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Major Disease Prevalence and Menstrual Characteristics in Infertile Female Korean Smokers

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We investigated the prevalence of smoking and factors associated with smoking in infertile Korean women. Smoking status, education, occupation, personal habits, past medical history, current illness, stress level, and menstrual characteristics were collected from self-report questionnaires. The Beck Depression Inventory (BDI) was used to assess the degree of depression. Data on the causes of infertility and levels of six reproductive hormones were collected from medical records. Among 785 women less than 42 years of age, the prevalence of current, secondhand, past, and never smokers were 12.7%, 45.7%, 0.9%, and 40.6%, respectively. Primary infertility was more frequent in secondhand smokers. Causes of infertility were similar among current, secondhand, and never smokers. Current smokers were less educated ($P < 0.001$) and more likely to consume alcohol than secondhand or never smokers ($P < 0.001$). Secondhand smokers slept less than current smokers ($P = 0.041$). Among several major diseases, only the prevalence of diabetes mellitus (4.0%) was significantly higher in current smokers than in secondhand smokers (0.0%, $P = 0.002$) or never smokers (0.6%, $P = 0.031$). The self-reported prevalence of depression, and the degree of depression were similar among women with different smoking statuses. There were no differences in menstrual characteristics or serum levels of six reproductive hormones between current, secondhand, and never smokers, even after excluding women with polycystic ovary syndrome. In conclusion, education/employment status, alcohol drinking, and the prevalence of primary infertility and diabetes mellitus were significantly different according to smoking status among infertile women.

Keywords: Infertility; Smoking; Depression; Menstruation; Education; Alcohol Drinking; Diabetes

INTRODUCTION

Smoking is known to negatively affect female reproductive function. It has been associated with diminished ovarian reserve, increased risk of infertility, and decreased rate of fertilization and pregnancy following in-vitro fertilization (IVF) treatment (1-5). In women undergoing IVF, the number of retrieved oocytes and live births were lower in smokers compared to never-smokers (4). However, in some studies, smoking was not associated with differences in the number of retrieved oocytes, fertilization rate, or miscarriage rate in IVF cycles (6-8). In a study of 127 Korean women undergoing intrauterine insemination (IUI) or IVF, pregnancy outcome was not affected by urinary cotinine positivity (9).

In a nationwide survey conducted by the Korean government, the incidence of smoking in 2012 was 43.6% in men and 7.9% in women aged 19 years or higher (10). In one study, the prevalence of positive urinary cotinine among infertile Korean women was 10.2%, which is higher than the rate reported in the nationwide survey (9). However, the prevalence of secondhand smoking was not reported among the infertile Korean women. Secondhand smoking has been associated with greater difficulty becoming pregnant and delayed conception in several studies (11-13). Moreover, epidemiologic studies investigating smoking-associated personal factors in infertile Korean women are not currently available.

Here, we report the results of a large-scale questionnaire-based survey performed in 6 infertility centers in Korea. By using a self-reported questionnaire along with hospital records, we assessed the prevalence of current, secondhand, past, and never smokers, and we investigated possible associations between smoking and personal habits, major diseases (including depression), menstrual characteristics, and reproductive hormone levels in infertile Korean women.

MATERIALS AND METHODS

Study subjects

This study was a part of a multicenter survey comprised of 1,000 infertile women. Six major fertility clinics in Korea participated

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in this study (Seoul National University Hospital, Seoul National University Bundang Hospital, Maria Infertility Clinic, Hamchoon Women's Clinic, CHA Medical Center, and Ajou University Hospital).

Women who visited the infertility clinics between April and December 2014 were asked to participate in the study. Among the 1,000 women who chose to participate during this time period, 129 women with unknown smoking status and 86 women over the age of 42 years were excluded. Women over the age of 42 years were excluded because they have higher incidence rates of major diseases, menstrual irregularity, and reproductive hormone levels. Thus, a total of 785 women were included in the analyses. Seven past smokers were excluded from the analysis of variable parameters according to smoking status because this group had a small number of subjects. Women who were past smokers as well secondhand smokers were assigned to the secondhand smokers group.

Questionnaires

All participating women anonymously completed a structured, self-report questionnaire. The questionnaire included age, weight, height, final level of education (high school, college or higher), job status (with or without job), alcohol consumption (yes or no), sleep hours per day, exercise habits (days per week of mild, moderate, vigorous, and weight-training exercise), obstetric history, past medical and surgical history, current illness, age at menarche, irregular menstrual period (yes or no), duration of menstrual flow (days), and dysmenorrhea (yes or no).

