Research Article

Epidemiologic aspects and risk factors associated with infertility in women undergoing assisted reproductive technology (ART) in north of Iran

Marzieh Zamaniyan1,2, Noushin Gordani3*, Paniz Bagheri4, Kaveh Jafari5, Sepideh Peyvandi2, Mojtaba Hajihoseini4, Robabeh Taheripanah6, Siavash Moradi7, Salomeh Peyvandi3 and Arman Alborzi2

1Diabetes Research Center, Mazandaran University of Medical Sciences, Sari, Iran
2Infertility Center, Department of Obstetrics and Gynecology, Mazandaran University of Medical Sciences, Sari, Iran
3Department of Obstetrics and Gynecology, Mazandaran University of Medical Sciences, Sari, Iran
4Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
5Mazandaran Heart Center, Mazandaran University of Medical Sciences, Sari, Iran
6Infertility and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
7Community Medicine Specialist, Gastrointestinal Cancer Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Abstract

Objective: This study aimed to investigating of the epidemiological aspects of infertility and related risk factors in infertile women.

Materials and methods: This cross-sectional study, carried out on 330 infertile women referred to two infertility treatment center of Imam Khomeini Hospital and Mother center in Sari, Iran, from April 2015 to March 2017.

Results: 54.5% of these women were in the age of 30-39 years, infertility duration in 55.2% was 1-5 years, Body mass index (BMI) in 44.5% of samples was 26-30 kg/m², 54.5% had diploma and associate degree. 63.6% lived in urban areas. 74.5 % of patients reported primary infertility. History of polycystic ovarian syndrome (PCOs) and pelvic inflammatory disease (PID) and poor ovarian reserve were the most common causes and risk factors for the infertility with prevalence 19.42%, 16.81% and 13.91%, respectively. Most underlying disease was thyroid disorders (54.5%). There was found statistically significant relationship between residents of urban areas and infertility duration, endometriosis and educational levels, miscarriage with thyroid. Data analysis performed using IBM SPSS 21 software and Chi-Square test (p < 0.05).

Conclusion: The results showed that women with infertility in north of Iran were more likely to be older, less educated, and also had overweight. They are more possible to have ovarian disorders. In these area, thyroid disease more common like Iodine deficient regions. Future research should be focused on the reasons why majority of women don’t seek treatment for the underline significant diseases that may be effects on ovarian function and fertility.

Introduction

Global estimates show that about 1.5 million couples encounter fertility problems [1,2]. Infertility is defined as being unable to pregnant after one year of trying to get without using contraceptive methods and agents. The incidence is based on the outcome (pregnancy or live birth) and the target population is from 1% to 5% [2]. The most important factors in infertility include pelvic inflammatory disease (PID), sexually transmitted diseases (STD), age, polycystic ovary syndrome (PCOs), and endometriosis [3-6]. Besides known diseases that affect women's fertility, socioeconomic factors can also affect women's fertility and cause problems [7,8]. The prevalence of mental disorders in infertile couples has
also been reported to be 33% and psychological factors along with physical (psychosomatic) factors must be considered in infertility treatment [9,10]. In most cases, infertility does not mean the absolute inability of people to be pregnant, but those who have need medical help to pregnancy [11]. Prevalence of infertility in the central areas of Mazandaran province in north of Iran is reported 4.9% and the rate of untreated infertility was only 5% [12].

Infertile women are more susceptible to physical, psychological, and social stressors because of infertility and its treatment than men. Sexual dysfunctions are also increased by Infertility. The pattern and prevalence of infertility is a good indicator of family health and planning for it, but data on reproductive health and its individual and social aspects are insufficiently available [13]. While the most important and rational approach to reducing the problem of infertility is, first, identifying the various causes of infertility and promoting reproductive health in order to prevent infertility. The epidemiological aspects and factors affecting infertility in developing countries are important. Infertility levels and patterns vary across countries and even across regions within a country [14]. Given that no studies have been conducted in the last ten years in Mazandaran province to investigate the risk factors of infertility, therefore, this study conducted to investigate the epidemiological aspects and risk factors associated with infertility in women undergoing ART in north of Iran, for early identification, prevention, and initiation of treatment.

