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Influence of a patient education and care program on women undergoing non-assisted reproductive technology fertility treatment

Akiko Mori[1] | Osamu Nishii[2] | Yasushi Takai[3] | Mikio Momoeda[4] |
Etsuko Kamisawa[5] | Kiyomi Shimizu[6] | Mieko Nozawa[7] | Yuri Takemura[8] |
Akihisa Fujimoto[2]

[1]Department of Nursing, School of Nursing, Shonan Kamakura University of Medical Sciences, Kanagawa, Japan

[2]Department of Obstetrics and Gynecology, Teikyo University School of Medicine Hospital Mizonokuchi, Kanagawa, Japan

[3]Department of Obstetrics and Gynecology, Saitama Ika Daigaku Sogo Iryo Center, Saitama, Japan

[4]Center for Advanced Reproduction, St. Luke's International University, Hospital, Tokyo, Japan

[5]Graduate School of Nursing, Kyoto Tachibana University, Kyoto, Japan

[6]Department of Nursing, School of Nursing, Josai International University, Chiba, Japan

[7]Department of Nursing, Tokyo University of Technology School of Health Sciences, Tokyo, Japan

[8]Denentoshi Ladies Clinic, Kanagawa, Japan

Correspondence
Akiko Mori, Department of Nursing, School of Nursing, Shonan Kamakura University of Medical Sciences, 1195-3 Yamasaki, Kamakura-shi, Kanagawa 247-0066, Japan.
Email: a.mori@sku.ac.jp

Abstract

Purpose: To determine the influence of a patient education and care program on the quality of life (QOL) of female patients undergoing non-assisted reproductive technology (ART) fertility treatment.

Methods: Participants completed the MOS 36-Item Short-Form Health Survey and fertility QOL (FertiQoL) questionnaires at baseline and at 3, 6, and 12 months of treatment. The responses of patients who underwent three sessions of the program (at baseline, 3 months, and 6 months of treatment) were compared with those of patients who did not receive the program.

Results: This study compared 69 patients who received an additional care program with 104 patients in the control group, all from 13 facilities. Treatment FertiQoL responses ($p = 0.004$) and treatment tolerability ($p = 0.043$) differed between the program and control groups at 3 months using the repeated measures mixed model. The cost of treatment per pregnancy was lower in the program group than in the control group.

Conclusion: The patient education and care program provided by reproductive fertility specialists or fertility nurses during non-ART fertility programs improves patient satisfaction.

KEYWORDS
fertility nursing, infertility treatment, outpatient, quality of life, reproductive medicine

1 | INTRODUCTION

According to the 15th Japanese National Fertility Survey (2015),[1] 18.2% of first-married couples undergo infertility investigation and treatment, with the number of couples seeking infertility treatment continuing to increase. Balancing infertility treatment and work is challenging for most patients. In 2018 surveys,[2,3] 14% of workers indicated that they had undergone or planned to undergo infertility treatment, and 87%–95.6% reported that it was difficult to balance infertility treatment and work. These surveys also found that women visit hospitals more often than men and are more burdened in terms of mental health, physical condition, and physical strength.[2] Furthermore, the average treatment cost per cycle has increased in the past 5 years.[3]

Infertility treatment is known to affect couples in various ways. Patients who do not understand the challenges of infertility treatment and who do not seek proper support experience psychological stress that may lead to cessation of treatment before it can be effective. Systematic support increases patients' interest in treatment procedures, and patient-centered health care directly affects patients' anxiety, depression, and quality of life (QOL).[4] The National Institute for Health and Care Excellence (NICE) guidelines [CG156][5] recommend patient-centered care and include evidence supporting patient self-care during pregnancy. Other guidelines recommend that medical professionals consider the values, preferences, and needs of patients when providing health care.[6] However, these guidelines are not recognized in Japan owing to differences between the social environments and medical systems in Japan compared with Europe, where the guidelines were established. Japanese guidelines focus on diagnoses and treatments; they contain little information regarding health care team collaboration or the psychological and lifestyle aspects of patients undergoing examinations and treatments.[7,8] Furthermore, nursing guidelines have not been sufficiently reviewed and evaluated.[9]

In 2016, the Cochrane Review[10] for psychoeducational interventions in infertility was published. This provided views on the effects of psychoeducational interventions on mental health and pregnancy rates based on 39 studies published up to 2015. In addition to the Cochrane review, another systematic review[11] also found that the effects of psychosocial interventions are unclear due to issues in the research methodology. Recently, many randomized controlled trials have been conducted with programs that impose group session or homework; however, most of them are aimed at patients undergoing assisted reproductive technology and are provided by researchers other than clinic medical staff.[12-16]

Infertility treatment is divided into non-assisted reproductive technology (non-ART) infertility treatments and assisted reproductive technology (ART). In Japan, government subsidies cover some ART, though it is mainly a self-financed medical treatment. Although most non-ART infertility treatments are paid for by insurance, additional education and care for patients are not standardized, and the availability of these services varies based on the medical institution. The effects of patient education and care programs, provided by reproductive medicine specialists or fertility nurses, on the treatment process of patients undergoing infertility treatment for the first time have not been investigated. Thus, this study aimed to clarify the influence of such a patient education and care program on the QOL of female patients undergoing non-ART infertility treatment.

2 | MATERIALS AND METHODS

This prospective study examined the influence of a clinical care program on female patients undergoing infertility treatment between April 28, 2017, and March 31, 2020.

