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Risk factors for resignation from work after starting infertility treatment among Japanese women: Japan-Female Employment and Mental health in Assisted reproductive technology (J-FEMA) study

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ABSTRACT

Objective To elucidate the risk factors associated with resignation from work of Japanese women undergoing infertility treatment.

Methods A total of 1727 female patients who attended a private fertility clinic in Japan participated in the Japan-Female Employment and Mental health in Assisted reproductive technology study. Questions related to demographic, clinical and socioeconomic characteristics were employed in the questionnaire. Out of the 1727 patients, 1075 patients who were working at the time of initiating infertility treatment and felt infertility treatment incompatible with work were included in the analysis. Risk factors for resignation were assessed by using multivariable logistic regression models.

Results Among 1075 working women who started infertility treatment, 179 (16.7%) subsequently resigned. Multivariable-adjusted ORs for resignation in those with lower educational background and infertility for ≥2 years were 1.58 (95% CI: 1.07 to 2.34) and 1.82 (95% CI: 1.15 to 2.89), respectively. The OR for resignation in non-permanent workers undergoing infertility treatment was 2.65 (95% CI: 1.61 to 4.37). While experiencing harassment in the workplace approached significance, lack of support from the company was significantly associated with resignation after starting infertility treatment, with ORs of 1.71 (95% CI: 0.98 to 2.99) and 1.91 (95% CI: 1.28 to 2.86), respectively.

Conclusion One-sixth of women resigned after starting infertility treatments. It was found that factors related to education, infertility duration and work environment were significantly associated with resignation. Reducing the physical and psychological burden endured by women, for example, by increasing employer-provided support, is vitally important in balancing infertility treatment with maintenance of work life.

Key messages

What is already known about this subject?

- Psychological distress brought about by infertility treatment is related to absence from work.
- The difficulties of combining work and infertility treatment are associated with job insecurity.
- Few preliminary studies show risk factors for resignation after starting infertility treatment despite continued high treatment expenses until the end of treatment.

What are the new findings?

- Lower educational background, longer duration of infertility, non-permanent worker, harassment experience in the workplace and lack of support within the company were identified as risk factors for resignation after initiating infertility treatment.

How might this impact on policy or clinical practice in the foreseeable future?

- Prior to infertility treatment, providing special care such as infertility treatment leave, in addition to psychological support, to those who have these risk factors may reduce the tendency of resigning from work.
- This finding may contribute to policy development to secure a healthy work life for patients undergoing infertility treatment.

INTRODUCTION

In the USA, Europe and high-income Asian counties, the number of women receiving treatments for infertility has increased in the recent years.[1–3] This phenomenon is largely understood in the context of increasing age at marriage and childbearing, as well as increasing attainment of higher education among women in the last half-century.[4–6] Nonetheless, ovarian function declines with age, with peak fertility occurring in the early 20s and decreasing at 32 years, with rapid subsequent declines in ovarian reserve from 35 to 38 years.[7] Gynaecological diseases that alter conception and successful pregnancy, including endometriosis and uterine myoma, also increase with the cumulative number of ovulations and menstruations. Given the complex interplay between these numerous social and biological factors, when women wish to have children later

after marriage, conception and successful pregnancy are more difficult. Since the first in vitro fertilisation (IVF) baby in the UK in 1978,[4] treatment for infertility has improved remarkably over the last several decades. Infertility treatments typically consist of either the timing method, artificial insemination with husband's semen or assisted reproductive technology (ART), which includes IVF and intracytoplasmic sperm injection (ICSI).[8]

In Japan, there has been a decline in the number of births to about half in the last 40 years, with 1 708 643 babies born in 1978 to 918 400 babies in 2018. Despite this, approximately 1 in 5.5 Japanese couples opts for infertility treatment and this number continues to increase.[9] The highest number of ART cases in the world is currently yielded in Japan,[2 3] with 447 790 cycles and 54 110 neonates—about 1 in 18.1 neonates born in 2016 were conceived via ART treatment.[3]

