

Evaluating the effect of nurses' supportive and educational care on GATA2 gene expression and quality of life in patients with endometriosis

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ABSTRACT

Endometriosis is one of the women's aggressive but benign diseases, formed by the presence of endometrial glands and stroma outside the uterine cavity. Various genes, including the GATA2 gene, are involved in the pathogenesis of endometriosis. Since this disease affects patients' quality of life, this study was conducted to investigate the effect of nurses' supportive and educational care on the quality of life of endometriosis patients and its role in GATA2 gene expression. For this purpose, 45 patients with endometriosis participated in this research, a semi-experimental before-and-after study. The instrument used was demographic information and quality of life questionnaires affiliated with Beckman Institute, which were completed in two stages before and after implementing patient training and support sessions. The real-time PCR technique was also used to evaluate the expression level of the GATA2 gene after obtaining endometrial tissue from patients before and after the intervention. Finally, the received information was analyzed using SPSS software and statistical tests. Based on the obtained results, the average quality of life score before the intervention was 51.73 ± 13.91 , and after the intervention was 60.46 ± 13.80 ($P < 0.001$). Also, in all four dimensions of quality of life, patients' average scores increased after the intervention compared to before the intervention. Still, this difference was significant only in the two dimensions of physical and mental health ($P < 0.001$). GATA2 gene expression before intervention was 0.35 ± 0.13 among endometriosis patients. After the intervention, its amount reached about three times, i.e., 0.96 ± 0.32 , which showed a significant difference between the two groups at the 5% probability level. In general, the results of this research confirmed the positive effect of educational and support programs in improving the quality of life of breast cancer patients. Therefore, it is suggested to design and implement such programs in a broader manner and based on patients' educational and support needs.

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Introduction

Endometriosis is one of the women's aggressive but benign diseases, which is formed by the presence of endometrial glands and uterine stroma outside of the endometrium and uterine muscle in the peritoneal and visceral surfaces of the female pelvis (1, 2). It affects about 15-20% of women of reproductive age. Endometriosis is a multifactorial disease caused by the interaction of genetic and environmental factors (2). Since the origin of endometriotic ectopic tissue and its pathogenesis are highly debated, various etiologies have been proposed. The most accepted of them is the theory of menstrual blood return (3). This theory is also called Implantation (4). According to it, the menstrual tissue and blood are withdrawn through the fallopian tubes, placed on the pelvic parts, and start growing and multiplying in the same area, leading to endometriosis. Other theories include coelomic metaplasia theory, embryonic remnant theory, lymphatic-vascular metastasis, hormonal factors, environmental pollution, and genetic factors in endometriosis. It is possible to treat endometriosis with medication or surgery (3, 5). In most cases, both treatments are done together. Surgical removal of scar tis-

sue is the most effective treatment with the lowest rate of endometriosis recurrence, which can significantly impact a patient's quality of life (6).

Quality of life is a concept that has been a challenging issue for many centuries. Still, in recent years, it has attracted particular attention for endometriosis patients and their survival rates and longevity (7). One of the reasons for the increased attention to this concept in the new era and more emphasis on the quality of life versus the quantity of life is that today survival is not the only consideration and people want a good quality of life and unlike in the past when the evaluation of the effect of treatment is based on recovery, disability. It was death. The quality of life is evaluated as one of the essential consequences and determining indicators of the effect of disease treatment (6).

Today, quality of life is sometimes used instead of health in various studies (6-8). But the quality of life includes more dimensions than health status and is influenced by more factors. Its main areas include physical, mental, social, and spiritual health (8). Although these areas can be separated and examined separately, there is an interaction between them and a disorder in each, which of the mentioned dimensions has a direct and significant

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effect on other measurements. One of the most important measures at this level is supportive, educational care and, as a result, increasing the quality of life of people with endometriosis (9). But unfortunately, not enough attention is paid to this issue. For example, Mjali et al.'s study (10) showed that most (63.6%) patients with endometriosis received moderate supportive care from nurses. In their research on self-care in patients with endometriosis, Vithana et al. (11) concluded that the self-care practices performed by the studied subjects were insufficient. In their belief, nurses play an essential and influential role in improving the quality of life of endometriosis patients by encouraging and promoting proper self-care due to their longer and more direct contact with the patient. In this way, patients can return to their everyday lives and return to society. Orem's theory can be helpful in this field and in achieving these goals (12). According to Orem's definition, self-care is the learned behavior that a person performs to maintain or promote life, health, well-being, and prevention and treatment of disease (13). According to this model, the patient must cooperate in self-care, and it is clear that a person needs awareness to accept such responsibility. Nurses are the most central members of the health team in meeting this existing need, which is necessary, along with training to improve behavioral skills in patients and self-sufficiency in self-care, to help patients make more efforts to control the disease and improve quality (14).