2.1 | Patients

Female patients aged <42 years with an infertility period of <2 years who underwent infertility treatment for the first time were included in this study. All patients were eligible for non-ART infertility treatments (including timing therapy, ovulation induction, or artificial insemination) and were diagnosed with either unexplained infertility, ovulation disorders, polycystic ovarian syndrome, or mild male infertility. Patients with complications of a previous surgery who did not require further treatment, patients with a history of miscarriage, or patients who had no experience in childbirth and child-rearing were also included in the study. All patients in this study were required to be able to read, write, and speak Japanese.

Patients who were eligible for *in vitro* fertilization and/or intracytoplasmic sperm injection and those with a history of infertility treatment at another hospital, complications that required treatment before or at the same time as infertility treatment (including endometriosis, uterine fibroids, ovarian cysts, abnormal glucose tolerance, psychiatric/nervous system disorders, cervical cytology abnormalities, and premature ovarian insufficiency), or a history of stillbirth or early neonatal mortality were excluded from the study.

The patients' age, occupation, history of pregnancy and delivery, medical history, comorbidities, duration of infertility, and type of infertility treatment were recorded.

2.2 | Sample size

The required sample size was calculated using PS-Power and Sample Size Calculation version 3.1.2 (D. Dupont and Walton D. Plummer, Jr., Freeware) based on data from a previous similar study,[17] and a δ value of 0.7, σ value of 2, α value of 0.05, and power of 0.8. The required sample size was 129, and the target sample size was 155 patients based on a dropout rate of 20%.

2.3 | Study design

Patients in the control group received standard medical examinations and treatment, while those in the program group received

standard medical examinations and treatment along with three 30-min sessions of the education and care program. These sessions were conducted at enrollment, then after 3 and 6 months of infertility treatment (Figure 1). All patients completed the 36-item MOS 36-Item Short-Form Health Survey (SF-36v2) of the comprehensive health-related QOL scale and the 36-item fertility quality of life (FertiQoL) tool scale (Japanese version) at enrollment and at 3, 6, and 12 months of treatment.

2.4 | Patient education and care program

The education and care program was provided by doctors and nurses who were familiar with reproductive medicine who had been trained specifically for this program prior to their participation in the study. The health care providers were trained to concentrate on patient care during the program using tools to understand patient needs, provide education, and care, and to evaluate the patient's achievement of the program goals. Patients were instructed to communicate with doctors using the notebooks provided, and nurses shared the patient information with doctors throughout the program period. The researchers set goals for the program and created three materials to support their achievement. The first was a booklet on examinations and treatments to supplement and strengthen the doctor's explanations. The second was a booklet that contained advice on psychological stress that patients may experience during treatment, and to convey the caregiver's closeness to the patient's feelings. The third was to encourage communication between patients and doctors by allowing both patients and doctors to record test results, treatment methods, or physical condition, and questions. These are in line with the advice of the routine psychosocial care guidelines of European Society of Human Reproduction (ESHRE) for fertility staff.[6] We also developed an interview sheet for nursing consultations so that nurses could understand the physical and living conditions of patients in detail; they could then utilize

this to provide appropriate information and advice tailored to each individual's requirements. Doctors and nurses ensured that a minimum of 30 min was used to communicate with patients. Doctors and nurses offering the program to patients were asked to attend a 2-h guidance workshop before participants were recruited into the program group. At the guidance workshop, researchers explained the program and used role-plays to demonstrate how to interact with patients in the program. Afterward, a question and answer session was held, and the answer sheets were edited and shared so that the protocol became clearer.

During the minimum 30-min session, doctors and nurses devoted themselves to patient care, by explaining and instructing patients how to use the "Infertility Guidance and Management- Examination & Treatment".

The nurse was able to understand the patient's needs using an interview sheet for consultations and gave each patient a booklet titled, "To Live Comfortably During Treatment" as a guide to instruct the patient and respond to consultations. The nurse provided the "My Treatment Notebook" and told the patients to fill it in appropriately and bring it at the time of the examination, to use it to communicate with the doctor. Furthermore, doctors and nurses were asked to continue sharing information at meetings, to evaluate the degree to which patients achieved the program's goals, and to fill out the program goal achievement evaluation sheet.

2.5 | Study outcomes and program goals

The primary outcome was the patient QOL measured using the SF-36v2 questionnaires, and the secondary outcome was the FertiQoL questionnaires in this study. Additional outcomes included treatment time required to achieve pregnancy, treatment cost, pregnancy rate, and withdrawal rate.