Stress level was assessed by the 10-point Likert scale question, from 1 (no stress) to 10 (unbearable stress). A feeling of despair lasting 2 or more weeks during the previous year was also recorded (yes or no).

Cause of infertility and serum reproductive hormone levels (luteinizing hormone [LH], follicle stimulating hormone [FSH], estradiol, basal or random thyroid stimulating hormone [TSH], prolactin, and anti-Müllerian hormone [AMH]) were collected from medical records. Basal levels were recorded for LH, FSH, and estradiol, and basal or random levels were recorded for TSH and AMH. The age-related decrease in AMH levels were taken into account, and we compared them as its absolute value as well as age-specific multiples of the median (MoM) value calculated using the Korean reference value for each corresponding age. In the analysis of serum levels of TSH, women diagnosed with thyroid disease were excluded.

Beck Depression Inventory (BDI)

We used a modified and validated Korean version of the BDI (14). This is a widely-used questionnaire, which contains 21 items. Each item describes a specific thought or behavior associated with depression and scores for each item range from 0 to 3. Scores from each item were summed and 4 degrees of depression were assigned; these included no depression (sum 0–9), mild depression (sum 10–15), moderate depression (sum 16–23), and severe depression (sum 24–63). Subjects with self-reported depression were excluded from the BDI analysis.

Statistical analysis

Analysis of variance (ANOVA) with Bonferroni post-hoc tests were used to compare numerical variables between current, secondhand, and never smokers. χ^2 or a Fisher's exact tests were used to compare proportions between groups. Statistical analysis was conducted using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). A P value below 0.05 was considered statistically significant. When missing data exceeded 25% of all subjects for a variable, the variable was not analyzed.

Ethics statement

The Institutional Review Board at each of the six hospitals (Seoul National University Hospital, Seoul National University Bundang Hospital, Maria Infertility Clinic, Hamchoon Women's Clinic, CHA Medical Center, and Ajou University Hospital) approved the study (IRB No. 1408-018-601, Seoul National University Hospital). Informed consent was obtained from all women prior to participation of the study.

RESULTS

Smoking status

Among 785 women, current, secondhand, past, and never smokers represented 12.7% (n = 100), 45.7% (n = 359), 0.9% (n = 7), and 40.6% (n = 319) of the study population, respectively. The prevalence of secondhand smoking among women that were not current smokers was 52.4%.

Participant characteristics

Age, age at marriage, body mass index (BMI), number of spontaneous or artificial abortion, and current number of children were similar between current, secondhand, and never smokers (Table 1). The proportion of primary infertility was significantly higher in the secondhand smokers (90.0%) than in current smokers (82.0%, $P = 0.035$) or never smokers (81.5%, $P = 0.002$). The cause of infertility did not differ based on smoking status (Table 1). Female factor infertility details are also shown in Table 1.

Participant habits

The proportion of women with college or higher education was significantly lower in current smokers (72.0%) than in secondhand (83.2%, $P < 0.001$) or never smokers (92.5%, $P = 0.012$) (Table 2). The proportion of employed women was highest in secondhand smokers (65.1%), and this was significantly higher than in never smokers (46.8%, $P < 0.001$).

Alcohol consumption was more prevalent in current smok-

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Table 1. Obstetric history and diagnosis of infertility

Parameters	Current smokers (n = 100)	Secondhand smokers (n = 359)	Never smokers (n = 319)	*P* value
Age, yr	34.5 ± 3.6	34.5 ± 3.6	34.5 ± 3.3	0.994
Age at marriage, yr	29.8 ± 4.3	30.4 ± 4.0	30.3 ± 3.7	0.336
BMI, kg/m^2	22.4 ± 3.4	21.7 ± 3.2	21.7 ± 3.3	0.104
No. of spontaneous abortion	0.7 ± 0.8	1.1 ± 1.0	1.0 ± 1.0	0.118
No. of artificial abortion	0.8 ± 0.9	0.4 ± 0.6	0.5 ± 0.7	0.082
Women with at least one abortion	38 (38.4)	109 (30.4)	107 (33.9)	0.282
No. of live births	0.5 ± 0.4	0.1 ± 0.1	0.1 ± 0.1	0.533
Primary infertility	82 (82.0)[a]	323 (90.0)[b]	260 (81.5)[c]	0.004
Secondary infertility	18 (18.0)	36 (10.0)	59 (18.5)	a–b: *P* = 0.035; b–c: *P* = 0.002
Cause of infertility				0.138
Male factor	16 (16.0)	70 (19.5)	76 (23.8)	
Female factor	32 (32.0)	106 (29.5)	72 (22.6)	
Combined	23 (23.0)	76 (21.2)	59 (18.5)	
Unexplained	29 (29.0)	107 (29.8)	112 (35.1)	
Female factor infertility				0.616
Tubal factor	24 (43.6)	85 (46.7)	52 (39.7)	
PCOS	15 (27.3)	56 (30.8)	37 (28.2)	
Other ovulatory factor	4 (7.3)	11 (6.0)	14 (10.7)	
Uterine factor	12 (21.8)	30 (16.5)	28 (21.4)	

Values are presented as number (%) or mean ± standard deviation.
BMI = body mass index, PCOS = polycystic ovary syndrome.