While more women are choosing to undergo infertility treatment, balancing infertility treatment with work is affected by various factors, including demographic, clinical and socioeconomic characteristics.[2 10–12] Maintaining employment can be challenging for women undergoing infertility treatments with regard to physical, mental and economical impacts. Notably, infertility treatment, especially ART procedures, may require frequent and sudden clinic visits depending on the individual's menstruation cycle—and as such, some women consequently decide to resign from their work despite continued high expenses until treatment success.[13] Moreover, ART is not covered by the Japanese National Health Insurance, and this adds further substantial out-of-pocket expenses.[14] The Japanese Government, Ministry of Health, Labour and Welfare, developed a financial subsidy programme to help reduce the economical impact on a specific infertility treatment including examinations.[15 16] As it varies among local government policies and largely depends on the contents of applicable procedures, the subsidy programmes benefit 150 000 Japanese yen (JPY) (approximately 1100 British pounds (GBP), converted with the average exchange rate in August 2020: 139.3 JPY/GBP) at maximum per one cycle of an IVF or ICSI, which generally costs JPY300 000–500 000 (2200–3600 GBP) in Japan. However, it is also restricted by frequency of treatments (≤6 times), annual household incomes (<JPY7.3 million, 52 420 GBP) and the age of wife (≤42 years). Thus, as many women receiving infertility treatment continue to struggle with unavoidable dilemmas in the workplace, an understanding of how society can best support working women undergoing infertility treatment is warranted.[7 10]

To our knowledge, there have been no large-scale epidemiological studies in Asia investigating resignation in female patients who undergo infertility treatment. The objective of this study was to clarify the risk factors for resignation in the included population. A clearer understanding of these factors may facilitate public institutions and companies to regulate and improve their support systems for women undergoing infertility treatments.

MATERIALS AND METHODS

Study population

The Japan-Female Employment and Mental health in ART (J-FEMA) study, organised in November 2017, is a cross-sectional, multicentre survey of female patients attending fertility clinics in Japan and which established a database of factors associated with infertility treatment in Japan. The study enrolled female patients aged ≥20 years who attended the following four fertility clinics: (1) Sugiyama Clinic Shinjuku in Tokyo (located on Honshu mainland, capital of Japan, with a population of 14 million residents); (2) Sugiyama Clinic Marunouchi in Tokyo; (3) Saint Mother Hospital Infertility Clinic in Fukuoka prefecture (located on Kyushu island, an urban-suburban area 650 miles southwest of Tokyo, with a population of 5 million residents) and (4) Takasaki ART Clinic in Gunma prefecture (located on Honshu mainland, a suburban-rural area 76 miles north of Tokyo, with a population of 2 million residents).[17] A total of 1727 female patients participated in the J-FEMA study between August and December 2018. As illustrated in figure 1, 1369 (79.3%) patients reported working at the time of initiation of their infertility treatment. Among these patients, 1075 felt that undergoing infertility treatment was incompatible with work and hence they were included in the analysis dataset because they were presumed struggling to stay at work with undergoing infertility treatment.

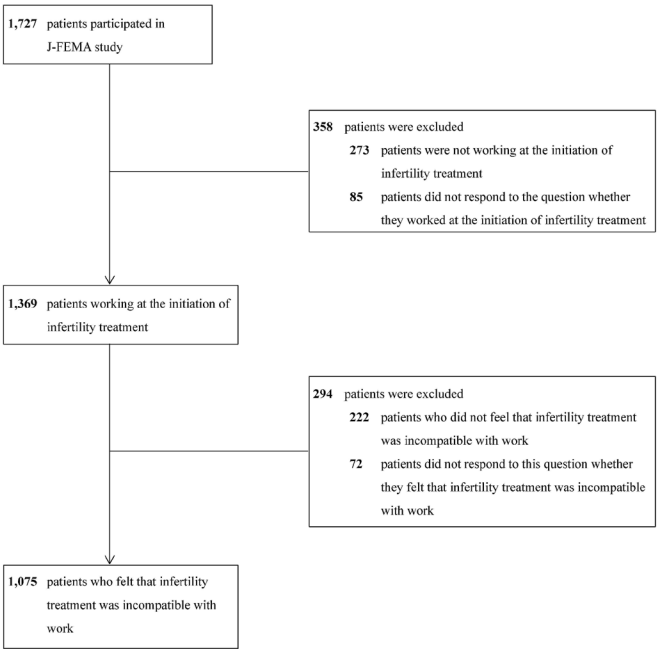

Figure 1 Flow chart of study population included in the analysis. J-FEMA, Japan-Female Employment and Mental health in Assisted reproductive technology.