The goals of the education and care program were as follows: (1) to explain the patient's diagnosis and infertility treatment; (2) to
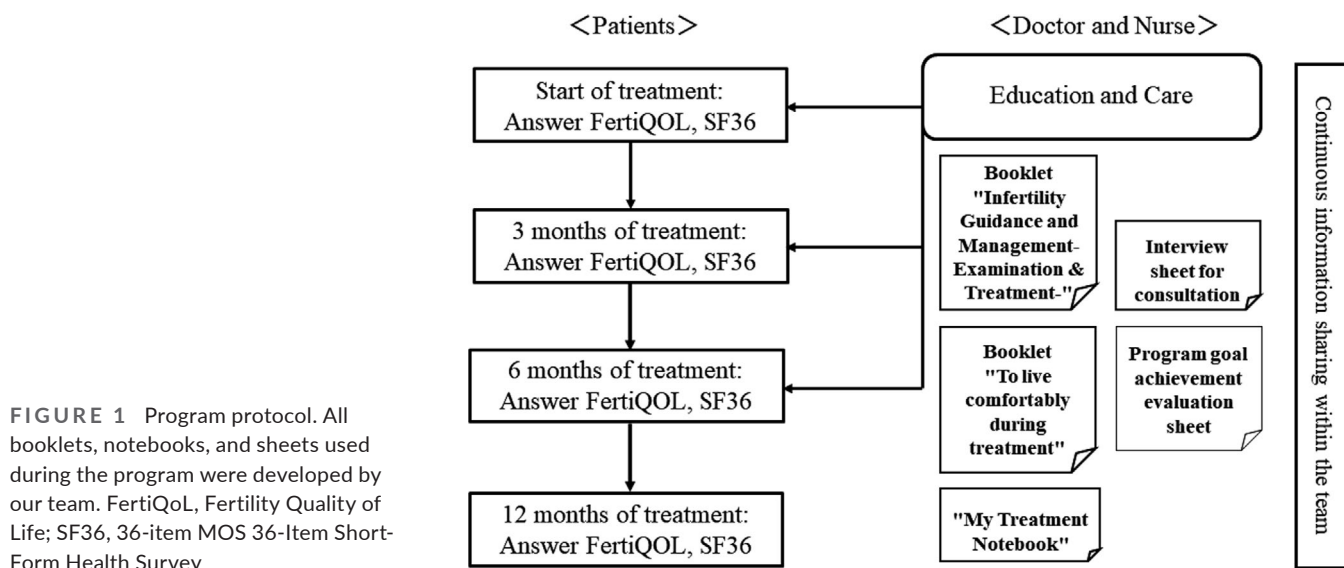

FIGURE 1 Program protocol. All booklets, notebooks, and sheets used during the program were developed by our team. FertiQoL, Fertility Quality of Life; SF36, 36-item MOS 36-Item Short-Form Health Survey

develop patient behaviors including asking questions and studying; (3) to help the patient describe her health condition clearly to the medical professionals; (4) to follow each patient's plan for her treatment; (5) to allow the patient to manage her daily life during treatment; and (6) to help the patient manage stress during treatment. The "Infertility Guidance and Management- Examination & Treatment" and "To Live Comfortably During Treatment" booklets, "My Treatment Notebook," and an interview sheet for consultations created specifically for this program were used to achieve the program's goals.

2.6 | Outcome indices

The SF-36v2 questionnaire was used as the primary outcome index. This questionnaire includes 36 items categorized into eight subscales, including one item regarding changes in health. The SF-36v2 is scored from 0 to 100 points, with higher scores indicating a higher QOL. The survey score can be compared with the national standard value of QOL. Summary scores of the physical, mental, and social components can also be determined.

The FertiQoL questionnaire was used as the secondary outcome index. The 36 items of this questionnaire include 34 items divided into six subscales, one item regarding physical health, and one item regarding overall life satisfaction. The questionnaire is scored from 0 to 100 points, with higher scores indicating a higher QOL. The FertiQoL can be divided into the core FertiQoL, comprising four subscales (emotional, mind/body, relational, and social), and the treatment FertiQoL, comprising two subscales (treatment environment and treatment tolerability). The Japanese version of the reliability coefficient Cronbach's α was 0.93 for the 34 items included in the six subscales of the FertiQoL, and the coefficients of each subscale ranged from 0.66 to 0.88.[19]

Additional outcomes measured included pregnancy rate, required length from treatment to achieving a positive pregnancy test (days from first visit to positive pregnancy test), infertility treatment costs (total medical expenses which were paid either by patients or by public insurance.), treatment withdrawal rate (the ratio of the total number of patients who did not come to the hospital to the number of patients at baseline), changes in lifestyle habits/physical function (including smoking, drinking, body mass index, and menstruation), and type of life events. To evaluate the goals of the program, a 13-item program goal achievement evaluation sheet and a 12-item questionnaire were completed by the nurses involved in the program.

2.7 | Statistical analyses

Descriptive statistics were used to analyze the characteristics of the participants. Continuous data are presented as means (standard deviations), and categorical data are presented as numbers (percentages). An unpaired t test or a cross-table chi-squared test and the number of Klamer correlations were used to compare the groups. Also, we used repeated measures mixed models to compare the groups. All statistical analyses were two-sided. Significance was set at $p < 0.05$, and all analyses were conducted using SPSS version 26.0 (IBM Corp.).

2.8 | Ethical considerations

This study was approved by the Research Ethics Committee of St. Luke's International University (approval date: April 28, 2017; approval number 17-A006) and was conducted according to the principles of the Declaration of Helsinki. All patients provided informed consent for their participation in this study.

3 | RESULTS

3.1 | Patients and facilities

A total of 173 female patients were included in this study. The control group included 104 patients who did not receive the additional education and care program. The program group included 69 patients who had received our education and care program.

We requested participation from 22 facilities nationwide and obtained consent from 17 facilities. At each participating facility, the control group was surveyed first. Once all patients in the control group completed the required surveys at 6 months, the participating facility was instructed to recruit patients for the program group. Of the 17 facilities that obtained consent, one experienced a decrease in nursing staff and three did not have any patients who met the inclusion criteria; therefore, the final analysis included data from 13 facilities. Eight facilities collected data for both the control and program groups, and five facilities collected data for either the control group ($n = 2$) or the program group ($n = 3$) owing to a lack of patients who met the inclusion criteria, a delay in the initiation of the study owing to a lengthy ethics review process, or personal preferences of patients.

