Effectiveness of Instructional Guidelines on Awareness and Perception of Premature Ovarian Insufficiency Women regarding Stem Cell -Based Ovarian Regeneration

Doaa Lotfi Afifi Alqersh (1), Hanan E. Nada⁽²⁾

Assistant Professor of Maternal & Newborn Health Nursing, Faculty of Nursing, Menoufia University.
 Lecturer of Maternal & Newborn Health Nursing, Faculty of Nursing, Menoufia University.

Abstract

Background: Premature ovarian insufficiency (POI) is defined as a partial or complete loss of ovarian endocrine function and fertility before the age of forty. **Aim**: was to evaluate the effectiveness of instructional guidelines on awareness and perception of premature ovarian insufficiency women regarding stem cell-based ovarian regeneration. **Methods**: A quasiexperimental one group pre-test/post-test design was conducted at Menoufia University Hospital with 152 women diagnosed with POI. Women completed a structured questionnaire, an awareness assessment questionnaire, and a perception assessment scale. **Results**: Postintervention, awareness levels and positive perception of stem cell therapy significantly improved (p < 0.001). Major barriers to treatment included high costs, limited treatment availability, and insufficient information (36.2%,29.6% & 21.4%) respectively. **Conclusion**: Instructional guidelines effectively enhanced awareness and perception of POI women regarding stem cell-based ovarian regeneration. **Recommendation**: These findings highlight the need for continued education and improved healthcare accessibility to support informed decision-making on emerging fertility treatments.

Keywords: Infertility, premature ovarian insufficiency, premature ovarian failure, regenerative medicine and stem cell therapy.

Introduction

Premature ovarian insufficiency (POI) refers to a partial or complete loss of ovarian endocrine function and fertility before the age of 40. POI, which is caused by early ovarian follicle depletion and premature follicle destruction, frequently coexists with amenorrhea and infertility (Torrealday, et al., 2017);(Ishizuka, 2021). The yearly prevalence of POI has been rising gradually (Park et al., 2021). The prevalence of POI varies according to demographic parameters such race, social status, economic status, and lifestyle. (Golezar et al., 2020). In this regard, in a Swedish national register study, 1.9% of women had POI in 2018 (Lagergren et al., 2018). Another study conducted in Iran found that between 3.2 to 5.9% of women suffer with POI; however, a meta-analysis conducted in 2019 found that the prevalence of POI worldwide was 3.7% (Golezar et al., 2019).

It was determined that over 70% of POI cases were idiopathic (Elfayomy et al., 2016). Nevertheless, new developments in whole-genome sequencing have shown that genetic factors account for at least 30% of these cases and chromosomal causes such as autoimmune ovarian damage with a

prevalence of 0.1% (Stuenkel and Gompel, **2023).** Infectious conditions, such as mumps oophoritis also may cause POI (Webber et al., 2016). The prevalence of iatrogenic POI, which includes ovarian operations and chemotherapy and radiation for cancer, ranges from 6% to 47% (Jiao et al., 2021). POI is rarely caused by environmental factors, such as exposure to harmful substances. These chemicals disrupt the endocrine system, whether they are synthetic or natural (Evangelinakis, et al., 2024). Finally, Lifestyle Factors may cause POI. Numerous studies have found a weak link between underweight and an earlier menopausal onset (Shelling & Ahmed, 2023).

Premature ovarian insufficiency (POI) is frequently associated with oligomenorrhea or amenorrhea lasting longer than four months and blood levels of folliclestimulating hormone (FSH) above 25 mIU/mL on at least two consecutive tests at 4-week intervals in women under 40 (Webber et al, 2016). A lack of estrogen before the natural menopause results in unpleasant symptoms such vaginal dryness, anxiety, depression, hot flashes, night sweats, and disturbed sleep. Additionally, it has been linked to a higher risk of osteoporosis, cardiovascular disease (CVD), and, to a lesser degree, neurodegenerative ageing (Stuenkel and Gompel, 2023). POI has a negative impact on the skeletal, cardiovascular, urogenital, and neurological systems in addition to psychological health and general quality of life (Webber et al., 2016).

