of PI specified to men, so we had to use a mathematical formula to estimate the prevalence of PI in men from the overall prevalence of PI in couples. Also, the number of studies about PI in the general population was extremely low (just two studies), and the estimated average may not be generalized to Iran as a whole. It is expressed that significant percentages of infertility cases are associated with male factors (26).

Consistent with this finding, other studies (22-27) reported that male factors played a greater role in primary infertility in couples. It is highlighted that an impairment in spermatogenic occurrence, which depends on the coordinated activities between multiple hormones, local secretory agents, and specific genes of the testis, may have a considerable role in male infertility (28). However, our results indicated the role of the female factor in the population is significantly more prominent than the male factor in fertility disorders, which may be due to the lack of any domestic research on the prevalence of PI in men. Additionally, the prevalence of PI in Iran seems to be higher than the world average. Therefore, it is crucially important to support the large number of couples who experience this problem. Our analysis suggests that a substantial percentage of couples and men in Iran are struggling with PI. Thus, the capability of health systems and societies to address this issue.

5. Conclusion

The prevalence of PI in different parts of Iran has been reported in infertile couples and the general population, there was no domestic study on the prevalence of PI in men, so there is a need for further studies and research in this field.

6. Appendix

6.1. Acknowledgements

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6.2. Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

6.3. Funding and support

None.

6.4. Author contribution

All the authors had the same contribution.

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Table 1: Prevalence of Primary infertility and infertility factors among the infertile patients referred to infertility treatment centers.

Author [ref.]	Study design-location	(% male)	PI Prevalence in referred couple	Male/female/both/unexplained factors	Mean (SD)or range of Age
Shagheib Sh., et al. 2018 (24)	Cross-sectional with census sampling-Sanandaj	579 infertile patients	64.3%	30.3%/52%/-/17.8%	35.6±7.6
Sepidarkish m., et al. 2016 (23)	Cross-sectional with simple random sampling- Tehran	405 infertile patients (41.5%)	70.9%	36%/21.7%/17.5%/24.8%	31.28 ± 5.42
Masoumi SZ., et al., 2015(29)	Cross-sectional with census sampling-Hamadan	1200 infertile men and women (43.9%)	69.5%	66%/88.9%/-/-	30-40
Karimpour Malekshah A., et al. 2011(27)	Cross-sectional with convenient sampling-Mazandaran	3734 infertile couples	78.7%	38.9%/34.7%/14.6%/11.8%	33±7
Kamali M., et al. 2007 (22)	Retrospective with systematic sampling-Tehran	2492 infertile couples	90.1%	50.5/28.6%/11.9%/9.3%	33.6±6.3
Weighted average: 81.26% (CI 95%: 81.1-81.43)		Estimated Primary infertility considering any male factors: (PI in couples)*(male F+ both F)= 46.35% (CI95%: 46.15-46.54)			

Table 2: Prevalence of Primary infertility and infertility factors in population-based studies of infertility.

Author [ref.]	Study design-location	Participants	PI Prevalence in couple	Male/female/both/unexplained factors	Mean (SD) Age of men
Kazemijaliseh H., et al. 2015(30)	cross-sectional with systematic random sampling-Tehran	1067 married women	17.3%	29.1%/51.6/4.7%/14.4%	-
Aflatoonian a., et al. 2009(31)	cross-sectional study with Cluster random Sampling-Yazd	5200 couples	3.48%	25.3%/57.5%/8%/9.2%	45.35±15.18
Weighted average: 5.76% (CI95%: 5.63-5.89) PI: primary infertility.		Estimated Primary infertility considering any male factors: (PI in couples)*(male F+ both F)= 1.93% (CI 95%: 1.89-1.97)			

PI: primary infertility.