3.2 | Patient characteristics

No significant differences were found between the characteristics of the control and that of the program groups (Table 1). In total, over 90% of the patients were employed. Patients in the program group were more likely to have irregular menstruation than those in the control group. The study flow chart is shown in Figure 2. The number of patients in the eight facilities that recruited participants in both the control group and the program group was 152, the number of patients in the two facilities that recruited participants into only the control group was 11, and the number of patients in the three facilities that recruited participants into only the program group was 10. There was no significant difference between the characteristics and the baselines of SF36 and FertiQoL in these three types of facilities.

TABLE 1 Patient characteristics

	Control group (n = 104)	Program group (n = 69)	p-value[a]
	[n/n, %] (%)	[n/n, %] (%)	(two-sided test)
Age (years)	32.7 ± 3.54 [103/104, 99.0]	32.3 ± 3.70 [68/69, 98.6]	0.447
Occupation	[98/104, 94.2]	[67/69, 97.1]	
Public officials	5/98 (5.1)	2/67 (3.0)	0.781
Office worker (regular employee)	48/98 (49.0)	35/67 (52.2)	
Office worker (Temporary staff)	4/98 (4.1)	2/67 (3.0)	
Self-employed / freelance	1/98 (1.0)	2/67 (3.0)	
Part-time job	14/98 (14.3)	6/67 (9.0)	
Housewife	16/98 (16.3)	11/67 (16.4)	
Unemployed	0	1/67 (1.5)	
Other	10/98 (10.2)	8/67 (11.9)	
Duration of infertility (months)	13.8 ± 12.31 [98/104, 94.2]	11.9 ± 6.02 [63/69, 91.3]	0.269
Height (cm)	158.7 ± 5.60 [103/104, 99.0]	160.2 ± 5.16 [66/69, 95.7]	0.091
Body weight (kg)	54.0 ± 9.12 [103/104, 99.0]	54.0 ± 7.04 [66/69, 95.7]	1
BMI	21.4 ± 3.24 [103/104, 99.0]	21.0 ± 2.46 [64/69, 92.8]	0.45
Smoking			
Yes	2 /102 (2.0)	3/65 (4.6)	0.326
Alcohol			
Yes	43/99 (43.4)	29/64 (45.3)	0.814
Irregular menses			
Yes	18/91 (19.8)	19/63 (30.2)	0.138
Menstrual symptoms			
Yes	50/89 (56.2)	37/61 (60.7)	0.585
History of pregnancy			
Yes	14/104 (13.5)	6/69 (8.7)	0.337
History of miscarriage			
Yes	9/103 (8.7)	5/68 (7.4)	0.746
Past history			
Yes	21/103 (20.4)	13/68 (19.1)	0.839
Present illness			
Yes	5/103 (4.9)	5/68 (7.4)	0.496

Note: Continuous data are presented as mean ± standard deviation. Categorical data are presented as ratio (percentage).

[n/n, %] (%); [A/B, %] A = Actual number of patients; B = Number of patients who can answer the item; % = A/B × 100

[a]p-value: Cramer's coefficient of association

3.3 | Primary outcome

The mean scores of all patients for each subscale of the SF-36v2 at baseline were as follows: physical functioning (PF) = 54.9, role physical (RP) = 51.5, body pain (BP) = 51.3, general health (GH) = 53.4, vitality (VT) = 47.8, social functioning (SF) = 49.9, role emotional (RE) = 48.8, mental health (MH) = 49.0, physical component summary (PCS) = 56.2, mental component summary (MCS) = 48.6, and role/social component summary (RCS) = 47.7. The scores of the VT, SF, RE, MH, MCS, and RCS subscales did not reach the national standard values at baseline or within 12 months of treatment (see Table S1). The SF-36v2 scores were not significantly different between the control and the program groups at any time point.