Questionnaires and variables

The analysis used an anonymous self-administered questionnaire developed for the study. In this study, those who reported that they had worked at initiation of infertility treatment and 'left the job' in response to the question 'why had the patient's work status changed after starting infertility treatment ("changed the job" or "left the job")' were defined as resigning from work. The questionnaire included the following data: age; age at marriage; age at initiation of ART; educational background; infertility treatment (duration of infertility and ART experience) and work environment including company size (<50, 50–999 and ≥1000 employees), employment type (permanent worker defined no fixed end date for their employment, non-permanent worker defined contract and part-time worker, self-employed and other workers), harassment experience in workplace after starting infertility treatment (yes or no) and infertility treatment-relevant support from company (yes or no). Variables were classified respectively into the following categories: age was categorised as <35, 35–39 or ≥40 years; educational background was categorised as university degree or more advanced ('higher educational background') versus other ('lower educational background') and

duration of infertility was categorised as <2 years versus ≥2 years.

Statistical analyses

Pearson's χ^2 test was used to describe the age-specific characteristics of patients, and the association between potential risk factors and employee resignation. The ORs of factors including resignation after adjustment for patient age, educational background, duration of infertility, employment type, harassment experience in workplace after starting infertility treatment and support from company were analysed using a multivariable logistic regression analysis (forced entry method). All statistical analyses were performed with IBM SPSS for Windows (V.25.0; IBM, Armonk, New York, USA). All probability values for statistical tests were two-tailed, and values of $p<0.05$ were regarded as statistically significant.

RESULTS

In the present study, 1075 Japanese female workers who reported working at the initiation of infertility treatment were included in the analysis. Mean and SD of age, age at marriage and age at initiation of ART were 37.5 (4.7), 32.2 (5.0) and 36.9 (8.8) years, respectively. The mean (SD) of infertility duration was 3.2 (2.7) years.

Demographic characteristics of the study population according to the patient resignation status are described in table 1. There was a total of 179 (16.7%) patients who resigned after starting infertility treatment. Resignation rates were significantly higher in those who had lower educational background ($p<0.01$), had been infertile for ≥2 years ($p<0.01$), were non-permanent workers ($p<0.001$), had any harassment experience in the workplace after starting infertility treatment ($p<0.01$) or had experienced lack of infertility treatment-relevant support from their company ($p<0.01$).

The results of the multivariable analysis of risk factors for resignation after starting infertility treatment are presented in table 2. The multivariable-adjusted OR and 95% CIs in those who had a lower versus higher educational background was 1.58 and 1.07–2.34, respectively. After adjustment, patients who had been infertile for ≥2 years showed a significantly higher risk of resigning (OR 1.82; 95% CI: 1.15 to 2.89) versus those with shorter duration of infertility. Similarly, OR of resignation in non-permanent workers was substantially higher at 2.65 (95% CI: 1.61 to 4.37) compared with that of permanent workers. Although the association of harassment experience in the workplace with resignation after starting infertility treatment approached significance (OR 1.71; 95% CI: 0.98 to 2.99), lack of company support was associated with a nearly doubled risk of resignation after starting infertility treatment (OR 1.91; 95% CI: 1.28 to 2.86).

DISCUSSION

As far as we know, this is the first large-scale study in Asia to study the risk of resignation in female patients who are employed at the initiation of infertility treatment. The present study revealed that over one-sixth of female patients who felt that infertility treatment was incompatible with work resigned after starting the treatment despite the continued expense the treatment requires.[13] The resignation rate in our study was substantially higher than that found previously (15.6% in 2018) among general female workers of prime working age (25–54 years).[18] The mean age of patients at marriage in our study (32.2 years) was slightly older than that of the general female population in Japan in 2018 (31.2 years).[5] In addition, the mean age of patients at initiation of ART was 36.9 years. Delivery by women at an advanced maternal age, which was previously rare, is no longer uncommon in the recent years.[19] However, as fertility peaks in the early 20s, decreasing at 35–38 years as the ovarian reserve rapidly decreases,[7] and the success rate of ART decreasing further with advanced age,[3] we reasonably assume that providing health support to patients undergoing infertility treatment is worth much attention.[20]

Our study revealed that five factors were significantly associated with resignation in women receiving infertility treatment. Lower educational background was significantly associated with resignation. Several studies have shown that lower education and female gender are strong predictors of long-term sickness absence and resignation.[21] Additionally, Cheng *et al*[22] also reported that lower educational attainment yields higher levels of job insecurity, while those who have professional attainments were found to have the lowest levels of job insecurity. In our study, although no significant difference was observed in the age at marriage between those with lower and higher educational attainment, factors such as age and age at initiation of ART, as well as duration of infertility, cost of infertility treatment, non-permanent worker and self-employed and others were significantly higher in those with lower education. By contrast, annual salaries of both patient and partner and the infertility treatment-relevant support from the patient's company were significantly lower in those with lower education (online supplemental table 1). In contrast to trends seen in higher educated patients,[4–6] this deduction may be explained by multiple factors, including lack of knowledge and consequent delayed access to infertility treatment and poor career-orientation[23] due to the lower educational background—although this is speculative because the reasons of resignation might not be always simple. However, education is a key dimension of socioeconomic position and a higher level of education provides knowledge, skills, values and attitudes that are likely to support healthier choices and protect one's self from job loss.[24]

