

Original Research

Infertility Prevalence and Associated Factors among Women in Seoul, South Korea: A Cross-Sectional Study

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Academic Editor: Ugo Indraccolo

Submitted: 15 December 2022 Revised: 10 January 2023 Accepted: 11 January 2023 Published: 10 March 2023

Abstract

Background: Infertility is not only a health problem that affects individuals but also a social problem that affects families, societies, and populations. Recently, although infertility rates have been increasing in Korea, there are few studies on this. This study aimed to investigate the prevalence of infertility among Korean women attempting to conceive and factors associated with this. **Methods:** This cross-sectional study was conducted from May to November 2019. Participants accessed the website of the Seoul Metropolitan Government, gave their consent to the study, and then answered the questionnaire. A total of 2274 women preparing for pregnancy were recruited and their data were analyzed. **Results:** Among the 2274 women, 443 (19.48%) were infertile. Of these infertile women, 320 (72.2%) had primary infertility and 123 (27.8%) had secondary infertility. The average period of primary infertility was 1.7 ± 1.1 years, whereas the period of secondary infertility was 2.2 ± 1.5 years. The average age of non-infertile and infertile women was 31.9 ± 3.2 years and 33.2 ± 3.8 years, respectively, a statistically significant difference ($p < 0.001$). Univariate analysis revealed various risk factors for infertility (educational level, social drinking, insomnia, bulimia, artificial abortion, and spontaneous abortion) that were statistically significant. Employment, anorexia, depression, and irregular menstruation showed a marginal significance. However, in the multivariate logistic regression analysis, age ≥ 35 years, body mass index ≥ 23 , and a history of artificial abortion were significant risk factors for infertility. **Conclusions:** This study identified the prevalence of infertility in Seoul and the associated factors of women's infertility. Further research is necessary to identify clinical and male-specific variables related to infertility. These studies are expected to be of great help to prevent infertility and increase the birth rate.

Keywords: infertility; prevalence; associated factors; Korean women

1. Introduction

Infertility is a global health problem and is increasing by 0.37% per year [1]. World health organization reported that 15% of reproductive-aged couples worldwide are affected by infertility [2]. The number of female patients treated for infertility in Korea increased from 146,235 in 2017 to 162,938 in 2021 [3]. If we include patients who are infertile but undiagnosed, the number will be higher.

A cross-sectional study conducted on 765 women in China showed that the prevalence of infertility among women aged 20–40 years was 24.58%, and age, history of gynecological surgeries and decreased ovarian reserve (DOR) may be associated to infertility [4]. A study conducted in Duala, Cameroon, reported an infertility prevalence of 19.2%, and suggested that sexual transmitted diseases (STD), uterine fibroids, dysmenorrhea, and abortion history in these women increased the risk of infertility [5].

Infertility should not be thought of as solely the problem of the infertility patient. Infertility causes psychologi-

cal problems such as anxiety and depression and affects the family and community to which the patient belongs as well as wider society [6]. In addition, it is expensive to receive fertility treatment, and many withdraw for this reason [7].

There is a paucity of research into the prevalence or associated factors of infertility in the context of Korea.

Thus, we aimed to fill a gap in the literature by investigating the infertility prevalence and associated factors of married women in Seoul, Korea, and their primary concerns while preparing for pregnancy.

2. Materials and Methods

2.1 Design and Study Population

This cross-sectional study was conducted in a community of 12 regional areas in Seoul, South Korea from 1 May 2019, to 30 November 2019. Women preparing for pregnancy visited the Seoul metropolitan government's website to participate in the program and voluntarily responded to the survey. The inclusion criteria were: (1) women prepar-