3.4 | Secondary outcome

The mean total FertiQoL score of all patients at baseline was 65.7 (SD 12.24), the mean core FertiQoL score was 71.3 (SD 15.53), and the mean treatment FertiQoL score was 69.2 (SD 12.80). The mean subscale scores at baseline were as follows: emotional = 59.6 (SD 18.08), mind/body = 59.9 (SD 18.10), relational = 71.6 (SD 17.04), social = 77.0 (SD 13.73), treatment environment = 68.1 (SD 16.44), and treatment tolerability = 62.0 (SD 14.40). The mean physical
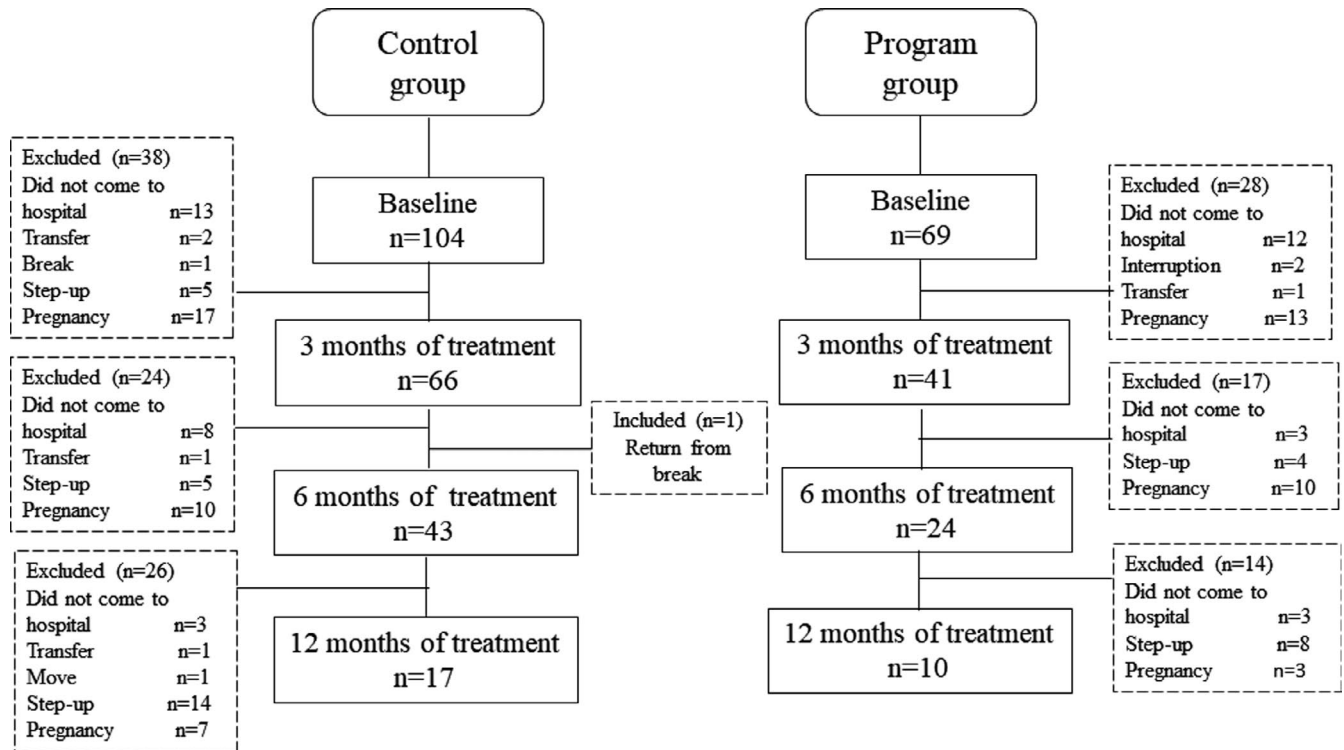
FIGURE 2 Patient flowchart

TABLE 2 Difference between groups in terms of changes in the treatment FertiQoL score using repeated measures mixed model

						95% CI: Difference of estimated mean	
Score (n = 17, 9)	Time	Difference of estimated mean (I–J)	SD	DF	p-value	Lower	Upper
Treatment FertiQoL score	Baseline	−5.011	5.087	24	1	−15.509	5.487
	3 months	−15.882	4.259	24	0.004**	−24.672	−7.092
	6 months	−7.941	4.753	24	0.431	−17.751	1.868
	12 months	−8.53	4.579	24	0.299	−17.982	0.921
Treatment tolerability	Baseline	−6.454	7.01	24	1	−20.922	8.014
	3 months	−16.176	5.859	24	0.043*	−28.269	−4.084
	6 months	−3.922	6.344	24	1	−17.016	9.173
	12 months	−2.696	7.498	24	1	−18.172	12.78
Treatment environment	Baseline	−2.941	4.977	24	1	−13.214	7.331
	3 months	−15.686	5.961	24	0.058	−27.989	−3.383
	6 months	−10.621	5.563	24	0.273	−22.103	0.861
	12 months	−12.84	4.885	24	0.059	−22.923	−2.758

Note: p-value: Bonferroni correction; $*p < 0.05$, $**p < 0.01$.

health score was 2.8, and the mean overall life satisfaction was 2.5 at baseline. No significant differences were found in the FertiQoL scores between the groups at baseline. The progress of FertiQoL is shown in the supplementary tables (Table S2). The treatment environment ($t = −3.507$, $p = 0.001$), treatment tolerability ($t = −2.229$, $p = 0.028$), and treatment FertiQoL ($t = −3.575$, $p = 0.001$) scores in the program group ($n = 41$) were significantly higher than those in the control group ($n = 66$) at 3 months. The treatment environment score remained significantly different between the control and the program groups at 6 months ($n = 24$; 63.9 ± 18.58 vs. $n = 43$; 55.9 ± 13.58 points; $t = −2.015$, $p = 0.048$) and 12 months ($n = 10$; 71.3 ± 15.23 vs. $n = 17$; 58.5 ± 9.73 points; $t = −2.629$, $p = 0.015$). Repeated measures mixed models' analysis was performed on the treatment FertiQoL (Table 2); the treatment FertiQoL scores ($p = 0.004$) and treatment tolerability ($p = 0.043$) differed between the two groups at 3 months (Figures 3–5).

No significant differences were found in the health status evaluation or satisfaction with QOL between the two groups at any time point.

3.5 | Additional outcome indices

Table 3 shows the treatment costs, methods, and outcomes. The treatment methods were significantly different between both groups at baseline, as artificial insemination and ovulation induction (via oral administration) were more common in the control group. No patients in the program group underwent artificial insemination at baseline. In both groups, the use of timing therapy decreased, and the use of artificial insemination increased over time.

The treatment withdrawal rate was higher in the program group (27.5%) than in the control group (22.1%), though the difference was not significant. Nurses cited the reason for withdrawing from treatment for busy patients' difficulty finding time to attend appointments. The reasons for withdrawal from treatment among patients who did not identify as busy were unclear.