Materials and methods

This cross-sectional study was conducted by investigating of the patients who referred to two infertility treatment center of Imam Khomeini Hospital and Mother center, Sari, in Iran, from April 2015 to March 2017. Study approved by the medical Ethical Committee of Mazandaran University of Medical Sciences with ethic code: (IR.MAZUMS.IMAMHOSPITAL.REC.1397.067). Sample size determined based on the study of Karimpour, et al. [12] that was reported, frequency of infertility in the central part of Mazandaran province was 13% and at the level of confidence = 95%, level of error (α) = 5% with the following formula, the minimum sample size was 173. But, according to the available statistics in the Infertility Centers, the number of samples increased with the discretion of statistical supervisor.

\[ n = \frac{Z^2 \cdot p(1-p)}{d^2} \]

The researchers reviewed the files of both infertility centers, extracted the required information from the files of women who had the inclusion criteria, and recorded them in the data collection questionnaire. The sampling method was accessible. Data collection questionnaire included: Demographic and social information (age, level of education, occupation, body mass index (BMI), residency, infertility characteristics (type and duration of infertility), underlying disease include: History of malignancy (lymphoma), thyroid disorder, hyperprolactinemia, hypertension, hypertriglyceridemia, diabetes, depression, anxiety.

Inclusion criteria include: women 18 years and older who were referred to infertility treatment and undergoing ART. Exclusion criteria include: women who had infertility problem only in their husbands. Data analysis performed using IBM SPSS 21 software and Chi-Square test.

Results

Demographic and infertility characteristics of all samples showed in table 1 and descriptive indicators of underlying disease in table 2. Among the participants, 67 (19.42%) had the history of (PCOs), 58 (16.81%) history of (PID), 48 (13.91%) poor ovarian reserve, 7 (2%) endometriosis, 7 (2%) uterus anatomical disorder, 11 (3.18%) history of uterine fibroma and 6 (1.73%) ovarian cyst, concurrent male infertility 46 (13.33) and 46 (13.3%) had a history of miscarriage.

Women who lived in urban areas had the highest rates of duration of infertility in 1-5 years and rural patients in

### Table 1: Demographic and infertility characteristics of infertile women.

| Variable                  | Frequency (N) (%) |
|---------------------------|-------------------|
| Age (years)               |                   |
| 18-29                     | 74 (22.4%)        |
| 30-39                     | 165 (54.5%)       |
| 40 ≥                      | 91 (27.6%)        |
| Education                 |                   |
| High school               | 81 (24.5%)        |
| Diploma & Associate Degree| 180 (54.5%)       |
| Bachelor’s degree and higher| 69 (20.9%)     |
| Occupation                |                   |
| Housewife                 | 275 (83.3%)       |
| Employee                  | 55 (16.7%)        |
| Residency                 |                   |
| Urban                     | 210 (63.6%)       |
| Rural                     | 120 (36.4%)       |
| Type of infertility       |                   |
| Primary                   | 244 (74.5%)       |
| Secondary                 | 66 (25.5%)        |
| Body mass index (BMI) kg/m²|                 |
| ≤ 18.5 (underweight)      | 16 (4.8%)         |
| 18.5-25 (Normal)          | 126 (38.2%)       |
| 26-30 (Overweight)        | 147 (44.5%)       |
| 31-35 (Obesity)           | 29 (8.8%)         |
| ≥ 36 (Severe obesity)     | 12 (3.6%)         |
| Duration of infertility (years)|           |
| 1-5                       | 182 (55.2%)       |
| 6-10                      | 112 (33.9%)       |
| 11-15                     | 25 (7.6%)         |
| 16-20                     | 8 (2.4%)          |
| 21+                       | 3 (0.9%)          |