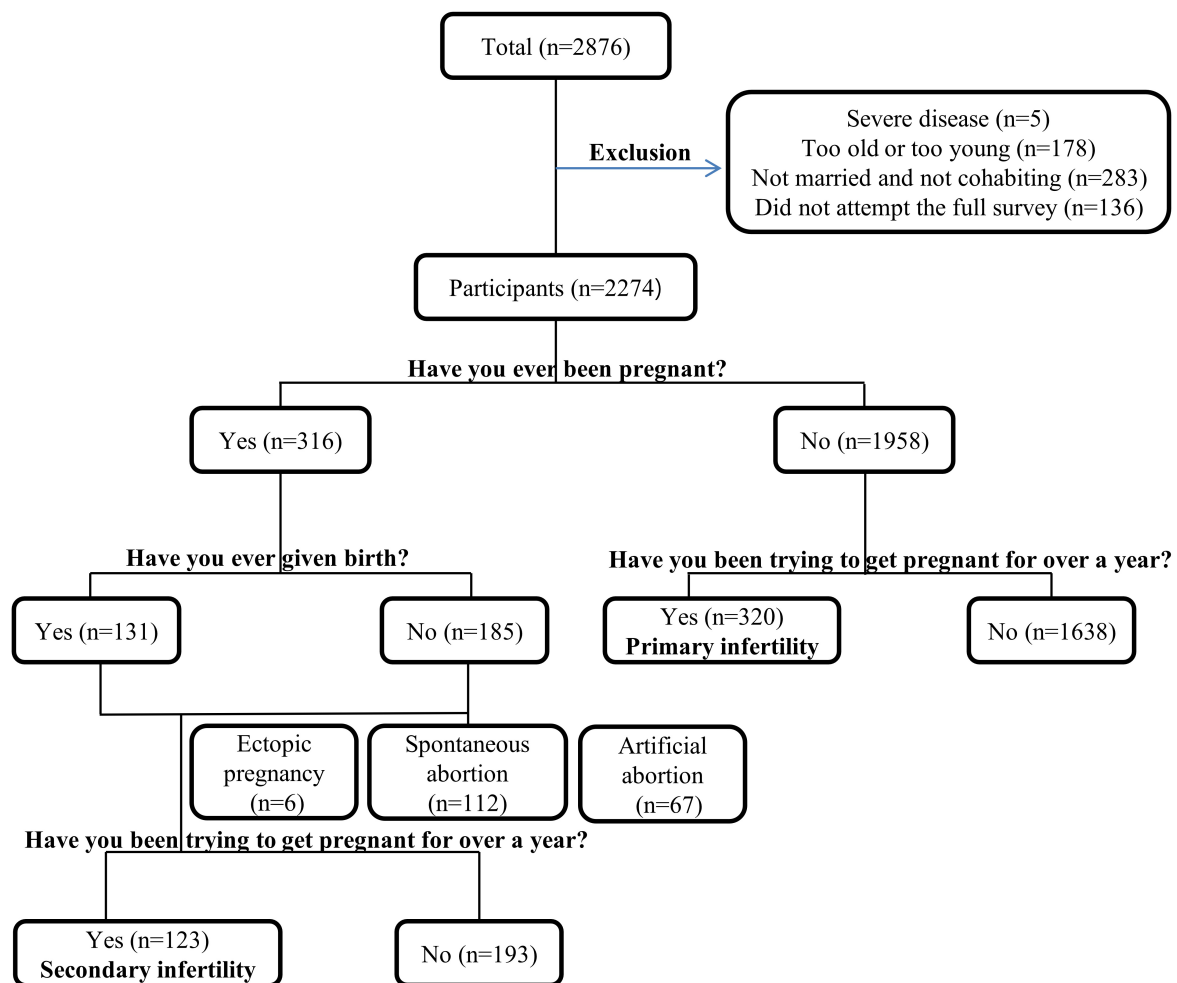


Fig. 1. Flow chart of the decision process to identify by questionnaire.

ing for pregnancy, (2) of childbearing age (20–45 years), and (3) married or cohabiting (4) who completed the questionnaire (Fig. 1). Following the survey, women who were evaluated as high-risk were treated by a specialist.

2.2 Survey and Data Collection

In this study, all data were collected using a questionnaire, which contained various elements associated with infertility risk factors. Both questions and answers were administered and collected through the website and patient consent was obtained for pre-progress data. The survey questionnaire was divided into 12 parts, with each part comprising detailed questions. The questions are as follow.

(1) Demographic characteristics: age, height, body weight, marital status (single, separated/divorced/widow, living with partner, married), occupation (managers, professionals and associated workers, clerical workers, service workers, sales workers, agro-fishery workers, functional workers and related functional workers, device machine operation and assembly workers, simple labor workers, soldiers, unemployed and students), education (high school graduation and below, above college–university), family

income (<3,000,000 won, or ≥3,000,000 won).

(2) Lifestyle and environment: drinking (Alcohol Use Disorders Identification Test–Korean (AUDIT-K)), smoking (amount per day, period), coffee (none, amount/day), sleeping (sound sleep, sleep disorder), exercise (none, times/week).

(3) Nutrition and eating habits: taking folic acid (none, yes), taking multi-vitamins (none, yes), taking iron (none, yes), regular diet (no, yes), vegetarian (no, yes), bulimia (no, diagnosed), anorexia (no, diagnosed).