Infertility treatments were advanced for more patients in the control group than for those in the program group, though the difference was not significant. The pregnancy rate was 32.7% in the control group and 39.1% in the program group, but the difference was not significant. The mean time to pregnancy of the control group (119 days) was not significantly different from that of the program group (127 days).

The mean total treatment cost of the control group (119 660 ± 107 558 Yen) was not significantly different from that of the program group (96 390 ± 92 946 Yen). The mean monthly treatment cost until pregnancy was 18 884 ± 20 765 Yen in the control group and 16 769 ± 11 410 Yen in the program group, which was not significantly different. The treatment cost required to achieve pregnancy per person (total treatment cost for each group/number of pregnancies) was 304 589 Yen in the control group and 155 707 Yen in the program group.
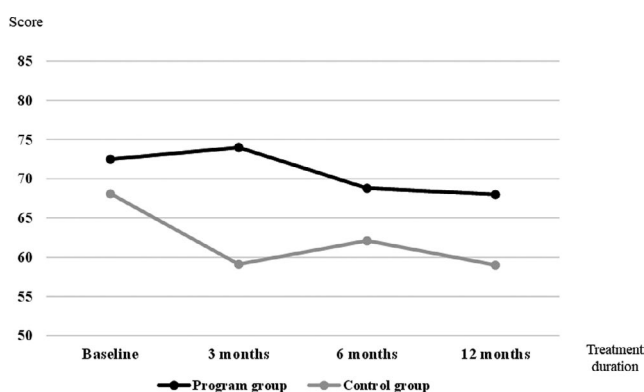

FIGURE 3 Treatment Fertility Quality of Life scores throughout the program. A *p*-value <0.05 was considered statistically significant

During the study period, one patient in the control group experienced miscarriage, one patient changed her place of residence, and two patients retired. In the program group, one patient experienced bereavement, one patient had an illness, and two patients changed their place of residence.

3.6 | Evaluation of the program

The goals of the program were evaluated at 3 and 6 months of treatment. The program goal achievement evaluation sheet was available in 53.7% of the patients (22/41) at 3 months and in 58.3% (14/24) at 6 months.

At 6 months, a higher percentage of patients achieved their goals of learning by themselves (50.0% vs 34.1%) of communicating their minds and views regarding their infertility treatment plan (50.0% vs 43.9%), of telling their doctor or nurse whether they were satisfied or not (45.8% vs 39.0%), of making lifestyle decisions for pregnancy (45.8% vs 39.0%), and of talking about how to deal with stress (37.5% vs 34.1%), than they did at 3 months. On the contrary, a slightly lower percentage of patients at 6 months achieved their goals of asking any question to a doctor (4.2% vs 7.3%), of observing and explaining their health conditions (41.7% vs 43.9%), of coordinating and managing their life undergoing infertility treatment (45.8% vs 46.3%), of understanding intensity and tendency of their stress (8.3% vs 9.3%), and of talking about their actual experiences of stress (25% vs 26.8%), than at 3 months. A lower percentage of patients achieved their goals of filling in the "My Treatment Notebook" (20.8% vs 29.3%), of using them for asking questions to their doctor or nurse (37.5% vs 43.9%), and of talking about coping skills to their actual experiences of stress (20.8% vs 26.8%), at 6 months than at 3 months.

Nurses at 11 of the participating facilities were asked to complete a questionnaire regarding the implementation of the program, and responses were received from 10 (90.9%) facilities. The same nurse provided education and care during all three sessions at 60% of the facilities and two sessions at 30% of the facilities. At 10% of the facilities, nurses were involved in only one education and care session. The sessions lasted the full 30 min at 70% of the facilities. The inability to take all 30 min of each session in the remaining 30% of the facilities was due to the lack of staff or patient preference. The program-specific booklets were used in eight (80%) to nine (90%) of the facilities. The notebook was used in five (50%) of the facilities, and the interview sheet was used in 90% of the facilities.

The reported difficulties in implementing the program included recruiting patients who met the inclusion criteria, securing 30 min of time for each session, and adjusting the patient's consultation date and the program nurse's working day. Some advantages of the program were patients' anxiety, and problems were addressed, and this led to a greater understanding of and support for the patient. Improved cooperation between the doctors and other team members was also reported. Nurses reported receiving more positive reactions than negative reactions from patients in the program.
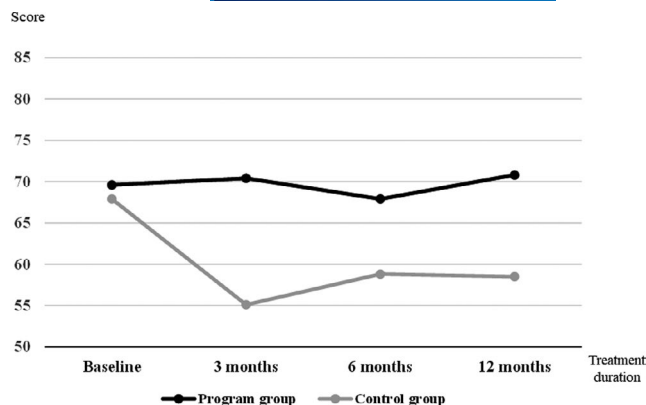
Score