Table 2. Educational level and job status

Education and job	Current smokers (n = 100)	Secondhand smokers (n = 359)	Never smokers (n = 319)	*P* value
High school	28 (28.0)	60 (16.8)	24 (7.5)	< 0.001
College or higher	72 (72.0)[a]	298 (83.2)[b]	295 (92.5)[c]	a–b: *P* < 0.001; a–c: *P* = 0.012; b–c: *P* < 0.001
With job	56 (56.6)	229 (65.1)[d]	148 (46.8)[e]	< 0.001
Without job	43 (43.4)	123 (34.9)	168 (53.2)	d–e: *P* < 0.001

Values are presented as number (%).

Table 3. Behavioral parameters

Behaviors	Current smokers (n = 100)	Secondhand smokers (n = 359)	Never smokers (n = 319)	*P* value
Alcohol drinking	86 (86.0)[a]	252 (70.8)[b]	207 (65.5)[c]	< 0.001 a–b: *P* = 0.002; a–c: *P* < 0.001
Sleep hours per day	7.7 ± 1.0[d]	7.4 ± 1.2[e]	7.5 ± 1.1	0.041 d–e: *P* = 0.048
Exercise per week				
Mild	5.6 ± 3.2	5.6 ± 3.6	5.5 ± 3.1	0.981
Moderate	1.0 ± 1.5	1.2 ± 1.5	1.0 ± 1.4	0.110
Vigorous	1.0 ± 1.5	1.1 ± 1.5	0.9 ± 1.4	0.592
Weight-training	0.6 ± 1.4[f]	0.5 ± 1.1[g]	0.3 ± 0.8[h]	0.017 f–g: *P* = 0.038; f–h: *P* = 0.006

Values are presented as number (%) or mean ± standard deviation.

ers (86.0%), and this was significantly higher than in secondhand smokers (70.8%, *P* = 0.002) or never smokers (65.5%, *P* < 0.001) (Table 3). Sleep duration was highest in current smokers, and this was significantly higher than that in secondhand smokers (7.7 vs. 7.4 hours, respectively, *P* = 0.041). The frequencies of mild, moderate, and vigorous exercise per week were similar between groups. However, the frequency of weight-training exercise was significantly higher in the current smokers (0.6 ± 1.4) than in secondhand smokers (0.5 ± 1.1, *P* = 0.038) or never smokers (0.3 ± 0.8, *P* = 0.006).

Table 4. Self-reported past medical history and current illness

Medical parameters	Current smokers (n = 100)	Secondhand smokers (n = 359)	Never smokers (n = 319)	*P* value
Past medical history				
Pelvic inflammatory disease	7 (7.0)	20 (5.6)	8 (2.5)	0.069
Venereal disease	2 (2.0)	3 (0.8)	1 (0.3)	0.191
Gynecologic surgery	21 (21.0)	62 (17.3)	52 (16.3)	0.556
Current illness				
Thyroid disease	5 (5.0)	14 (3.9)	14 (4.4)	0.877
Diabetes mellitus	4 (4.0)[a]	0 (0)[b]	2 (0.6)[c]	0.001 a–b: *P* = 0.002; a–c: *P* = 0.031
Hypertension	1 (1.0)	10 (2.8)	6 (1.9)	0.496
Dyslipidemia	1 (1.0)	7 (1.9)	4 (1.3)	0.780
Asthma	6 (6.0)	16 (4.5)	21 (6.6)	0.470
Tuberculosis	0 (0)	0 (0)	0 (0)	Cannot evaluate
Depression	2 (2.0)	14 (3.9)	5 (1.6)	0.156

Values are presented as number (%).