Evidence shows that patients with endometriosis have higher oxidative stress and inflammatory and pro-inflammatory cytokines levels (15, 16). To reduce these symptoms and increase the healing process and the quality of life of patients, the researchers emphasized the studies of appropriate interventions because it has been seen that the level of oxidizing indicators is high in the secretions and uterine fluids of people who have endometriosis (16). Recently, a third category of transcription factors has been introduced, the lack of which contributes to the development of infertility diseases (17). These factors include some Zinc Finger Transcription Factor (GATA) proteins, which naturally participate in cell proliferation and differentiation and increase cell differentiation (18). The impaired function or reduced expression of these factors due to the lack of differentiation of the affected cells and cell cycle exit contribute to the development of endometriosis (19). The family of GATA transcription factors in mammals consists of 6 members GATA1-GATA6. Also, based on its role in red blood cell differentiation, GATA2 is likely to effectively induce the growth and essential characteristics of endometriosis precursor cells (20).

Therefore, in the current study, the effect of nurses' supportive and educational care was evaluated on the quality of life and GATA2 gene expression in patients with endometriosis.

Materials and Methods

Patients' information and life quality evaluations

This research was a semi-experimental before and after study in which 45 patients with endometriosis participated in 2021. Sampling was done as available, and according to the recent studies on the quality of life, the entry criteria for the study were selected (21, 22). The entry criteria included being 65-18 years old, reading and writing literacy, physical and mental strength, and willingness to partici-

pate in the study. The exclusion criteria did not want to continue participating in the study and lack of access to the participants during the study for any reason (including death). Three questionnaires were used for demographic information, examination of Oram's health status, and quality of life. The demographic information questionnaire by the researcher based on the research conducted in this field includes the variables of patient age, age at diagnosis, duration of disease, age of first pregnancy, period of first breastfeeding, history of other conditions, and history of endometriosis among relatives and education level.

In this study, the participant's quality of life was assessed using the standard tool for evaluating the quality of life of endometriosis patients related to the National Medical Center and Beckman Research Institute. This tool examines the quality of life of women with endometriosis in 4 dimensions physical, mental, social, and spiritual health and includes 44 items. Each item is scored based on 0 to 10. This way, a score of zero is assigned to the worst situation, and a score of 10 is assigned to the best situation. The scoring in several cases (41, 33-37, 31, 17-29, 10, 9, 1-7) in this tool is reversed compared to other cases. Also, items 1 to 8 of this questionnaire (a total of 80 points) were for the physical dimension, items 9 to 30 (a total of 220 points) were for the psychological dimension, and items 31 to 37 (a total of 70 points) were for the social dimension, and finally, items 38 to 44 (a total of 70 points) were for the spiritual dimension. The highest sample the research unit can get after completing this tool is 440, and the lowest score is zero.

In this research, due to the different number of questions in each field, to compare the average scores of different dimensions of quality of life, the scores obtained in each dimension were first multiplied by 100 and then divided by the maximum score of that dimension. As a result, all scores obtained ranged from 0 to 100.

Regarding the validity of this tool, the face and content validity method was used. Also, two indices, Content Validity Ratio (CVR) and Content Validity Index (CVI), were used, and CVR of more than 0.51 (minimum value set by Lavashe for 14 experts) and CVI of more than 0.79 were obtained. The internal consistency method was also used for the reliability of the tool; In this way, Cronbach's alpha coefficient was calculated after completing the questionnaires by the people participating in the research, and the reliability coefficient was 0.8.

To implement the intervention, the researcher first explained all the work steps to each of the patients in simple language, and they were allowed to make a decision to participate in the study and then proceed to obtain written informed consent and complete demographic information questionnaires, check the health status. The quality of life was measured before the intervention, and patients were invited to participate in 8-45 minute sessions held on Wednesdays every week in the hospital.

In this research, the quality of life questionnaire scores, which the patients completed before the intervention, were recorded as a pre-test. Based on the questionnaire to check the health status of Orem, the self-care needs of the patients were determined. The educational sessions were held in groups and based on the identified needs of the patients according to Orem's self-care model, with familiarization with endometriosis and how to adapt to this disease, the ways of treatment, and its complications, type

of nutrition, spiritual health, mental health, and physical therapy of organs were held (21, 22).