### Table 2: Descriptive indicators of underlying disease of infertile women.

| Underlying systemic disease | Frequency (N) (%) |
|----------------------------|-------------------|
| History of malignancy (lymphoma) | 1 (1.13%)        |
| Thyroid disorder            | 48 (54.5%)        |
| Hyperprolactinemia          | 7 (7.9%)          |
| Hypertension                | 9 (10.2%)         |
| Hypertriglyceridemia        | 3 (3.4%)          |
| Diabetes                    | 12 (13.6%)        |
| Depression                  | 2 (2.2%)          |
| Anxiety                     | 7 (7.9%)          |
6-10 years. There was a statistically significant relationship between the duration of infertility and the residency in urban area, so that the higher percentage of urban patients had shorter infertility duration ($p = 0.001$). Also, there was a significant relationship between endometriosis and level of education ($p = 0.04$), women with lower level of education were more likely to had endometriosis. The relationship between miscarriage and thyroid disorder was confirmed ($p = 0.04$). 22% of women who suffer from thyroid disorder had a history of miscarriage. 16% of people lived in an urban area had miscarriage, but this rate was reduced to 9% in rural areas. Although the miscarriage rate was higher in urban than rural areas, but there was no significant relationship between miscarriage and place of residency ($p = 0.07$). ($p < 0.05$ was significant).

Discussion

This study aimed to investigate the epidemiological aspects of female infertility and the results show that most of patients (54.5%) were over 30 years and 22.4% under 30 years. Kamali, et al. [15] reported the most common age group of infertile women was 19-24 years old. This result differed from result of our study, but in another study in Nigeria by Ikechuba, et al. [16] infertile women 25 - 34 years were 67.2%. Correia, et al. [7] showed that older patients are more likely to have infertility. Kelly, et al. [9] also reported similar results. Perhaps the reason of the difference in results of various studies, is the cultural differences and time difference between studies, because in recent years, especially in Iran, the age of marriage has increased, which can be one of the important causes of increased infertility [17]. Because the increasing age of marriage in many societies today, infertility rate has increased, so dropping the fertility ability of older women can be expected [18]. Although more and more women are pursuing higher education at universities every day and may delay their first or subsequent pregnancy, informing this group of women in health planning is beneficial in reducing infertility and reducing time to pregnancy.

Our study showed that 79% of infertile patients had lower level of education, and only 21% of infertile women had a bachelor’s degree or higher. A 2014 study of Correia, et al. [7] showed that women with infertility had lower education which was like to our study. Also, there was a significant relationship between endometriosis and educational level. Patients with lower level of education had more endometriosis. Prevalence of endometriosis in infertile women has been reported as 9% – 50% [19]. Endometriosis is one of the major causes of infertility, although there are mechanisms, such as ovarian dysfunction, luteal insufficiency, but Luteinized follicles, recurrent miscarriages, and intrauterine inflammation have also been proposed [21].

The results of this study showed that 44.5% of patients were overweight and over 11% had severe obesity and obesity. Correia, et al. like the present study identified overweight and obesity as important factors in female infertility and reported a significant relationship between them [7]. Consistent with these results, Kelly, et al. [9] showed that infertility patients had higher weights than other females. Javadim, et al. [22] examined the smoking status, caffeine intake, and BMI of infertile women and found that obese patients had significantly higher rates of infertility. In our study, almost no cigarette and caffeine-related diseases were present, which could be due to cultural difference.

History of PCOs and PID were the most important causes of infertility in patients in the present study. According to results of Mohebbi, et al., most important causes of infertility was ovarian disorders, which was in line with the present study. They showed that patients with PCOs were younger than the healthy group and also had higher testosterone levels [23]. In our study, thyroid dysfunction and diabetes in infertile women were 54.5% and 13.6% respectively. Infertility was not significantly associated with underlying disease. Miscarriage was significantly associated with thyroid disorder. Considering to the endemic nature of hypothyroidism in the north of Iran and its association with miscarriage in infertile women, more serious perinatal treatment should be considered in infertile women seeking modern infertility treatment.