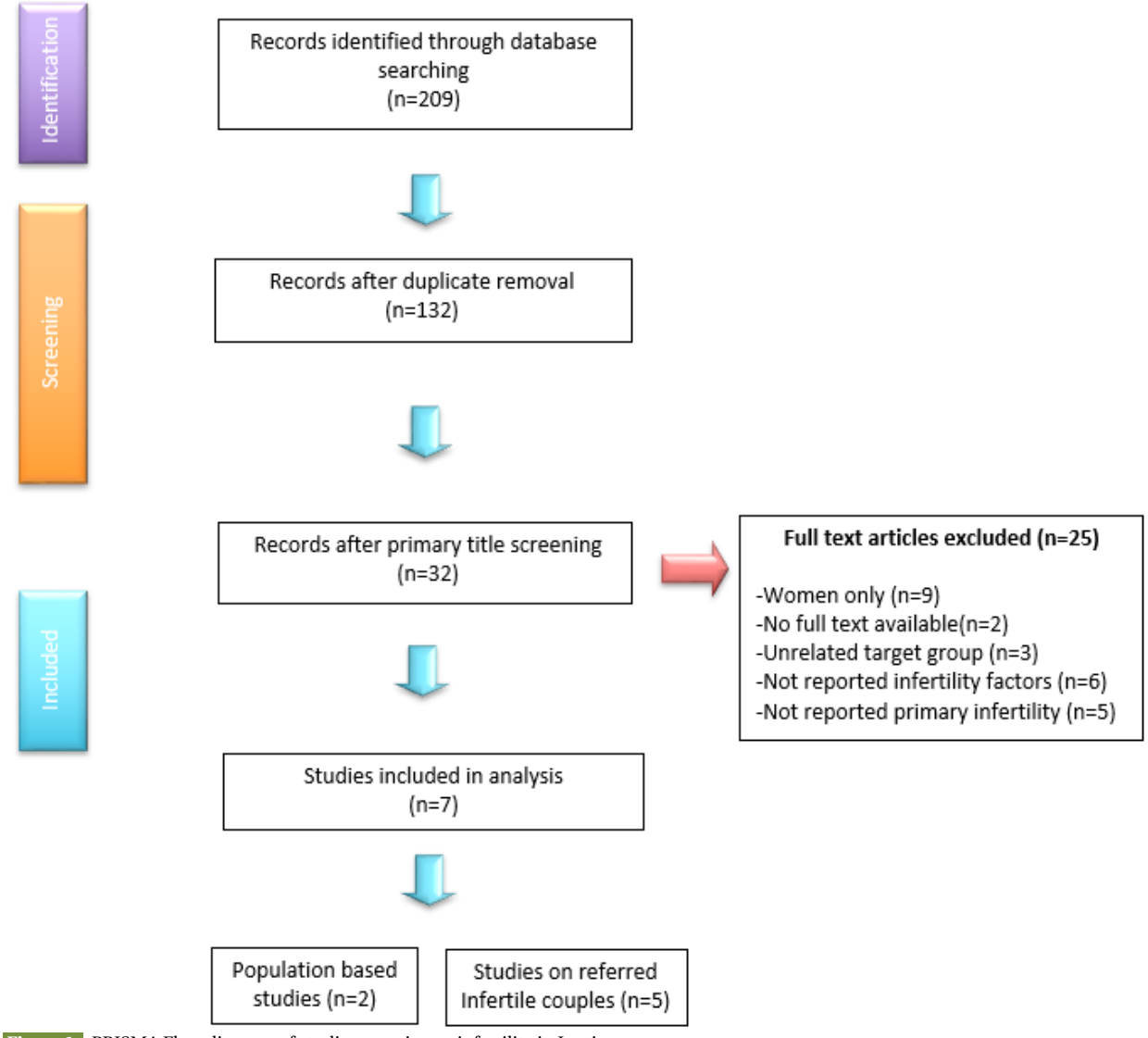

Figure 1: PRISMA Flow diagram of studies on primary infertility in Iranian men.