The traditional infertility therapies, including assisted reproductive technology,

are often futile for many women (Kim and Kim, 2024). Stem cell (SC) therapy has recently demonstrated potential in restoring the diminished ovarian reserve in POI patients (Ling et al., 2019) because they have the ability to proliferate indefinitely and have the potential for pluripotent differentiation. Their pluripotency and capacity for self-renewal make them an choice appealing therapeutic for transplantation (Petrou et al., 2020). Stem cells are divided into three categories according to where they come from: induced pluripotent stem cells (iPSCs), adult stem cells (ASCs), and embryonic stem cells (ESCs). Bone marrow (BM), adipose tissue (AT), menstrual blood, umbilical cord (UC), amniotic fluid. amniotic membrane. placenta, and endometrial are among the tissues that contain mesenchymal stem cells (MSCs), a subset of ASCs. Patients with POI may benefit from stem cell treatment (SCT) to restore their oocytes and ovarian function (Huang et al., 2023); (Herraiz et al., 2018).

Perception is how one interprets reality and awareness is knowledge of a situation. The primary nursing responsibility is to provide education, instruction, counselling, support, and follow-up. Nurses should give enough education to women with early ovarian insufficiency in order to increase their awareness and perspective (Fenton, 2015) ;(Paschou et al., 2020). In addition to providing adequate time for education and compassionate communication, it is essential to tailor care for women with POI through a customized needs assessment and a treatment plan developed through collaborative decision-making (Lambrinoudaki et al., 2021).

Significance of the Study

Premature ovarian insufficiency (POI) is an essential reproductive health problem with prevalence has been rising gradually among women of childbearing age, leading to infertility, hormonal imbalances, and long-term health complications (**Park et al.**, **2021**). Stem-cell-based ovarian regeneration has emerged as a promising strategy for ovarian function restoration; however, awareness and perception of this innovative therapy among women with POI remain low.

This study is significant as it evaluates the effectiveness of instructional guidelines in improving awareness and perception of POI women regarding stem-cell-based ovarian regeneration. Enhancing women's understanding of this emerging therapy can empower them to make knowledgeable choices regarding their reproductive wellbeing and increase their confidence in considering innovative treatment options.

Furthermore, the study highlights the role of nursing professionals in providing education, counselling, and support to POI patients, emphasizing the importance of patient-centered care. By identifying gaps in knowledge and perception, this research contributes to the development of targeted educational interventions that can be integrated into healthcare settings to improve patient outcomes.

Operational Definitions:

Awareness: is a state of consciousness Perception: is a process of understanding

Aim of the Study

The current study aimed to investigate the effectiveness of instructional guidelines

on awareness and perception of premature ovarian insufficiency women regarding stem cell- based ovarian regeneration.

Research Hypotheses

- H1:Women with premature ovarian insufficiency (POI) who receive a nursing instructional guideline will exhibit an improvement in awareness regarding stem cell-based ovarian regeneration compared to before.
- **H2:**Women with premature ovarian insufficiency (POI) who receive a nursing instructional guideline will exhibit an improvement in perception regarding stem cell-based ovarian regeneration compared to before.

Subjects and Methods

Research Design:

The current study adopted a quasiexperimental research design with one group pre-test and post-test to evaluate the effectiveness of instructional guidelines on the awareness and perception of women diagnosed with premature ovarian insufficiency (POI) regarding stem-cellbased ovarian regeneration.

Settings:

The current study was carried out at the obstetrics and gynecology outpatient clinic at Menoufia University Hospital, Shebin El Koom, Menoufia Governorate. This is a university–affiliated hospital, with the primary role in education, as well as providing free and paid medical services during pregnancy, labor, and postpartum period. Additionally, it provides family planning services, as well as care for women with infertility, and gynecological problems. Also, this setting is governmental and known to have a high flow rate of women suffering from gynecological problems from both rural and urban areas.

Sampling:

Sample: A purposive sample of 152 women with POI, came to outpatient clinic seeking medical advice regarding infertility, was recruited according to the following criteria:

Inclusion Criteria:

- Women aged 20–40 years diagnosed with POI.
- Women available during the period of data collection.
- Women who agreed to participate in the study and given informed consent.

Exclusion Criteria:

- Women with chronic health conditions that could interfere with participation.