(4) History of disease: panic disorder, depression, epilepsy, hypertension, diabetes, thyroid disease, rheumatism, Behçet’s disease, asthma, liver disease, kidney disease, cancer, and others.

(5) Anxiety and depression: Hospital Anxiety Depression Scale (HADS).

(6) Sexually transmitted diseases: syphilis, gonorrhea, acquired immunodeficiency syndrome (AIDS), chlamydia, genital herpes, and others.

(7) Vaccination: rubella, chickenpox, hepatitis B, human papilloma virus (HPV), COVID-19.

(8) Medication history: prescription drugs, non-

Table 1. Demographic, lifestyle, medical, psychological, and obstetric factors in fertile and infertile women.

Factors		Infertility (n = 443)	Non-infertility (n = 1831)	<i>p</i>
Demographic factors, N (%) or Mean ± SD				
Age (y)		33.2 ± 3.8	31.9 ± 3.2	<0.001
BMI (kg/m ²)		21.5 ± 3.0	20.9 ± 2.5	<0.001
Job	White	329 (74.3)	1431 (78.2)	0.079
	Blue	114 (25.7)	400 (21.8)	
Education	≤High school	39 (8.8)	95 (5.2)	0.004
	College or university	404 (91.2)	1736 (94.8)	
Family income (won)	<3,000,000	100 (22.6)	353 (19.3)	0.119
	≥3,000,000	343 (77.4)	1478 (80.7)	
Lifestyle factors				
Exercise (per week)	<1	178 (40.2)	787 (43.0)	0.284
	≥1	265 (59.8)	1044 (57.0)	
Multivitamins	Non-use	256 (57.8)	996 (54.4)	0.198
	Use	187 (42.2)	835 (45.6)	
Coffee	No	115 (26.0)	439 (24.0)	0.383
	Yes	328 (74.0)	1392 (76.0)	
Social drinking	Non-drinker	92 (20.8)	261 (14.3)	0.001
	Drinker	351 (79.2)	1570 (85.7)	
Cigarette smoking	Non-smoker	399 (90.1)	1658 (90.6)	0.756
	Smoker	44 (9.9)	173 (9.4)	
Medical factors				
Insomnia	No	316 (71.3)	1399 (76.4)	0.026
	Yes	127 (28.7)	432 (23.6)	
Bulimia	No	372 (84.0)	1611 (88.0)	0.023
	Yes	71 (16.0)	220 (12.0)	
Anorexia	No	440 (99.3)	1289 (99.9)	0.109
	Yes	3 (0.7)	2 (0.1)	
Psycho-anxiety factor				
Screen of anxiety	Negative	388 (87.6)	1643 (89.7)	0.189
	Positive	55 (12.4)	188 (10.3)	
Screen of depression	Negative	370 (83.5)	1594 (87.1)	0.052
	Positive	73 (16.5)	237 (12.9)	
Obstetric factors				
Menstruation	Regular	330 (74.5)	1431 (78.2)	0.098
	Irregular	113 (25.5)	400 (21.8)	
Dysmenorrhea	Non-severe	334 (75.4)	1432 (78.2)	0.141
	Severe	100 (24.6)	355 (21.8)	
Artificial abortion	No	409 (92.3)	1798 (98.2)	<0.001
	Yes	34 (7.7)	33 (1.8)	
Spontaneous abortion	No	410 (92.6)	1752 (95.7)	0.006
	Yes	33 (7.4)	79 (4.3)	

SD, standard deviation; BMI, body mass index.

prescription drugs, traditional medicine, and others.

(9) Family history: intellectual disability, birth of a baby with physical disabilities, autistic family members, hereditary diseases, and other.

(10) Menstruation history: menstruation regularity and dysmenorrhea.

(11) Obstetric history: contraception, gravidity, parity, live birth, preterm birth, incompetent internal os of the cervix (IIOC), small for gestational age (SGA), sudden death of a newborn baby (SIDS), and infertility.

(12) What are your main concerns regarding preg-

nancy preparation? Pick one of the following:

1. Fetal malformations and disorders
2. Marital health illness
3. Advanced age
4. Stress
5. Infertility
6. Parenting
7. Weight
8. Lifestyle habits
9. Economic problems

Table 2. Multivariate logistic regression analysis of infertility in preconception care.