In each meeting, necessary explanations were given about one of the cases, and during the sessions, the questions and problems of the patients were answered. Also, to support the patients, things such as individual referral to a psychologist, nurse practitioner, palliative medicine, nutritionist, and meeting with the treated patients were done. Finally, pamphlets and educational CDs were provided to the patients to understand the issue better and remind them of essential points. In the last session, according to the previous appointment, a general test of the learned material was taken, and the items that needed retraining were identified, and in a 6-hour session, usually one-day training, all the required materials were reviewed in an intensive form. Finally, we collected the quality of life of 45 patients with endometriosis after the intervention was measured using a quality of life questionnaire and all the obtained information.

Evaluation of GATA2 gene expression

The endometriosis patients under study removed endometrial tissue samples using pipel. Similarly, the consent form of the patients to cooperate in the project and informed that their names and personal information would not be available to the public was read and signed by the individual. Each tissue was divided into 50-100mg pieces. Then, to protect the tissue's genetic material and preserve it better, about 500 microliters of RNA Later liquid were poured on the samples. The tissues were immediately transferred to a freezer at -80 degrees Celsius.

RNA extraction from frozen tissue samples was performed by Trizol (Invitrogen, USA) according to the protocol. Nanodrop device (Thermo Scientific, Germany) was used to quantitatively and qualitatively check the purity of the extracted RNAs. To perform the next steps, the RNA samples must be free of contamination for genomic DNA. Before cDNA synthesis, RNA samples extracted by the enzyme (#EN0521-Fermentas, DNase I) (Thermo Scientific, Germany) were treated for 30 minutes in a thermostat (Eppendorf, USA) at a temperature of 37 °C. Then 2µl of 50 mM EDTA was added to each of the samples, and they were incubated again for 5-7 minutes at 65°C to inactivate the DNase I enzyme. According to its protocol, this study used a cDNA synthesis kit (scientific, Germany) for cDNA synthesis. Then, the quality and non-contamination of the synthesized cDNA samples compared to DNA were measured by performing the Control-PCR reaction, and finally, the synthesized cDNAs were stored at -20°C.

To check the level of GATA2 gene expression, primers were designed with Generunner and Perlprimer, Primer 3 software, and the quality of the primers was checked on Nucleotide Blast and Primer Blas websites (<http://blast.ncbi.nlm.nih.gov.com>). The β-Actin primers were de-

signed as housekeeping primers to control gene expression. The sequence and information of the primers are presented in Table 1.

The reactions were performed using Cybergreen (Applied Bios, USA) and a detector system. Each reaction contained 10 µl of SYBR® Premix Ex Taq II, 3pmol of GATA2 primer, 25ng/µl of synthesized cDNA, which was made up to 20 µl with water. The concentration of β-actin primers was considered equal to the concentration of the same expression primer for each reaction. Each reaction was carried out with temperature and initial conditioning conditions at 95 degrees Celsius for 10 minutes, followed by 40 cycles including 95 degrees Celsius for 15 seconds and 60 degrees Celsius for 1 minute. All the reactions were repeated twice to increase accuracy, and positive and negative control experiments were performed each time. The obtained information was processed by software 7500 version 2.0.1. Finally, the values of CT (cycles where the fluorescence value is higher than the background value) were calculated using the obtained results.

Statistical analyses

The quality of life of 45 patients with endometriosis after the intervention was measured using a quality-of-life questionnaire, and all the obtained information was collected. Data analysis was also done with the help of SPSS statistical software and using descriptive indicators (prevalence, percentage, mean, standard deviation), and an analysis of paired t was done at the significance level of P<0.05. Also, GATA2 gene expression was evaluated in endometriosis patients. SPSS software and the One-Way ANOVA statistical method were used to check the significance of the data. The Chi-square test was also used to compare qualitative variables. A P-value less than 0.05 were considered for all analyses.

Results

The average age of the patients was 44.68±8.43, and 68.9% were between 40-59 years old. Their average age when the disease was diagnosed was 43.77 ± 8.34. The education of 62.2% was a high school degree, and the duration of infection in 80% of the samples was less than one year. In 91.1% of people, there was no history of this disease in relatives. The average age of first pregnancy and breastfeeding was reported as 19.14±2.69 and 19.87±2.70, respectively. The paired t-test shows the scores of people in the four dimensions of quality of life before and after the intervention and the difference between the two, shown in Table 2. In all four dimensions of quality of life, the average score of people increased after the intervention compared to before the intervention. Still, this difference is significant only in the two dimensions of physical and mental health (P<0.001). Also, regarding the general

Table1. The sequence of expression primers designed for β-Actin and GATA2..