In this study, it was found that longer duration (≥2 years) of infertility was also significantly associated with resignation. Although longer durations of treatment might allow for more opportunities for resignation due to the longer period of observation, infertility is in itself a risk factor for adverse pregnancy outcomes, and longer durations of infertility are associated with greater risk.[25] As longer duration to conceive has been robustly associated with greater distress,[13 26] the interactions between emotional and physical problems associated with infertility treatment are complex and likely to be compounded by the difficulties of combining work, treatment and associated job insecurity.[27] In addition, the initial eagerness to seek treatment may diminish over time, with patients having more likely to consider the idea of infertility as a reality.[28] Female workers who have been infertile for ≥2 years might already have a higher risk for resignation at the time of the diagnosis of infertility.[8] The National Institute of Clinical Excellence guidelines propose an immediate IVF cycle for those meeting formal criteria providing that duration of regular unprotected intercourse is longer than 2 years.[29] Considering age and success rates, patients may tend to focus more on their infertility treatment rather than staying at work.

Non-permanent workers resigned from work have significantly higher rates than permanent employees. Based on the Survey on Employment Trends conducted by the Japanese Government in 2018, the average (SD) of proportion of non-permanent female workers is 53.4% (14.1) in Japan.[18] The higher proportion of permanent workers in our study might be considered because of

Table 1 Demographic characteristics of the study population by resignation status in those who had worked at initiation of infertility treatment and felt that infertility treatment was incompatible with work

	Number (%)							
Variables categories	**Total**		**Not resigned**		**Resigned**		**Resignation rate (%)**	**P value***
N	1018		839	(78.0)	179	(16.7)	16.7	
Age (years)								
<35	274	(27.3)	225	(27.2)	49	(27.4)	17.9	0.97
35–39	358	(35.6)	293	(35.5)	65	(36.3)	18.2	
≥40	373	(37.1)	308	(37.3)	65	(36.3)	17.4	
Age at marriage (years)								
<35	587	(66.2)	473	(65.3)	114	(69.9)	19.4	0.21
35–39	215	(24.2)	184	(25.4)	31	(19.0)	14.4	
≥40	85	(9.6)	67	(9.3)	18	(11.0)	21.2	
Age at initiation of ART (years)								
<35	216	(31.7)	168	(30.2)	48	(38.1)	22.2	0.23
35–39	266	(39.0)	221	(39.7)	45	(35.7)	16.9	
≥40	200	(29.3)	167	(30.0)	33	(26.2)	16.5	
Educational background†								
Higher	544	(53.8)	468	(56.2)	76	(42.5)	14.0	<0.01
Lower	468	(46.2)	365	(43.8)	103	(57.5)	22.0	
Duration of infertility (years)‡								
<2	304	(31.6)	267	(33.8)	37	(21.5)	12.2	<0.01
≥2	659	(68.4)	524	(66.2)	135	(78.5)	20.5	
ART experience								
No	262	(26.1)	217	(26.2)	45	(25.3)	17.2	0.79
Yes	743	(73.9)	610	(73.8)	133	(74.7)	17.9	
Company size at the initiation of infertility treatment (employees)								
<50	219	(32.6)	162	(32.7)	57	(32.4)	26.0	0.67
50–999	231	(34.4)	166	(33.5)	65	(36.9)	28.1	
≥1000	221	(32.9)	167	(33.7)	54	(30.7)	24.4	
Employment type at the initiation of infertility treatment								
Permanent worker§	475	(70.6)	374	(74.7)	101	(58.7)	21.3	<0.001
Non-permanent worker§	99	(14.7)	54	(10.8)	45	(26.2)	45.5	
Self-employed and others	99	(14.7)	73	(14.6)	26	(15.1)	26.3	
Harassment experience in workplace due to infertility treatment								
No	889	(90.7)	743	(92.1)	146	(84.4)	16.4	<0.01
Yes	91	(9.3)	64	(7.9)	27	(15.6)	29.7	
Infertility treatment-relevant support from company¶								
Yes	401	(42.2)	347	(44.5)	54	(31.4)	13.5	<0.01
No	550	(57.8)	432	(55.5)	118	(68.6)	21.5	