	Odds ratio	Confidence interval	<i>p</i>
Age (≥ 35 years)	1.089	1.056, 1.123	<0.001
BMI (≥ 23.0 kg/m ²)	1.561	1.200, 2.031	0.001
Education (\leq High school)	0.767	0.507, 1.162	0.211
Social drinking (drinker vs. non-drinker)	0.657	0.499, 0.864	0.003
Insomnia	1.151	0.903, 1.467	0.256
Bulimia	1.242	0.914, 1.687	0.166
History of artificial abortion	4.088	2.464, 6.782	<0.001

BMI, body mass index.

2.3 Definition and Standard Diagnosis

The definition of infertility, as is commonly known, is the failure to fall pregnant after 12 months of regular and unprotected sexual intercourse [8]. Primary infertility refers to no conception ever occurring, and secondary infertility is where there has been at least one prior pregnancy.

The occupation was divided into white worker and blue worker.

Alcohol consumption was tested with Alcohol Use Disorders Identification Test–Korean (AUDIT-K) [9]. Up to a total score of 19, was classified low risk (social drinkers), and 20 points or more were classified as high risk (problem drinkers). Alcohol consumption was divided into non-drinker, social drinker, and problem drinker.

Depression and anxiety were measured using the verified Hospital Anxiety and Depression Scale (HADS) [10, 11].

In the World Health Organization (WHO) body mass index (BMI) Classifications, a BMI >25 is considered overweight, but it is divided into <23 - normal weight and ≥ 23 - overweight according to Koreans, who have relatively low obesity rates [12].

2.4 Statistical Analysis

Students' *t*-test was performed to analyze continuous variables. The chi-squared test or Fisher's exact test was used for categorical variables. Finally, multiple logistic regression analysis was performed to estimate the odds ratio of infertility, considering confounders such as age, BMI, education level, alcohol, insomnia, bulimia, and history of artificial abortion. All statistical analyses were performed using R software, version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria). *p* values were based on a two-sided significance level of 0.05.

3. Results

3.1 Prevalence of Infertility and Characteristics of the Study Participants – Infertility vs. Non-Infertility Groups

Of the 2274 respondents, 443 (19.48%) were infertile. Among infertile women, primary infertility was identified in 320 (72.2%) respondents, whereas secondary infertility was identified in 123 (27.8%) cases. The average length of primary infertility was 1.7 ± 1.1 years, whereas that of

secondary infertility was 2.2 ± 1.5 years. The average ages of the infertility and non-infertility groups were 33.2 ± 3.8 years and 31.9 ± 3.2 years, respectively, and their difference was statistically significant ($p < 0.001$). The average BMI of these two groups was 21.5 ± 3.0 kg/m² and 20.9 ± 2.5 kg/m², respectively; the BMI of the infertility group was statistically significantly higher than that of the non-infertility group ($p < 0.001$). Respondents with a lower educational level (high school or lower) exhibited higher fertility ($p < 0.001$). Further, the infertility rate was lower in the social drinking group than in the non-drinking group ($p < 0.001$), and there was no problem drinking (AUDIT-K score ≥ 20) among the participants. Additionally, the infertility rate was higher among respondents with insomnia; however, these groups did not have particularly high anxiety or depression scores ($p < 0.001$). Respondents with bulimia also had a higher infertility rate. Regarding obstetric factors, the infertility rate was higher among respondents that experienced artificial or spontaneous abortion ($p < 0.001$) (Table 1).

3.2 Risk Factors for Infertility

Statistically significant risk factors for infertility were age ≥ 35 years, BMI ≥ 23 kg/m², educational level lower than high school, social drinking, insomnia, bulimia, and artificial and spontaneous abortion. Employment, anorexia, depression, and irregular menstruation showed marginal significance. However, in the multivariate logistic regression analysis, age ≥ 35 years, BMI ≥ 23 kg/m², and a history of artificial abortion were found to be significant risk factors for infertility (Table 2, Fig. 2).

3.3 Infertility Rate According to Age

As age increased, the infertility rate increased as follows: 14.2% (under the age of 30 years), 17.4% (30–34 years), 28.8% (35–39 years), and 37.9% (>40 years) (Fig. 3).