Medical history and current illness

Self-reported history of pelvic inflammatory disease, venereal disease, or gynecologic surgery was similar between groups (Table 4). The prevalence of thyroid disease, hypertension, dyslipidemia, asthma, tuberculosis, or depression was also similar between groups; however, the prevalence of diabetes mellitus was

Table 5. Stress and degree of depression

Mental status	Current smokers (n = 100)	Secondhand smokers (n = 359)	Never smokers (n = 319)	*P* value
Stress (0–10)	5.6 ± 1.6	5.9 ± 1.5[a]	5.6 ± 1.5[b]	0.019 a–b: *P* = 0.017
Self-reported despair	18 (18.0)	59 (16.4)	44 (13.8)	0.502
Self-reported treatment for despair	0/18 (0)[c]	9/57 (15.8)	11/42 (26.2)[d]	0.044 c–d: *P* = 0.024
BDI score (0–63)*	8.6 ± 6.5	7.9 ± 6.1	7.2 ± 5.9	0.107
Degree of depression*				0.118
No (0–9)	54 (61.4)	205 (65.7)	204 (70.3)	
Mild (10–15)	22 (25.0)	77 (24.7)	54 (18.6)	
Moderate (16–23)	8 (9.1)	21 (6.7)	29 (10.0)	
Severe (24–63)	4 (4.5)	9 (2.9)	3 (1.0)	
Mild-to-severe (10–63)	34 (38.6)	107 (34.3)	86 (29.7)	0.227
Moderate-to-severe (16–63)	12 (13.6)	30 (9.6)	32 (11.0)	0.616

Values are presented as number (%) or mean ± standard deviation.
BDI = Beck Depression Inventory.
*Women with self-reported depression and women who did not complete the BDI were excluded.

Table 6. Menstrual characteristics

Menstrual parameters	Current smokers	Secondhand smokers	Never smokers	*P* value
Overall, No.	100	359	319	
Age at menarche, yr	13.7 ± 1.5	13.5 ± 1.5	13.4 ± 1.9	0.165
Duration of menstrual flow, day	5.0 ± 1.3	5.3 ± 1.6	5.3 ± 1.5	0.294
Presence of irregular period	20 (20.0)	48 (13.4)	38 (11.9)	0.082
Presence of dysmenorrhea	59 (59.0)	213 (59.3)	197 (61.8)	0.297
After excluding women with PCOS, No.	83	299	274	
Age at menarche, yr	13.7 ± 1.6	13.5 ± 1.6	13.4 ± 1.9	0.267
Duration of menstrual flow, day	5.0 ± 1.3	5.2 ± 1.6	5.3 ± 1.5	0.281
Presence of irregular period	9 (10.8)	24 (8.0)	23 (8.4)	0.628
Presence of dysmenorrhea	52 (62.7)	180 (60.2)	174 (63.5)	0.340

Values are presented as number (%) or mean ± standard deviation.
PCOS = polycystic ovary syndrome.

Table 7. Serum levels of reproductive hormones

Hormones	Current smokers (n = 100)	Secondhand smokers (n = 359)	Never smokers (n = 319)	*P* value
AMH, ng/mL	4.8 ± 5.1	4.6 ± 4.3	4.8 ± 4.7	0.810
AMH (MoM)	1.3 ± 1.2	1.3 ± 1.0	1.4 ± 1.3	0.586
LH, IU/L	5.5 ± 4.9	5.5 ± 3.3	5.7 ± 3.4	0.866
FSH, IU/L	8.7 ± 8.5	7.8 ± 3.7	8.1 ± 8.4	0.608
Estradiol, pg/mL	46.0 ± 22.0	47.0 ± 41.0	48.0 ± 53.0	0.935
TSH, μIU/mL*	1.9 ± 1.0	2.2 ± 1.8	2.0 ± 1.1	0.110
Prolactin, ng/mL	13.5 ± 15.2	16.5 ± 24.1	14.0 ± 13.3	0.207
No. of women with				
TSH > 2.5 μIU/mL*	20 (24.4)	87 (30.0)	61 (23.5)	0.204
TSH > 4.0 μIU/mL*	2 (2.4)	22 (7.6)	11 (4.2)	0.091
Prolactin ≥ 20 ng/mL	9 (10.3)	51 (16.8)	29 (10.6)	0.061

Values are presented as number (%) or mean ± standard deviation.
AMH = anti-Müllerian hormone, MoM = multiples of the median, LH = luteinizing hormone, FSH = follicle stimulating hormone, TSH = thyroid stimulating hormone.
*Women with known thyroid disease were excluded.

significantly higher in current smokers (4.0%) than in secondhand smokers (0.0%, *P* = 0.002) or never smokers (0.6%, *P* = 0.031).