Gene		Primer Sequences	PCR Product Length
β-Actin	Forward	5'-CAAGATCATTGCTCCTCCTG-3'	95bp
β-Actin	Reverse	5'-ATCCACATCTGCTGGAAGG-3'	
GATA2	Forward	5'-TCCAGTACCGAGAGAAAGCCTA-3'	150bp
GATA2	Reverse	5'-GCAGGATGTCATAGGTCACG-3'	

Table 2. Comparison of different aspects for the life quality of the participants in the research before and after the intervention.

Dimensions of life quality	Mean ± Standard deviation			P-value
	Before Intervention	After Intervention	Difference	
physical health	53.83 ± 15.22	68.75 ± 15.55	17.12 ± 14.91	0.001*
mental health	45.62 ± 19.07	55.46 ± 18.36	18.11 ± 9.83	0.001*
Social health	45.26 ± 20.85	49.65 ± 18.50	16.68 ± 4.38	0.085
mental health	74.98 ± 10.36	77.55 ± 11.12	10.54 ± 2.57	0.0109
Average overall score	51.73 ± 13.91	60.46 ± 13.80	13.77 ± 8.73	0.001*

*: Based on the results obtained at the error level of 5% (P<0.05), the scores of people in the dimensions of physical and mental health and overall quality of life are known to be significant.

dimension of quality of life before and after the intervention, it was observed that before the intervention, the average score of the sample of people on the quality of life increased to 51.73±13.91. After the intervention, this score increased to 60.46±13.80 and based on this, the score of the people on the quality of life in the post-test compared to the pre-test, an average of 13.77 ± 8.73 units increased. The effect of nurses' supportive and educational care on the quality of life of endometriosis patients is known to be significant (P<0.001).

According to the analysis, GATA2 gene expression before intervention was 0.35 ± 0.13 among endometriosis patients. After the intervention, its amount reached about three times, i.e., 0.96 ± 0.32, which showed a significant difference between the two groups at the 5% probability level (Figure 1).

Discussion

The results of the present study aimed to investigate the effect of nurses' supportive and educational care on the quality of life of endometriosis patients and its role in GATA2 gene expression. Our results showed that the patient's quality of life improved after implementing nurses' supportive and educational care, which aligns with the study of Della Corte et al. (7). In their study, the quality of life improved significantly after applying the self-care model in the test group compared to the control group. According to their belief, in the self-care program, a person learns activities that take responsibility for his health. It also improves the ability to communicate with the surrounding environment, perform adaptive actions and behaviors, and as a result, improve the quality of one's life. Similarly, the Das et al. study (23) results in implementing the self-care education program to enhance the quality of life of patients with esophageal cancer are consistent with the present research findings.

Regarding the different aspects of the quality of life, it was observed in this research that the physical health dimension of the patients had increased the most, and this increase was found to be significant, which is in line with the study of Olayide et al. (24). So that in their research, to investigate the effect of education on the quality of life of breast cancer patients, they concluded that after counseling and education in the field of breast cancer treatment and standard care, the quality of life of patients has increased in all aspects. But the most significant increase was related to the physical element (25). Wang et al. (26) and Warzecha et al. (8) also reached the same conclusion regarding the quality of life of hemodialysis patients and the elderly

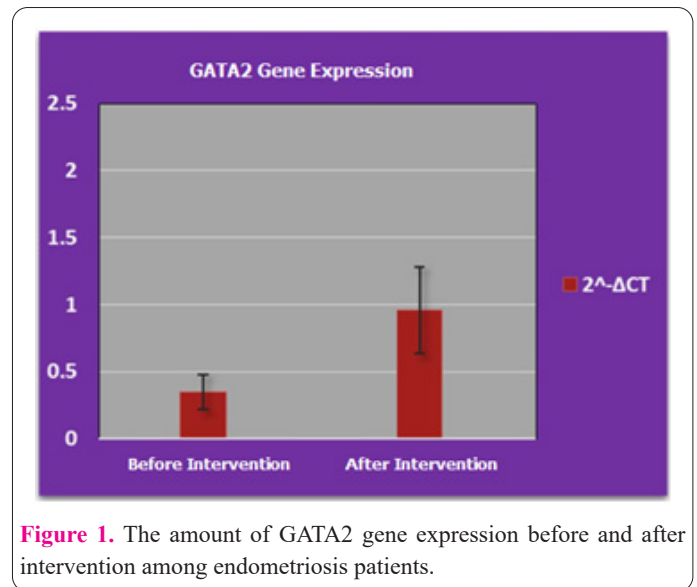


Figure 1. The amount of GATA2 gene expression before and after intervention among endometriosis patients.