3.4 Participants' Main Concerns as They Prepare for Pregnancy

We asked the participants what they were most worried about vis-à-vis their pregnancy and provided them with nine options (fetal malformations and disorders, health and illness, weight, advanced age, infertility, stress, par-

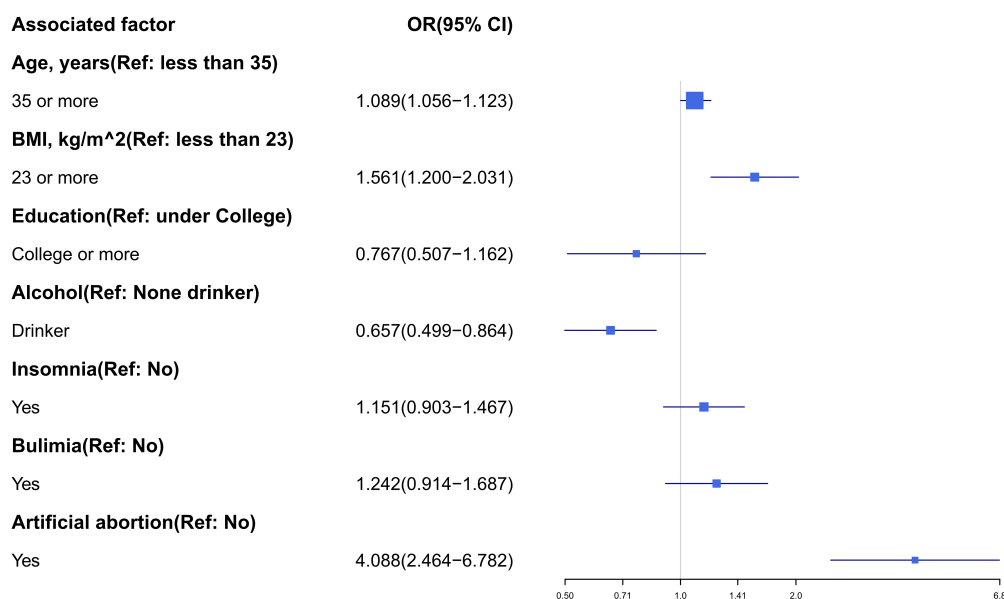


Fig. 2. Multivariate logistic regression analysis of infertility in preconception care. BMI, body mass index; OR, odds ratio; CI, confidence interval.

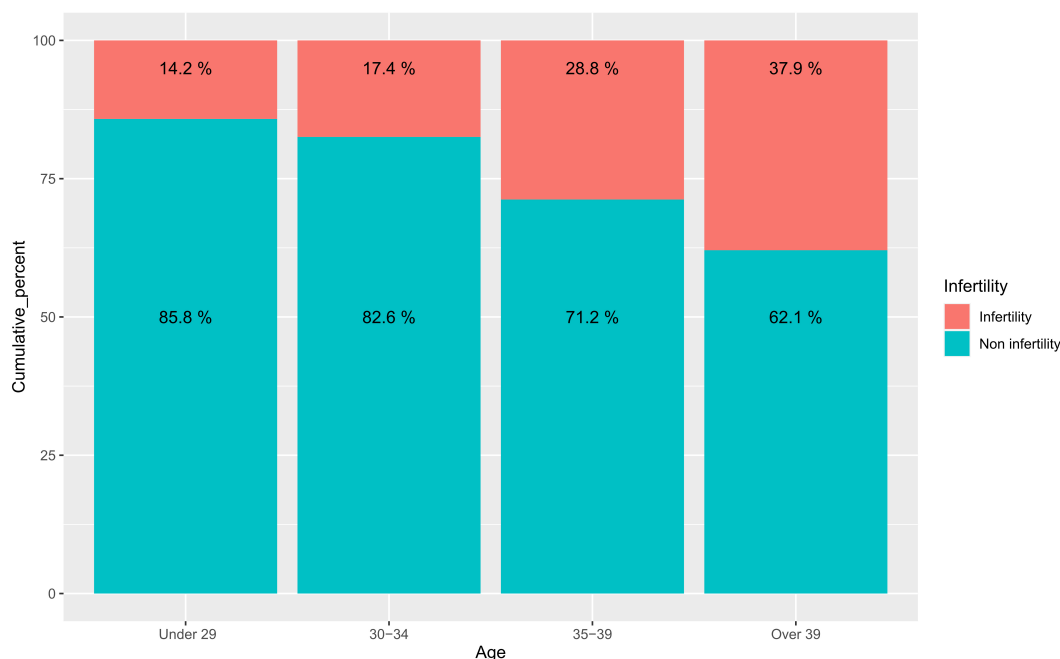


Fig. 3. Infertility ratio according to age classification.

enting, economic problems, and lifestyle habits). The biggest concerns they face while preparing for pregnancy included fetal malformations and disorders (24.89%), infertility (20.93%), marital health and illness (18.77%), advanced age (16.93%), stress (7.6%) and parenting (5.49%) in order (Fig. 4).