Stress and BDI

Daily stress level was highest in the secondhand smokers and was significantly higher than that in never smokers (5.9 vs. 5.6, respectively, *P* = 0.017) (Table 5). The percentage of women who reported despair in the past year was similar between groups, but none of the current smokers received treatment for despair. After excluding women with self-reported depression and women who did not complete the BDI, there were no differences between groups for the mean BDI score or the prevalence of mild,

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Table 8. Serum levels of reproductive hormones after excluding women with polycystic ovary syndrome

Hormones	Current smokers (n = 83)	Secondhand smokers (n = 299)	Never smokers (n = 274)	*P* value
AMH, ng/mL	2.9 ± 2.2	3.4 ± 2.7	3.6 ± 2.9	0.179
AMH (MoM)	0.9 ± 0.7	1.1 ± 0.8	1.0 ± 0.8	0.483
LH, IU/L	5.2 ± 4.9	4.9 ± 2.2	5.4 ± 2.9	0.231
FSH, IU/L	9.3 ± 9.1	8.1 ± 4.0	8.4 ± 9.1	0.593
Estradiol, pg/mL	44.0 ± 22.0	47.0 ± 41.0	49.0 ± 57.0	0.915
TSH, μIU/mL*	1.8 ± 1.0	2.2 ± 1.5	2.0 ± 1.2	0.123
Prolactin, ng/mL	13.9 ± 16.6	17.5 ± 26.5	14.4 ± 14.3	0.205
No. of women with				
TSH > 2.5 μIU/mL*	15 (18.0)	74 (24.7)	50 (18.2)	0.078
TSH > 4.0 μIU/mL*	1 (1.2)	17 (5.7)	10 (3.6)	0.146
Prolactin ≥ 20 ng/mL	8 (9.6)	45 (15.1)	27 (9.9)	0.086

Values are presented as number (%) or mean ± standard deviation.
AMH = anti-Müllerian hormone, MoM = multiples of the median, LH = luteinizing hormone, FSH = follicle stimulating hormone, TSH = thyroid stimulating hormone.
*Women with known thyroid disease were excluded.

moderate, and severe depression.

Gynecologic characteristics

The age at menarche, duration of menstrual flow, and percentage of women reporting an irregular period or dysmenorrhea were all comparable between groups (Table 6). Similarly, comparable menstrual characteristics were also observed after excluding women with known polycystic ovary syndrome (n = 122). Reproductive hormone serum levels did not differ between groups (Table 7), and similar serum hormone levels were observed after excluding women with known polycystic ovary syndrome (Table 8).

DISCUSSION

Here we firstly reported the prevalence of current, secondhand, and never smokers in infertile Korean women. The observed prevalence of current and active smoking (12.7%) was slightly higher than the 7.9% among women aged ≥ 19 from a nationwide survey reported by the Korean government and the 10.2% observed among infertile Korean women based on urinary cotinine measurement (9,10).

In the previous researches, the prevalence of secondhand smoking has been reported in two manners. In some studies, the prevalence of secondhand smoking was reported as the proportion of secondhand smokers among all women. The National Health and Nutrition Examination Survey (NHANES) III (1988–1991) estimated 33% of all women in the United States were secondhand smokers based on self-reports (15). When calculated likewise, the prevalence of secondhand smoking in our study was 45.7%. Considering the lower prevalence of current female smokers in Korea compared to the United States (7.9% vs. 18.8%, respectively), this is considerably high (10,16). Secondhand smoking has also been reported as the proportion of secondhand smokers among those who are not current smokers. The second and third US National Reports on Human Exposure to Environmental Chemicals (part of NHANES; NHANES 1999–2000, 2001–2002, respectively) reported measurable urinary cotinine in approximately 50% of women who were not current smokers (17). In a study based on the 2008 Korea National Survey for Environmental Pollutants in the Human Body, the prevalence of self-reported secondhand smoking among women who were not current smokers was 39.2% (18). Calculated based on this method, the prevalence of secondhand smoking was 52.4% in our study, which was a 13.2% absolute difference. This difference may have been due to our subjects being comprised of infertile women under high stress, or it may have been due to the different distribution of employed women in our study group compared to that in the general population.

Secondhand smoking has been associated with difficulty becoming pregnant, delayed conception, increased pregnancy losses, increased risk of preterm labor, and increased incidence of chromosomal abnormalities and congenital malformations (12,13,17,19). The influence of secondhand smoking, compared to direct smoking, on natural or IVF pregnancy have not been studied in depth, and needs further investigation.

In the present study, current smokers were less educated and more likely to consume alcohol than secondhand or never smokers. Although a strong association between smoking behavior and lower educational status or alcohol consumption has previously been reported (20), we firstly confirmed these relationships in infertile women.