Sample Size Calculation:

Based on data from literature (*Eldesouky*, 2019), considering level of significance of 5%, and power of study of 80%, the sample size can be calculated using the following formula:

$$n = \frac{2(Z\alpha/2 + Z\beta)^2 \times p (1-p)}{(d)^2}$$

where, p = pooled proportion obtained from previous study; d = expected difference in proportion of events; $Z_{\alpha/2}$ =1.96 (for 5% level of significance) and Z_{β} = 0.84 (for 80% power of study). Therefore,

 $n = \frac{2(1.96 + 0.84)^2 \times 0.95(1 - 0.95)}{(0.07)^2} = 152.$

Accordingly, the sample size required is 152.

Data Collection Tools:

Tool I. Structured Interviewing Questionnaire.

This tool was developed by researchers to

collect baseline data, including:

Part 1, Socio-demographic data (Age, education level, residence, occupation, income) and BMI.

Part 2, **Obstetric and medical history** (age of menarche, age at onset of menstrual irregularities, presence of menopausal symptoms, gravidity, number of living children, associated medical conditions, etc.....)

Tool II: Awareness Assessment Questionnaire.

This questionnaire was developed by researchers to assess participants' basic knowledge of POI, knowledge of stem cells, understanding the mechanism of stem-cell therapy, awareness of ovarian regeneration, awareness of risks and limitations, perceived benefits of treatment, trust in healthcare providers, most significant barriers preventing from pursuing of stem-cell therapy, participants' expectations regarding the timeframe for seeing results from stemcell therapy, participants' confidence in healthcare providers' recommendations regarding stem-cell therapy, etc.

Each item in the Awareness Assessment Questionnaire was scored based on the participant's ability to provide accurate and complete answers. The scoring system was designed to categorize participants' levels of awareness into two distinct categories: correct and incorrect.

Scoring Scale for Each Item:

- Correct response: 2 points.
- Incorrect response or "I don't know": 1 point.

The total score was determined by summing the points for all questions in the questionnaire.

Interpretation of the Total Score:

- Poor Awareness: <50% of the total score.
- Fair Awareness: 50%–75% of the total score.
- Good Awareness: >75% of the total score.

Tool III: Perception Assessment Scale. This tool was developed by researchers to cover participant's stem-cell therapy perception and belief scale, decisionmaking and accessibility, support and social factors, ethical and emotional considerations, and belief in scientific advancements.

Scoring System for the Perception Assessment Scale:

Each item was scored based on the participant's response:

- Agree: 3 points
- Neutral: 2 points
- Disagree: 1 point

The total score was calculated by summing the scores for all items.

Categorization of perception levels:

- Positive perception: ≥70% of the total score.
- Neutral perception: 50%-69%.
- Negative perception: <50%.

Validity and Reliability:

The tools were reviewed by five experts in the field of maternity nursing for testing its content validity. The tools were validated for clarity, relevancy, and content completeness. The appropriate improvements were made. Internal consistency was measured using Cronbach's Alpha coefficients. The Cronbach's alpha value of the Perception Belief Scale is 0.902, and of the Awareness Assessment Questionnaire is 0.898. A value above 0.70 is considered acceptable for reliability.

Ethical Considerations:

Ethical approval was obtained from Scientific Research the Ethics Faculty of Committee. Nursing, Menoufia University on 20 September, 2023. Also, women who agreed to participate in the study provided informed written consent after being explained the study's purpose and importance. In addition, each woman was given a summary of the research intervention before agreeing to participate in the trial. Similarly, the researchers emphasized that participation in the study is fully voluntary, and women were advised that they could leave at any time without providing reasons. The coding of data ensured anonymity and confidentiality.

Pilot Study:

A pilot study was conducted with 10% of the sample to evaluate the feasibility and applicability of the data collection tools. Minor adjustments were made based on feedback from the pilot study. The pilot participants were excluded from the final sample.

Procedure:

The study was conducted in five phases over six months from the

beginning of July, 2024 to the end of November, 2024.

<u>1. Preparatory Phase:</u>

Official approval to perform the study was received from the aforementioned setting's relevant authorities. In addition, a review of relevant literature was conducted to design data gathering techniques, as well as instructional guidelines and teaching materials.