4. Discussion

This cross-sectional study demonstrated that the infertility prevalence in a sample of Korean women was about

19.48% and age, low education, social drinking, history of artificial or spontaneous abortion, insomnia, and bulimia are associated factors that may be related to infertility. In multivariate analysis, age, BMI, social drinking, and history of artificial abortion were found to be related to infertility. The infertility rate increased with age, with 14.2% under the age of 29, 17.4% between the ages of 30 and 34, 28.8% between the ages of 35 and 39, and 37.9% over the age of 39. It was shown that the biggest worries for women preparing for pregnancy are fetal malformation or disorders, and infertility.

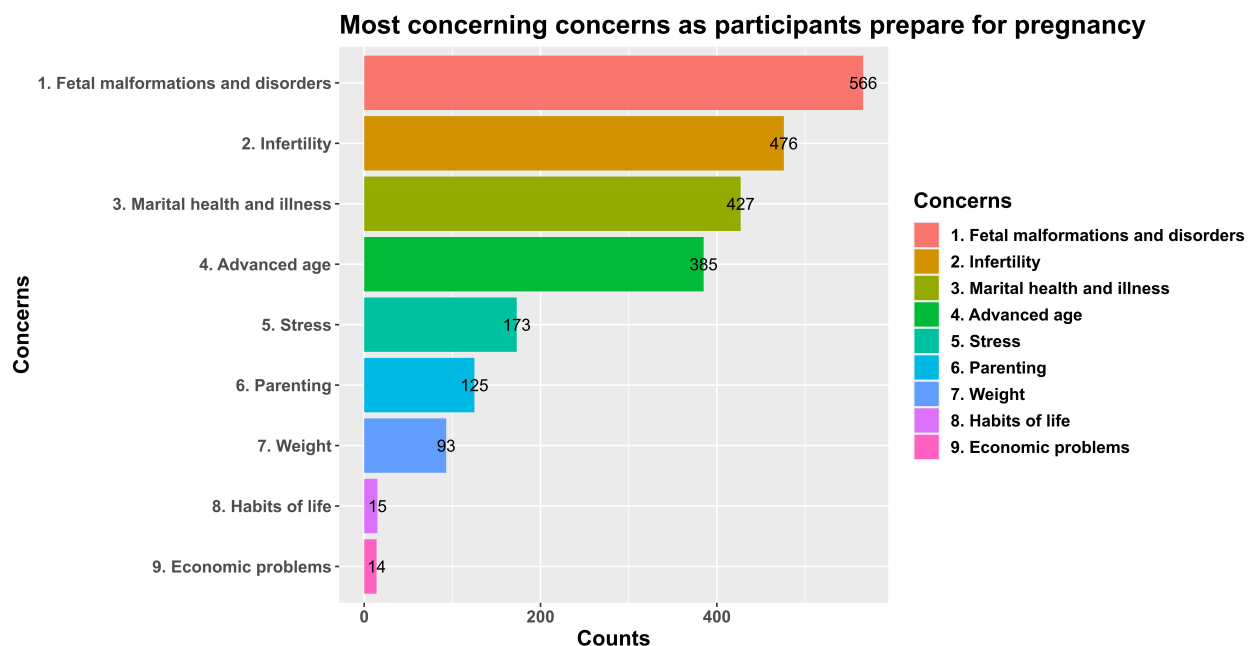


Fig. 4. Participants' main concerns as they prepare for pregnancy.

Globally, infertility prevalence is about 15%, and the rate of treatment for infertility in Korea is 20%. There are many reasons for this, but the main one is advanced age at marriage, that is, the advanced age of people preparing for pregnancy.

Although fertility declines with age in both men and women, this effect has a stronger correlation with maternal age. Prior studies have shown that fertility decreases at 32 years of age, with an increase in the rate of decline after 37 years of age [13]. The causes of age-related infertility are multifactorial. There is a demonstrated decrease in oocyte number as women progress through their reproductive years [14]. Furthermore, the rates of miscarriage and chromosomal abnormalities increase with maternal age [15]. Aging is also associated with an increase in disorders that may impair fertility, such as tubal disease, leiomyomas, and endometriosis [13]. Further, the impact of age-related behaviors (e.g., decreased sexual activity) on fertility is difficult to quantify.