Conclusion

The results of this study showed that infertile women were older, with a lower level of education and overweight or obesity. Also, those had ovarian disorders, PCOs, which is one of the causes of their infertility. Future research should be focused on the reasons why majority of women don’t seek the underline significant diseases that may be effects on ovarian function and fertility.

Acknowledgement

This study was supported by Mazandaran University of Medical Science. The authors have no conflicts of interest to declare.

References

1. Boivin J, Bunling L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007; 22: 1506-1512. PubMed: https://pubmed.ncbi.nlm.nih.gov/17376819/

2. Zhou Z, Zheng D, Wu H, Li R, Xu S, et al. Epidemiology of infertility in China: a population based study. BJOG. 2018; 125: 432-441. PubMed: https://pubmed.ncbi.nlm.nih.gov/29030908/
3. Tao X, Ge SQ, Chen L, Cai LS, Hwang MF, et al. Relationships between female infertility and female genital infections and pelvic inflammatory disease: a population-based nested controlled study. Clinics. 2018; 73: e364. PubMed: https://pubmed.ncbi.nlm.nih.gov/30110069/

4. Den Heijer CD, Hoebe CJ, Driessen JH, Wolffs P, Van Den Broek IV, et al. Chlamydia trachomatis and the risk of pelvic inflammatory disease, ectopic pregnancy, and female infertility: a retrospective cohort study among primary care patients. Clin Infect Dis. 2019; 69: 1517-1525. PubMed: https://pubmed.ncbi.nlm.nih.gov/31504315/

5. Silvestris E, de Pergola G, Rosania R, Loverro G. Obesity as disruptor of the female fertility. Reprod Biol Endocrinol. 2018; 16: 22. PubMed: https://pubmed.ncbi.nlm.nih.gov/29523133/

6. Deyhoul N, Mohamaddoost T, Hosseini M. Infertility-related risk factors: a systematic review. Int J Women's Health Reprod Sci. 2017; 5: 24-29.

7. Correia S, Rodrigues T, Barros H. Socioeconomic variations in female fertility impairment: a study in a cohort of Portuguese mothers. BMJ open. 2014; 4: e003985. PubMed: https://pubmed.ncbi.nlm.nih.gov/24384900/

8. Shreffler KM, Greil AL, McQuillan J. Responding to infertility: Lessons from a growing body of research and suggested guidelines for practice. Family relations. 2017; 66: 644-658. PubMed: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5798475/

9. Kelly-Weeder S, Cox CL. The impact of lifestyle risk factors on female infertility. Women & Health. 2007; 44: 1-23.

10. Gmyrek GB, Sieradzka U, Goluda M, Gabryś M, Sozański R, et al. Flow cytometric evaluation of intracellular cytokine synthesis in peripheral mononuclear cells of women with endometriosis. Immunol Invest. 2008; 37: 43-61. PubMed: https://pubmed.ncbi.nlm.nih.gov/18214799/

11. Tanbo T, Fedorcsak P. Endometriosis associated infertility: aspects of pathophysiological mechanisms and treatment options. Acta Obstet Gynecol Scand. 2017; 96: 659-667. PubMed: https://pubmed.ncbi.nlm.nih.gov/27998009/

12. Javadi M. Study of the status of smoking, receiving caffeine and mass index of infertile and healthy 25-25 years old women. 2017; 20: 10-7.

13. Karimpour Malekshah A, Esmailenejad Moghaddam A, Moslemizadeh N, Peivandi S, Barzegarnejad A, et al. Infertility in Mazandaran province - north of Iran: an etiological study. Iran J Reprod Med. 2011; 9: 21-24. PubMed: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4212141/