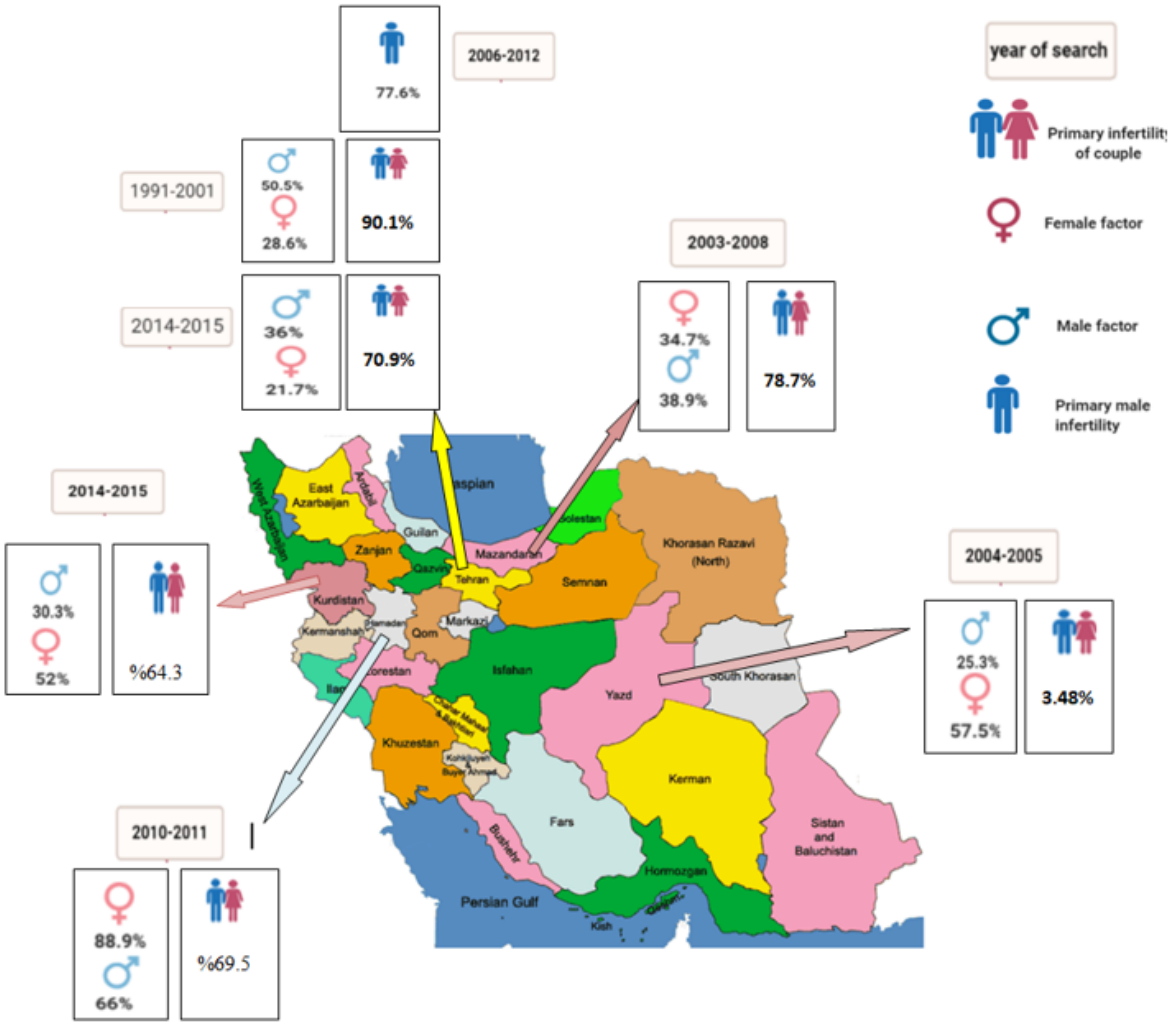

Figure 2: Iran map containing percentages of primary infertility of couples and male. This Figure demonstrates rates of primary infertility cases in each region (Tehran, Sanandaj, Mazandaran, Hamedan, Yazd.) due to male and female factor involvement.