FIGURE 4 Treatment environment scores throughout the program. A *p*-value <0.05 was considered statistically significant
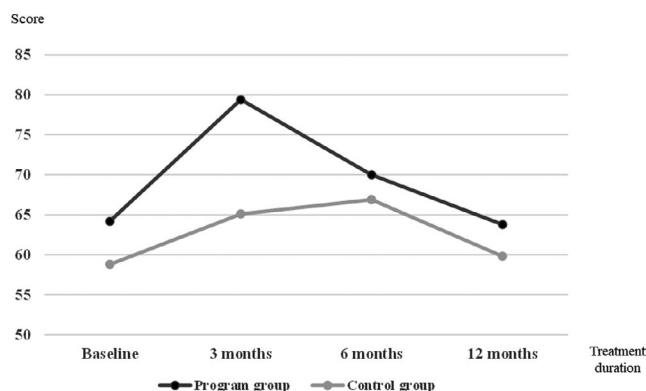
Score

FIGURE 5 Treatment tolerability scores throughout the program. A *p*-value <0.05 was considered statistically significant

4 | DISCUSSION

The education and care program was found to influence the treatment FertiQoL scores of female patients undergoing non-ART infertility treatment. Thus, the results of this study suggest that a program in collaboration with a reproductive medicine specialist and fertility nurse could have a positive effect on patients' QOL. Moreover, the treatment cost required to achieve pregnancy per person was lower in the program group than in the control group. Regarding treatment costs, there was a difference in treatment methods between the two groups, with patients in the control group having artificial insemination, but patients in the program group did not have artificial insemination at baseline; thus, differences in treatment methods may have affected the cost.

4.1 | SF36-v2 and FertiQoL scores in women undergoing non-ART fertility treatment

The mean score of the SF-36v2 for healthy women aged 30–39 years has been reported as lower than the national standard value for MH

and MCS only.[18] Scores for the subscales of the SF-36v2, excluding the PF and GH subscales, have also been reported to be lower than the national standard value.[17] In this study, the scores for the VT, SF, RE, and MH subscales and MCS and RCS were lower than the national standard values, indicating that women undergoing treatment for infertility have a lower psychosocial QOL than healthy women of the same age. The mean total FertiQoL score in this study was 65.7 points, which is slightly higher than that reported in a previous Japanese study (average total FertiQoL, 62.4–63.7 points)[19,20] and that of a previous international study (*n* = 930, average total FertiQoL, 55.4 points), which obtained data from the USA, Australia/New Zealand, Canada, and the UK,[21] as well as that of a Chinese study (*n* = 151, average total FertiQoL, 63.34 points).[22] In our study, the mean score of the emotional subscale (sadness, loss, depression, and anger) was the lowest and the relational subscale was the highest among the subscales, and this was similar to the results of a Turkish study.[23]

4.2 | Program outcomes

In our study, no differences were found in the SF-36v2 scores of the control or program groups at any time point, indicating that the program implemented in this study had little effect on the SF-36v2 scores. In a cluster randomized controlled trial of female patients undergoing non-ART infertility treatment in Japan, intervention effects were observed in the RP, RE, and PCS subscales.[17] The lack of a significant difference in these subscales in our study may be due to differences in the content and method of the intervention program. The number of patients may have provided insufficient power to detect a significant difference.

The treatment FertiQoL score and treatment tolerability were significantly different between the two groups at 3 months, indicating the effect of the program. Although no significant difference was observed in the treatment environment, a tendency for a difference between the two groups at 3 and 12 months was noted. These results may indicate that the program temporarily maintained patient satisfaction regarding the relationship with medical staff, patient understanding, and patient care. However, no differences in emotional, mind/body, relational, and social subscales, or in the core FertiQoL scores, were found between the program and the control groups, suggesting that the education and care program had no effect on these scores. These results may be attributed to the fact that this program was provided by medical professionals at medical institutions and aimed to promote patient understanding of the treatment and to coordinate the treatment with the patient's daily life. A longitudinal study reported that the overall impression of the facility, environment, and equipment inside the facility, and adequate time to discuss concerns with medical staff affected patients' satisfaction with treatment.[24] This program dedicates a specific time for the education and care of patients with infertility, and this may have influenced the treatment environment score. There are few intervention studies for subjects who are not patients receiving ART. In an