The decrease in follicular number has been associated with a concurrent decrease in oocyte quality [16]. An increase in the rate of chromosomal abnormalities and miscarriage has been observed with advancing maternal age [17]. Studies suggest that most oocytes from women older than 40 years of age are chromosomally abnormal. Trisomy is the most common chromosomal abnormality observed with increasing age [18,19]. The increase in aneuploidy in older oocytes is due to meiotic non-disjunction [20]. Total prevalence per 10,000 births was 22.0 (95% confidence interval (CI) 21.7–22.4) for trisomy 21, 5.0 (95% CI 4.8–5.1) for trisomy 18 and 2.0 (95% CI 1.9–2.2) for trisomy 13; live birth prevalence was 11.2 (95% CI 10.9–11.5) for trisomy 21, 1.04 (95% CI 0.96–1.12) for trisomy 18 and 0.48 (95%

CI 0.43–0.54) for trisomy 13. There was an increase in total and total corrected prevalence of all three trisomies over time, mainly explained by increasing maternal age [21].

Multiple studies have showed that obese women take longer to conceive. Wise *et al.* [22] showed that the fecundability ratios decreased as BMI increased [23]. Obesity can affect several stages leading to pregnancy, the first being the H-P-O axis. Obese women have higher circulating levels of insulin, a stimulus for ovarian androgen production [24]. These androgens are aromatized to estrogen, leading to negative feedback on the hypothalamic-pituitary-ovarian (H-P-O) axis and gonadotrophic production [25]. This induces menstrual abnormalities and ovulatory dysfunctions. Second, obesity can affect oocytes. Obese women need increasing dosages of drugs and require more time to grow follicles during *in vitro* procedures [26,27]. The number of eggs collected is low and the cancellation rate is high [28]. Obese women undergoing *in vitro* fertilization (IVF) have an altered follicular environment, with higher levels of insulin, triglycerides, and markers of inflammation, such as lactated and C-reactive protein (CRP), in follicular fluid [29]. Statistically significant BMI reduction was observed when myo-inositol, which is related to insulin control, or glycemic control agent was administered to patients with polycystic ovary syndrome who were overweight or obese [30]. In addition, obesity can affect the embryo. Metwally *et al.* [31] noted that obesity may adversely affect embryo quality in young women (<35 years) undergoing *in vitro* fertilization/Intracytoplasmic Sperm Injection (IVF/ICSI), in while the oocyte quality is not affected. Leary *et al.* [32] demonstrated that embryos of women with BMI ≥ 25 kg/m² were less likely to develop after fertilization, and those that did, reached the morula stage more quickly. *In vitro*, leptin

has a stimulating effect on human trophoblastic stem cell growth, and its inhibition decreases proliferation and dramatically increases apoptosis [33]. Tonically elevated levels of leptin in obesity may decrease the sensitivity of the trophoblast to its effects.

Obesity can also affect the endometrium. After reviewing 450 donor-oocyte frozen embryo transfer cycles, Dessolle *et al.* [34] stated that BMI was an independent predictor of clinical pregnancy. Inflammatory pathways are critically important reproductive events such as follicle rupture at the time of ovulation and invasion of the trophoblast into the receptive endometrium.

This study found that infertility was higher in the low-educated group, which has also been reported in previous studies. Infertility treatments are significantly associated with a higher socioeconomic position. Thus, women and men with lower levels of education and occupational classifications were less likely to seek help. Individuals seeking treatment for infertility are more likely to be better educated and in higher-status occupations, and they typically have children later in life [35]. In Korea, when the infertility group was divided into upper-, middle-, and low-income levels, the birth rate increased in tandem with income [36].

In a study conducted in Finland, from 2006 to 2010, 1.9% of all singleton pregnancies were achieved via IVF; however, the proportion varied substantially among socioeconomic groups, ranging from 1.2% (annual range: 0.9–1.5%) among blue-collar workers to 3.2% (annual range 2.8–4.2%) among white-collar workers. Moreover, 85% of all women giving birth following IVF belonged to the two highest socioeconomic groups [37].

Furthermore, socioeconomic status exhibited a significant positive correlation with antral follicle count and anti-Müllerian hormone levels ($r = +0.524$ and $p = 0.000$ and $r = +0.659$ and $p = 0.000$, respectively), as well as a significant negative correlation with follicle-stimulating hormone levels ($r = -0.498$ and $p = 0.000$) [38].