*Pearson's χ^2 test.
†Educational background: university and graduate school as 'higher educational background'; and junior high school, high school and junior college/technical school/university dropout as 'lower educational background'.
‡The median duration of infertility.
§Permanent worker defined no fixed end date for their employment; non-permanent worker defined contract and part-time worker; self-employed and other worker.
¶Infertility treatment-relevant support including, but not limited to, reduction in work-hours, hours-leave and flexible working style.
ART, assisted reproductive technology.

treatment cost and flexibility in work life-treatment balance, and not everyone can undergo infertility treatment, especially ART treatment. Therefore, patients who undergo infertility treatment tend to be permanent workers and they may be over-represented in this study. However, our findings are in accordance with prior study showing the risk for sick leave in shift workers compared with scheduled workers.[12] Suga *et al*[30] previously reported that non-regular employees more frequently changed their occupations five times more than regular employees do; part-time and short-term contract employees were 12 times more likely to have occupation changes. Non-permanent workers have substantially more barriers to taking the frequent or sudden leaves of absence that are frequently required during infertility treatment while still being engaged in their jobs.[26] Temporary agency work is considered a more unfavourable employment status than those with permanent work arrangements and has been associated with precarious labour and life situations.[31] In contrast, permanent workers may opt to continue working out of economic necessity,[30] as well as a fear that job security at a similar pay and position might not be wholly guaranteed on returning to work after childbearing.[32] A reduction of fertility after job loss is one of the many difficulties women face when re-establishing their careers.[33] Workplace structures that provide a choice of working styles for women wanting to conceive or give birth should cater to non-permanent staff.[20]

Table 2 Associations with resignation after starting infertility treatment in those who had worked at initiation of infertility treatment who felt that infertility treatment was incompatible with work

Variables categories	Multivariable OR (95% CI)*	P value
Age (years)		
<35	1.00	
35–39	0.81 (0.50 to 1.33)	0.41
≥40	0.87 (0.53 to 1.43)	0.58
Educational background†		
Higher	1.00	
Lower	1.58 (1.07 to 2.34)	0.02
Duration of infertility (years)‡		
<2	1.00	
≥2	1.82 (1.15 to 2.89)	0.01
Employment type at the initiation of infertility treatment		
Permanent worker§	1.00	
Non-permanent worker§	2.65 (1.61 to 4.37)	<0.001
Self-employed and others	1.23 (0.70 to 2.15)	0.47
Harassment experience in workplace due to infertility treatment		
No	1.00	
Yes	1.71 (0.98 to 2.99)	0.06
Infertility treatment-relevant support from company¶		
Yes	1.00	
No	1.91 (1.28 to 2.86)	<0.01

Further information regarding the characteristics of patients subanalysed by educational background are shown in online supplemental table 1.
*Each OR was adjusted for all other variables in the table.
†Educational background: university and graduate school as 'higher educational background'; and junior high school, high school and junior college/technical school/university dropout as 'lower educational background'.
‡The median duration of infertility.
§Permanent worker defined no fixed end date for their employment; non-permanent worker defined contract and part-time worker; self-employed and other worker.
¶Infertility treatment-relevant support including, but not limited to, reduction in work-hours, hours-leave and flexible working style.

Although significantly more women who resigned from their work reported an experience of harassment at the workplace, this association, though approaching statistical significance, did not remain significant after a multivariable analysis. In our study, 1 in 11 patients experienced harassment in their workplace during infertility treatment. This was lower than that reported in 'Pregnancy and Maternity-Related Discrimination and Disadvantage: Experiences of Mothers', published by the government of the UK, in which 20% of mothers experienced harassment or negative comments related to pregnancy or flexible working from their employer and/or colleagues.[34] Chan *et al*[10] reported that gender-based workplace bullying is experienced by nearly 40% of general female employees. However, our study showed that one-third of those who felt harassment eventually resigned from work, which was much higher than the 17.1% resignation rate in female workers in a general population in 2018.[18]