TABLE 3 Treatment methods and outcomes

	Control group (n = 104)	Program group (n = 69)	p-value[a]
	[n/n, %] (%)	[n/n, %] (%)	(two-sided test)
Type of treatment			
Baseline			
Timing therapy	87/103 (84.5)	55/64 (85.9)	0.003
Artificial insemination	8/103 (7.8)	0	
Ovulation induction (Oral)	8/103 (7.8)	2/64 (3.1)	
Ovulation induction (Injection)	0	1/64 (1.6)	
Ovulation induction (Self-injection)	0	1/64 (1.6)	
Other	0	4/64 (6.3)	
3 months of treatment			
Timing therapy	34/64 (53.1)	18/35 (51.4)	0.457
Artificial insemination	18/64 (28.1)	8/35 (22.9)	
Ovulation induction (Oral)	10/64 (15.6)	6/35 (17.1)	
Ovulation induction (Injection)	1/64 (1.6)	0	
Ovulation induction (Self-injection)	1/64 (1.6)	1/35 (2.9)	
Other	0	2/35 (5.7)	
6 months of treatment			
Timing therapy	10/43 (23.3)	6/23 (26.1)	0.395
Artificial insemination	27/43 (62.8)	12/23 (52.2)	
Ovulation induction (Oral)	4/43 (9.3)	4/23 (17.4)	
Ovulation induction (Injection)	0	1/23 (4.3)	
Ovulation induction (Self-injection)	2/43 (4.7)	0	
Other	0	0	
12 months of treatment			
Timing therapy	2/14 (14.3)	2/9 (22.2)	0.297
Artificial insemination	11/14 (78.6)	4/9 (44.4)	
Ovulation induction (Oral)	1/14 (7.1)	2/9 (22.2)	
Ovulation induction (Injection)	0	1/9 (11.1)	
Ovulation induction (Self-injection)	0	0	
Other	0	0	
Transfer or move			
Yes	5/104 (4.8)	1/69 (1.4)	0.404
Did not come to hospital			
Yes	23/104 (22.1)	19/69 (27.5)	0.47
Step up to ART			
Yes	25/104 (24.0)	11/69 (15.9)	0.252
Pregnancy			
Yes	34/104 (32.7)	27/69 (39.1)	0.419
Duration until pregnancy (day)	119.2 ± 82.75 [33/34, 97.1]	126.8 ± 84.85 [25/27, 92.6]	0.732
Total average treatment cost (yen)	119 660 ± 107 558 [84/104, 80.8]	96 390 ± 92 946 [42/69, 60.9]	0.234
The average monthly treatment cost until pregnancy (yen)	18 884 ± 20 765 [32/34, 94.1]	16 769 ± 11 410 [25/27, 92.6]	0.649
The treatment cost required to establish a pregnancy for one person (yen)	304 589	155 707	

Note: Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as ratio (percentage) [n/n, %] (%); [A/B,%] A = Actual number of patients; B = Number of patients who can answer the item; % = A/B × 100

[a]p-value: Cramer's coefficient of association.

intervention study that was conducted to educate patients undergoing artificial insemination about coping strategies, researchers held a few sessions apart from outpatient setting, and this was effective for specific coping strategies for patients.[14] However, the education and care program of this study contributes to maintaining a good relationship between patients and medical staff by dedicating a small amount of time to frequently collaborate with doctors and nurses regarding daily medical care.

No significant differences were found in the treatment withdrawal rate, pregnancy rate, or duration until pregnancy between both groups. However, the average monthly treatment cost until pregnancy and the treatment cost required to establish pregnancy for one person were lower in the program group than it was in the control group. As mentioned above, it is undeniable that treatment cost may have affected our findings because some patients in the control group had advanced to artificial insemination and were not in the program group at baseline. However, the difference in the patient's QOL means that patients participated in the treatment process with careful consideration and satisfaction, which also influenced the choice of treatment method; as a result, the cost of treatment may have been suppressed. A larger study is needed to verify these results.

4.3 | Evaluation of the program

In 60% of the facilities in this study, patients were able to meet the same program nurse in all education and care sessions, while in 40% of facilities they talked to program nurses only twice or once, out of three occasions in this study. In this regard, we acknowledge that there were challenges with protocol compliance in the program. On the contrary, 70% of the facilities in this study reserved 30 min for the program; hence, the interview sheet was used frequently and was considered to be an indispensable tool for implementation of the patient's assessment. However, nurses could not evaluate the achievements of goals for all patients in the program group, suggesting that assessment of patients' goals was challenging for nurses. However, nurses could assess the patients' behaviors and evaluations of the program, confirming that nurses spent a substantial amount of time with the patients. In turn, the program improved the practices of the nurses, as it deepened their understanding of patients and improved their patient rapport through repeated education and care sessions; this was achieved despite difficulties such as patient recruitment, workload, and adjustment to the new program. The relationships established during the education and care sessions are believed to have contributed to the high treatment environment score of the FertiQoL in the program group.

4.4 | Suggestions for team care in non-ART fertility treatment

Multidisciplinary teams in reproductive medicine often focus on ART treatments that manipulate embryos and gametes. However,

the results of this study suggest that non-ART infertility treatments provided by a collaborative team of doctors and nurses result in improved medical staff relationships and patient understanding and satisfaction. Therefore, we recommend the implementation of multidisciplinary teams during non-ART infertility treatments.

4.5 | Study limitations

This study has some limitations that have not already been discussed. First, the results of the SF-36v2 questionnaire should be interpreted with care as the target sample size was not reached within the study period; this was because only a few patients met the inclusion criteria, and securing nursing staff for daily patient recruitment during data collection was difficult owing to their busy working schedules. Second, the program was not evaluated by the patients. It is important to determine the patients' perception of the program and how the program affected the patients' QOL. Randomized controlled trials should be conducted to verify the results of this study and determine the most effective aspects of the program. Implementation research is required to promote the introduction and dissemination of this program.

5 | CONCLUSION

While the program used in this study did not affect the patients' SF-36v2 scores, the program group had higher treatment FertiQoL scores than the control group, indicating that the program may temporarily maintain the relationship between health care providers and patients. In addition, the cost required to achieve pregnancy per patient was lower in the program group than in the control group, although the length of treatment required before pregnancy, pregnancy rate, and treatment withdrawal rate were not significantly different between the groups.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

This study was approved by the Research Ethics Committee of St. Luke's International University (approval date: April 28, 2017; approval number 17-A006).

HUMAN RIGHTS STATEMENTS AND INFORMED CONSENT

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation

(institutional and national) and with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from all patients for being included in the study.

ORCID

Akiko Mori https://orcid.org/0000-0001-7879-4048
Yasushi Takai https://orcid.org/0000-0002-3872-8481

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.