Employed women were more prevalent in the group of secondhand smokers, and this may be related to more frequent exposure to secondhand smoke in their workplace. Although the age at marriage was not significantly different among groups, working women tend to try to get pregnant later in life, and this may be an explanation why secondhand smokers were more likely to be diagnosed with primary infertility than current smokers or never smokers. This may also explain why sleep time was comparable between current smokers and never smokers but significantly shorter in secondhand smokers. Occupational status may also be responsible for the high stress level observed in secondhand smokers. Stress level was not significantly different between current and never smokers. While there may be no association between smoking and stress level in these two groups, an alternative interpretation is also possible. Current smokers may have been under more stressful conditions that were relieved by smoking (or by the accompanied alcohol consumption). This speculation is supported by the fact that fewer current smokers sought for treatment for self-reported depression, despite a similar prevalence for depression between all three groups. A survey report from the American Psychological Association indicated a stress level of 4.8 in women in the general

population. The stress level found in our study was slightly higher in all three groups (5.6, 5.9, and 5.6 in current, secondhand, and never smokers, respectively), likely reflecting the stressful environment infertile women face.

Exercise patterns were similar between groups, but current smokers did weight-training exercise more frequently than secondhand smokers or never smokers. However, the absolute frequency was less than once a week in all three groups, and thus the small difference may not have any clinical significance.

The prevalence of diabetes mellitus (4.0%) was significantly higher in current smokers than in secondhand smokers (0.0%) or never smokers (0.6%). This finding is consistent with the existing literature, as smoking is a well-known risk factor for diabetes mellitus (21,22). Several cohort studies in Korea have also reported that smoking was associated with an increased risk for developing diabetes (23,24); a 55% increase in the risk of diabetes was reported among men and women who smoked 20 cigarettes a day (24).

Infertile women are prone to emotional instability, and depression is one of the most important conditions possibly associated with infertility, although controversy exists (25-28). The prevalence of self-reported depression was 2.7%, and, according to the BDI inventory, mild-to-severe depression and moderate-to-severe depression were found in 32.9% and 10.7% of women, respectively. Although we did not directly compare the prevalence of depression between infertile and fertile women, the prevalence of depression observed in our study was higher than in previous reports. As many as 20%–50% of women undergoing IVF cycles were found to have mild-to-moderate symptoms associated with depression, and 2% had severe symptoms. Further, symptoms gradually worsened after failed cycles (29-32). Although we did not find a significant difference in the degree of depression based on smoking status in infertile women, we are the first to report the prevalence of depression in infertile women in Korea.

Among the 97.3% of women who had never been diagnosed with depression, moderate-to-severe depression assessed by the BDI which required professional counseling was as high as 10.7%. In addition, only 9.5% of patients with a previous depression diagnosis and 16.5% of women who experienced despair received treatment for those conditions. Infertility practitioners should be aware of the risk of depression in infertile women. Based on our findings, screening for depression and appropriate expert consultation is highly recommended in infertile women.

In the present study, there were no differences in menstrual characteristics or serum reproductive hormone levels based on smoking status. A close association between smoking and menstrual irregularity or serum TSH level has been reported in non-infertile women (1,33-35). The effect of smoking on serum prolactin level showed conflicting results in previous studies (36-38). It must be emphasized that our study population included infertile women with a relatively low prevalence of smoking compared to western countries, and this might explain why smoking habits were not significantly associated with reproductive hormone levels; further research in this area is needed. Higher FSH, fewer antral follicle counts, and lower AMH values in smokers were reported in several studies. However, the influence of smoking on ovarian reserve is largely controversial (1,34,35,39,40).

Our study has several limitations. Questionnaire-based studies are intrinsically susceptible to recall bias, and intentional false responses may have been presented. Further, this was a cross-sectional study, and therefore did not allow for the establishment of causal relationships. Another limitation was subject heterogeneity, as participants were recruited at various stages of fertility treatments. Finally, information on follow-up treatments and pregnancy outcomes were not available.

In conclusion, higher probability of concurrent alcohol drinking, higher prevalence of diabetes mellitus, and lower education status were found in current smokers compared to never smokers. On the other hand, higher prevalence of primary infertility, higher proportion of employed women and lower education status were found in secondhand smokers compared to never smokers.

DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conceptualization: Jee BC. Data curation: Shin JJ, Jee BC, Kim H, Kim SH. Formal analysis: Shin JJ. Investigation: Shin JJ. Writing - original draft: Shin JJ. Writing - review & editing: Shin JJ, Jee BC.