Another identified risk factor for resignation investigated in this study is the lack of employer support for patients. Those who had not received support from their company had a significantly higher risk of resignation compared with those who felt adequately supported. Most patients who undergo infertility treatment have anxiety about the uncertainty in their future.[35] Infertility distress has been previously observed to be higher in unemployed women, women with difficulty in taking time off work and women who paid for treatment expenses by themselves.[26] In addition to clinical emphasis to improve service delivery and to assess the need for psychological counselling, larger social contexts and social science frameworks will also be important.[36] Formalised infertility treatment leave programmes may be important to stabilise working conditions and promote an understanding among all workers of the necessity of such programmes in the workplace.[30]

Most importantly, job displacement reduces average fertility. Fertility decline has been strongly associated with unemployment increase—a relationship that remains significant at all ages.[37] Difficulties experienced in combining treatment and work suggest that increased support is needed and hence must be considered. In the past seven decades, the total fertility rate (TFR) was reduced to half, with global TFR decreasing to 2.4.[1] As replacement level fertility is essential to maintain population size in high-income countries,[1 7] infertility has been recognised by WHO as a critical public health issue. Although many countries have prompted various pronatal policies such as fertility subsidies, childcare allowances and fertility-related pension schemes in the hope of boosting fertility rates,[38] none of these policies directly promotes earlier age at childbearing.[39] In Japan, TFR has been in a similar decline, decreasing to just 1.42 in 2018[5]; the number of births in 2018 was 918 400 and this figure continued to fall to fewer than 900 000 in 2019—the lowest level since Japan's Vital Statistics survey in 1899.[5] One in 5.5 Japanese couples has encountered problems with fertility requiring examination and treatment.[8 9] Although several policies and guidelines have been enacted in Japan in an attempt to reverse these trends, they have focused almost exclusively on general healthcare, maternity care, prenatal and perinatal health management and child-care.[14 40] Establishing and improving social systems including, but not limited to, the alleviation of family income restriction for subsidisation that enables infertile women, regardless of educational level and employment type, to pursue lifestyles conducive to childbearing, while actively working is a pressing issue. Specific workplace policies, guidance for supervisors and flexibility in fertility clinic times due to the requirement of sudden and frequent leaves for numerous tests and treatments would significantly help employees during their treatment and would greatly reduce the psychological distress, thereby potentially influencing physical health and treatment outcomes.[27]

The strength of the present study investigating factors of infertility treatment associated with resignation from work was its comprehensive survey design, widely conducted in female patients attending fertility clinics. The large sample size allowed us to robustly examine the associations of infertility-related and work-related factors with regard to resignation after adjustment of multiple clinically and socially relevant confounders despite some missing data. Nonetheless, several limitations warrant discussion. First, the J-FEMA study was based on a self-reported questionnaire without face-to-face interviews or diagnoses by clinical specialists. Thus, it was susceptible to recall or information bias, and the possibility that patients might have misunderstood the meanings of questions or misremembered their responses cannot be entirely ruled out. However, the association between infertility treatment and resignation is likely not to have been overestimated as our study population excluded those who failed to answer questions regarding being subject to harassment or receiving support from their company. Second, reasons for resignation are likely complex and multifactorial, and not solely due to infertility treatment. Although some workers may have not been forced to resign, this was not explored in the questionnaire and, therefore, the association between infertility treatment and resignation might be overestimated in this case. However,

given that other unexplored positive factors, such as partner income and family support may help women to better balance infertility treatments and work, we do not expect this limitation to drastically affect the trends identified in our analysis. In future studies, more structured questions using other tools such as dynamic-response surveys may provide further clarity to these important questions.

In conclusion, one-sixth of female patients who felt that infertility treatment was incompatible with work resigned from work after starting infertility treatment despite ongoing treatment expenses. Risk factors related to educational background, infertility duration and work situation were identified as significantly associated with resignation in female workers attending fertility clinics. Further longitudinal and prospective studies are warranted to more comprehensively understand the association between infertility treatment and work life. This understanding will facilitate and secure a healthy work life for patients undergoing infertility treatment.

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Contributors IY provided substantial contribution to the conception, analysing data, drafting of the manuscript. ME contributed to the substantial design of the work, acquisition of data, drafting of the manuscript and critical revisions and obtained the funding of the study. KK contributed to the design of the work and made critical revisions. KT contributed to the analysis of data and also participated in the critical revisions in the paper. YI helped in the analysis of data and made critical revisions. SS helped in the interpretation of the data and critical revision. KM contributed to the interpretation of data and critical revision. YU, GAD, AI, ST and TT helped in the interpretation of data and critical revision. AT, RS and YK contributed to the acquisition of data and critical revision. KN and YS helped in the acquisition of data and critical revision of the paper.

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