Regarding anxiety and stress levels, women in the low social class presented higher scores on the State Anxiety Scale, compared with those in the medium and higher social classes. The results also revealed that women's social class influenced their perceived personal stress and trait anxiety levels [39].

Several authors have insisted that abortion is associated with infertility. Reasonable grounds for a link between abortion and infertility include cervical damage, infections, pelvic inflammatory disease, incomplete abortion, intrauterine adhesion, endometrial thinning, and psychological factors. The above six factors have been explored as possible links between abortion and infertility—some with good supporting evidence and some with less; however, taken together, these factors point to an as yet unclear but significant level of risk [40].

Previous studies reported that prior surgical uterine evacuation may increase the relative risk of infertility [41].

Verhoeve *et al.* [42] demonstrated that women with secondary infertility and a history of artificial abortion had a significantly increased risk of tubal pathology.

Among women planning a pregnancy, waiting times to conception exceeding 12 months have been associated with spontaneous abortion [43]. Additionally, women with a previous miscarriage had a 13% decrease, and women with at least 2 previous miscarriages, a 35% decrease, in fecundability compared with women who had only a live birth [44]. Delays in achieving conception and increased rates of pregnancy loss share common risk factors such as advancing age, maternal obesity, cigarette smoking, alcohol, medical disorder and gynecological disorder [45]. Gray *et al.* [43] found a 1.7-fold adjusted risk of spontaneous abortion among women with a history of a delay of one or more years prior to pregnancy. Among women with a history of subfertility, the rate of early pregnancy loss was 68%, whereas among women with no delay in conception, the rate was 22% [43]. Arge *et al.* [46] in a recent Norwegian cohort study, reported that fecundability decreased as the number of prior miscarriages increased.

However, the relationship between sleep and fertility remains largely unknown. Kloss *et al.* [47] insisted that stress, sleep dysregulation, and circadian misalignment are potentially relevant to infertility. There are at least three possible pathways by which sleep disturbance may be related to infertility: hypothalamic-pituitary-adrenal (HPA) axis activation, which precipitates sleep disturbance; altered sleep duration and/or sleep continuity disturbance may interfere with reproduction or result in further increased HPA activation; and circadian dysrhythmia (independent of HPA axis activation, sleep duration and/or sleep continuity disturbance) may result in infertility [47].

Fetal malformation and disorder appear to be the most common concerns of women preparing for pregnancy. In Korea, nuchal translucency is measured and brain malformations such as anencephaly are screened by ultrasound at around 12 weeks of gestation. In addition, the other fetal anomalies can be detected through high-resolution ultrasound at 20 to 24 weeks of gestation. The next most common concerns are infertility, maternal health, and advanced age in that order. This is probably because of higher age at marriage and first childbirth.

To our knowledge, ours is the first community-based study to analyze infertility risk factors in Seoul, Korea. Data from 2274 people were analyzed. In this study, age, low educational level, social drinking, insomnia, bulimia, artificial abortion, and spontaneous abortion were found to be associated factors for infertility. However, the limitations of this study include the following: occupational group and educational background were not examined in greater detail, the causes of infertility were not examined comprehensively, and the risk factors for male infertility were not analyzed.

5. Conclusions

The results of this analytical survey conducted as part of a project of community-based preconception care for men and women of childbearing age in Seoul, identify several significant variables related to female infertility. These results could provide valuable insights for policymaking aiming to prevent infertility and increase birth rates. Further studies could comprehensively investigate physiological and biochemical tests related to infertility, as well as variables related to male infertility.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

HJL—Acquired patient data, and drafted the manuscript, created figures and tables; JYH—Conception, design, statistical analysis, provided guidance, responsible for the accuracy and integrity of the work presented here; HZC—Statistical analysis, created figures and tables; BJN—Interpretation of data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final version of manuscript.

Ethics Approval and Consent to Participate

This study was conducted with ethical approval from the Institutional Review Board (IRB) of Ilsan Paik Hospital, Inje University College of Medicine (2020-07-042-002). All participants provided their written informed consent after receiving a complete explanation of the study protocol.

Acknowledgment

We would like to express our gratitude to all those who helped us during the writing of this manuscript.

Funding

As a part of the survey conducted by the Seoul Metropolitan Government, all expenses for the survey were borne by the Seoul Metropolitan Government. Except for the survey process, there was no external funding for any process of writing and submitting the thesis.

Conflict of Interest

The authors declare no conflict of interest.

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