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REFERENCES

1. Freour T, Masson D, Mirallie S, Jean M, Bach K, Dejoie T, Barriere P. Active smoking compromises IVF outcome and affects ovarian reserve. *Reprod Biomed Online* 2008; 16: 96-102.
2. Augood C, Duckitt K, Templeton AA. Smoking and female infertility: a systematic review and meta-analysis. *Hum Reprod* 1998; 13: 1532-9.
3. Crha I, Hrubá D, Fiala J, Ventruba P, Záková J, Petrenko M. The outcome of infertility treatment by in-vitro fertilisation in smoking and non-smoking women. *Cent Eur J Public Health* 2001; 9: 64-8.

 https://doi.org/10.3346/jkms.2017.32.2.321

4. Klonoff-Cohen H, Natarajan L, Marrs R, Yee B. Effects of female and male smoking on success rates of IVF and gamete intra-Fallopian transfer. *Hum Reprod* 2001; 16: 1382-90.
5. Gruber I, Just A, Birner M, Lösch A. Effect of a woman's smoking status on oocyte, zygote, and day 3 pre-embryo quality in in vitro fertilization and embryo transfer program. *Fertil Steril* 2008; 90: 1249-52.
6. Firns S, Cruzat VF, Keane KN, Joesbury KA, Lee AH, Newsholme P, Yovich JL. The effect of cigarette smoking, alcohol consumption and fruit and vegetable consumption on IVF outcomes: a review and presentation of original data. *Reprod Biol Endocrinol* 2015; 13: 134.
7. Lintsen AM, Pasker-de Jong PC, de Boer EJ, Burger CW, Jansen CA, Braat DD, van Leeuwen FE. Effects of subfertility cause, smoking and body weight on the success rate of IVF. *Hum Reprod* 2005; 20: 1867-75.
8. Kornya L, Bódis J, Verzár Z, Török A, Tinneberg HR. Cigarette smoking and infertility. *Hum Reprod* 1998; 13: 3576.
9. Kim H, Kim SK, Yu EJ, Lee JR, Jee BC, Suh CS, Kim SH. The prevalence of positive urinary cotinine tests in Korean infertile couples and the effect of smoking on assisted conception outcomes. *Clin Exp Reprod Med* 2015; 42: 136-42.
10. Ministry of Health and Welfare, Korea Centers for Disease Control and Prevention. Korea Health Statistics 2012: Korea National Health and Nutrition Examination Survey (KNHANES V-3). Cheongwon: Korea Centers for Disease Control and Prevention, 2013.
11. Neal MS, Hughes EG, Holloway AC, Foster WG. Sidestream smoking is equally as damaging as mainstream smoking on IVF outcomes. *Hum Reprod* 2005; 20: 2531-5.
12. Peppone LJ, Piazza KM, Mahoney MC, Morrow GR, Mustian KM, Palesh OG, Hyland A. Associations between adult and childhood secondhand smoke exposures and fecundity and fetal loss among women who visited a cancer hospital. *Tob Control* 2009; 18: 115-20.
13. Hull MG, North K, Taylor H, Farrow A, Ford WC; The Avon Longitudinal Study of Pregnancy and Childhood Study Team. Delayed conception and active and passive smoking. *Fertil Steril* 2000; 74: 725-33.
14. Rhee MK, Lee YH, Jung HY, Choi JH, Kim SH, Kim YK, Lee SK. A standardization study of Beck depression inventory II—Korean version (K-BDI): validity. *Korean J Psychopathol* 1995; 4: 96-104.
15. Pirkle JL, Flegal KM, Bernert JT, Brody DJ, Etzel RA, Maurer KR. Exposure of the US population to environmental tobacco smoke: the third National Health and Nutrition Examination Survey, 1988 to 1991. *JAMA* 1996; 275: 1233-40.
16. Centers for Disease Control and Prevention (US). Current cigarette smoking among adults in the United States [Internet]. Available at http://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/ [accessed on 27 July 2016].
17. Meeker JD, Benedict MD. Infertility, pregnancy loss and adverse birth outcomes in relation to maternal secondhand tobacco smoke exposure. *Curr Womens Health Rev* 2013; 9: 41-9.
18. Lee SR, Lee CK, Im H, Yang W, Urm SH, Yu SD, Lee JH, Suh CH, Kim KH, Son BC, et al. Secondhand smoke exposure and urine cotinine concentrations by occupation among Korean workers: results from the 2008 Korea national survey for environmental pollutants in the human body. *J Occup Environ Hyg* 2014; 11: 314-25.