in their studies, respectively, and it was found that the average scores of people in the dimension of physical health were significantly higher after training. Because one of the most critical aspects of the quality of life that is disturbed by endometriosis is the physical dimension, and seeking help from a specialist and getting to know the solutions to deal with problems and many other things that are all related to a person's performance status. Significantly, it positively affects performing daily activities and, consequently, the life quality of endometriosis patients.

Patients' mental health is another dimension of life quality, which in this study has been significantly increased by implementing supportive and educational care from nurses before the intervention. Endometriosis treatment is associated with many psychological pressures, some of which reduce the quality of life and lead to anxiety or depression. In a study conducted by van Barneveld et al. (27) to investigate depression and anxiety in women with endometriosis, it was shown that the level of depression and anxiety in the patient group was significantly higher compared to the healthy group. In Casalechi et al.'s research (28), patients rated the treatment's psychological side effects, such as anger, anxiety, or worry, as more severe than the physical side effects, such as abortion. However, the self-care program and the improvement of information and awareness about the disease can reduce anxiety, strengthen a person's perception of life goals, reduce mood disorders, and improve patients' adaptability and adaptive behaviors. Therefore, it can enhance the quality of life, similar to Mińko et al.'s research (29). They investigated the effect of a self-care program on the quality of life of 70 acute

leukemia patients undergoing chemotherapy. They found that implementing this program significantly improved the quality of life and especially the psychological dimension in the test group compared to the control group. Omar et al. (30) conducted a study on 200 people with lung cancer, and nurses provided the participants with adequate care in preventing depression during 6 to 8 sessions per month through telephone calls. However, the positive effect of the results was determined very late (after 32 months). In this regard, Yela et al. (31) concluded that the short-term results were obtained through usual nursing care and support and face-to-face training compared to telephone training and support.

Regarding the two dimensions of social health and spiritual health, it was found in this study that the average score of people increased after the intervention compared to before the intervention, but this difference was not significant. Regarding social health, it can be said that endometriosis restricts people's social activities and affects their relationships and access to interpersonal resources. As a result, it increases the possibility of reducing communication with others and their isolation in society (32). In many types of research, we have seen that at the end of the treatment, the social health of endometriosis patients was lower than at the beginning of the treatment period. Based on this, a minimal change or even a constant change in the quality of life score and especially the social health of patients is considered a success for researchers (33, 34).

Regarding the dimension of spiritual health, the results obtained align with the study of Golchin et al. The lives of clients have improved. But the difference created regarding the spiritual dimension before and after the intervention was not significant, although Symonds et al.'s research (35) showed that spiritual health strongly affects endometriosis patients. Spiritual and religious peace may be even more important than physical and mental health, reminding us of the need to pay special attention in this field, identify influential factors, and carry out appropriate interventions to improve spiritual health.

One of the critical results of the current research was the significant increase in GATA2 levels in patients after the intervention. The results of the present study are consistent with the results of some researchers who stated that endometriosis leads to a decrease in the expression of the GATA family gene (36, 37). In the study of endometriosis, researchers found that many genes are involved in the improvement and development of this disease, among which the GATA family could be mentioned (37). The studies show that endometriosis is caused by changes in some members of the GATA family, such as GATA2 (38). Incomplete function or reduced expression of this factor due to the lack of differentiation of the affected cells and cell cycle exit are involved in the development of endometriosis (39). The research shows that the change of crucial molecules or signaling pathways, by influencing cell proliferation, migration, and invasion, can be effective on the level of oxidative damage and inflammation and, as a result, the occurrence and progression of this disease (39). However, modifiable factors such as nutrition and physical activity help prevent and treat this disease by regulating and modulating it (40). Also, our study showed that support educational interventions for endometriosis patients positively affect the quality of life and the expression of this gene.

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Authors' contribution

This study was done by the author named in this article, and the author accepts all liabilities resulting from claims which relate to this article and its contents.

Conflicts of interest

There are no conflicts of interest.

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Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Statements and Declarations

The author declares that no conflict of interest is associated with this study.

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