19. Meeker JD, Missmer SA, Cramer DW, Hauser R. Maternal exposure to second-hand tobacco smoke and pregnancy outcome among couples undergoing assisted reproduction. *Hum Reprod* 2007; 22: 337-45.
20. Wagenknecht LE, Perkins LL, Cutter GR, Sidney S, Burke GL, Manolio TA, Jacobs DR Jr, Liu KA, Friedman GD, Hughes GH, et al. Cigarette smoking behavior is strongly related to educational status: the CARDIA study. *Prev Med* 1990; 19: 158-69.
21. InterAct Consortium, Spijkerman AM, van der A DL, Nilsson PM, Ardanaz E, Gavrila D, Agudo A, Arriola L, Balkau B, Beulens JW, et al. Smoking and long-term risk of type 2 diabetes: the EPIC-InterAct study in European populations. *Diabetes Care* 2014; 37: 3164-71.
22. Will JC, Galuska DA, Ford ES, Mokdad A, Calle EE. Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study. *Int J Epidemiol* 2001; 30: 540-6.
23. Cho NH, Chan JC, Jang HC, Lim S, Kim HL, Choi SH. Cigarette smoking is an independent risk factor for type 2 diabetes: a four-year community-based prospective study. *Clin Endocrinol (Oxf)* 2009; 71: 679-85.
24. Jee SH, Foong AW, Hur NW, Samet JM. Smoking and risk for diabetes incidence and mortality in Korean men and women. *Diabetes Care* 2010; 33: 2567-72.
25. Biringer E, Howard LM, Kessler U, Stewart R, Mykletun A. Is infertility really associated with higher levels of mental distress in the female population? Results from the North-Trøndelag Health Study and the Medical Birth Registry of Norway. *J Psychosom Obstet Gynaecol* 2015; 36: 38-45.
26. Greil AL. Infertility and psychological distress: a critical review of the literature. *Soc Sci Med* 1997; 45: 1679-704.
27. Domar AD, Broome A, Zuttermeister PC, Seibel M, Friedman R. The prevalence and predictability of depression in infertile women. *Fertil Steril* 1992; 58: 1158-63.
28. 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.
29. Demyttenaere K, Bonte L, Gheldof M, Vervaeke M, Meuleman C, Vanderschuerem D, D'Hooghe T. Coping style and depression level influence outcome in in vitro fertilization. *Fertil Steril* 1998; 69: 1026-33.
30. Pasch LA, Gregorich SE, Katz PK, Millstein SG, Nachtigall RD, Bleil ME, Adler NE. Psychological distress and in vitro fertilization outcome. *Fertil Steril* 2012; 98: 459-64.
31. Volgsten H, Skoog Svanberg A, Ekselius L, Lundkvist O, Sundström Poromaa I. Risk factors for psychiatric disorders in infertile women and men undergoing in vitro fertilization treatment. *Fertil Steril* 2010; 93: 1088-96.
32. Lawson AK, Klock SC, Pavone ME, Hirshfeld-Cytron J, Smith KN, Kazer RR. Prospective study of depression and anxiety in female fertility preservation and infertility patients. *Fertil Steril* 2014; 102: 1377-84.
33. Windham GC, Elkin EP, Swan SH, Waller KO, Fenster L. Cigarette smoking and effects on menstrual function. *Obstet Gynecol* 1999; 93: 59-65.
34. Belin RM, Astor BC, Powe NR, Ladenson PW. Smoke exposure is associated with a lower prevalence of serum thyroid autoantibodies and thyrotropin concentration elevation and a higher prevalence of mild thyrotropin concentration suppression in the third National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab* 2004; 89: 6077-86.
35. Jorde R, Sundsfjord J. Serum TSH levels in smokers and non-smokers. The 5th Tromsø study. *Exp Clin Endocrinol Diabetes* 2006; 114: 343-7.
36. Baron JA. Cigarette smoking and Parkinson's disease. *Neurology* 1986; 36: 1490-6.
37. Al-Turki HA. Effect of smoking on reproductive hormones and semen parameters of infertile Saudi Arabians. *Urol Ann* 2015; 7: 63-6.

38. Baron JA, Bulbrook RD, Wang DY, Kwa HG. Cigarette smoking and prolactin in women. *Br Med J (Clin Res Ed)* 1986; 293: 482-3.
39. Asvold BO, Bjøro T, Nilsen TI, Vatten LJ. Tobacco smoking and thyroid function: a population-based study. *Arch Intern Med* 2007; 167: 1428-32.
40. Caserta D, Bordi G, Di Segni N, D'Ambrosio A, Mallozzi M, Moscarini M. The influence of cigarette smoking on a population of infertile men and women. *Arch Gynecol Obstet* 2013; 287: 813-8.

https://doi.org/10.3346/jkms.2017.32.2.321