2. Assessment and Interviewing Phase:

The researchers interviewed а woman who satisfied the inclusion criteria in a secluded, comfortable room within the health care unit. During this interview, the researchers introduced themselves to the women and discussed the purpose, relevance, nature, contents, and timeline of the study. Baseline data were collected, and pre-test was done to assess awareness and perception of POI women regarding stem cell therapy for ovarian regeneration. Each interview took approximately 25-30 minutes. The questions were presented in simple, clear Arabic to ensure that all participants could understand and provide accurate answers.

3. Planning Phase:

The instructional guidelines and educational materials were developed based on pre-test results and included:

- General information: Definition, causes, and complications of POI.

- **Treatment options:** Stem-cell-based ovarian regeneration (mechanism, benefits, risks).
- **Practical advice:** Recommendations on lifestyle habits, stress management, and treatment adherence.

<u>4. Implementation Phase:</u> includes 3 sessions

<u>Session 1</u>: Introduction to POI 1. Goal:

To provide women with a comprehensive understanding of POI, its causes, symptoms, and complications, as well as conventional fertility treatment options.

Objectives:-

- Increase awareness about POI as a reproductive health condition.
- Explain the physiological effects of POI and its impact on fertility and overall health.

2. Time:

- 45–60 minutes
- 3. Content:
- Definition of POI: A condition when ovarian function starts to deteriorate before the age of 40.
- Causes: Genetic factors, autoimmune disorders, idiopathic causes.
- Symptoms: Irregular or absent periods, hot flashes, mood swings, infertility, and early menopausal symptoms.
- Complications: Osteoporosis, cardiovascular issues, and emotional distress.
- Management of POI:-

- Hormone replacement therapy (HRT) to manage menopausal symptoms.
- Assisted reproductive technologies (ART) such as IVF/ICSI.
- Limitations of Conventional Treatments: Limited success rates, high costs, and the inability to restore natural ovarian function in many cases.

4. Teaching Methods:

- Interactive Lecture: Using PowerPoint slides with visual aids to explain medical concepts.
- Discussion: Participants were encouraged to discuss their experiences and ask questions.
- Printed Pamphlets: Distributed to provide a summary of the session's content in simple Arabic with illustrations to enhance understanding.

5. Educational Aids:

- PowerPoint presentation with images of the female reproductive system to explain POI.
- Visual flowcharts show the progression from normal ovarian function to POI.

<u>Session 2:</u> Stem-Cell-Based Ovarian Regeneration and Healthy Practices during Treatment

1. Goal:

To educate women about stem-cellbased ovarian regeneration, including its potential benefits, risks, limitations, and the importance of adopting healthy practices during fertility treatment.

Objectives:

- Enhance women's understanding of stem-cell therapy as an emerging treatment option.
- Clarify the potential benefits and limitations of stem-cell-based ovarian regeneration.

2. Time:

- 45–60 minutes

3. Content:

- Introduction to Stem-Cell Therapy:
 - Definition of stem cells and their regenerative properties.
 - Types of stem cells (e.g., autologous stem cells from the patient's own body).
- Mechanism of Action:
 - How stem-cell therapy aids in ovarian tissue repair, supports follicular development, and improves hormone production.
- Potential Benefits:
 - Restoration of ovarian function.
 - Improved hormone balance.
 - Potential to enhance fertility outcomes.
- Risks and Limitations:
 - Uncertainty of long-term outcomes due to the experimental nature of the treatment.
 - Financial costs and ethical considerations (e.g., use of certain types of stem cells).

4. Teaching Methods:

- Interactive Lecture: Using PowerPoint slides with visual aids to explain medical concepts.
- Discussion: Participants were urged to ask questions and share their experiences.
- Printed Pamphlets: Distributed to provide a summary of the session's content in simple Arabic with illustrations to enhance understanding.

5. Educational Aids:

- PowerPoint presentation with images of the female reproductive system to explain POI.
- Visual flowcharts show the progression from normal ovarian function to POI.

5. Evaluation Phase:

- Immediate feedback: The session ended with a brief questions and answers discussion to ensure participants understood the content.
- Post-intervention assessment: Conducted one month after the educational sessions using the same tools (Tool II and Tool III) to measure changes in awareness and perception.

Statistical Analysis

The statistical software SPSS for Windows version 20.0 (SPSS, Chicago, IL) was used for all analyses. Categorical data were presented as numbers and percentages. Variables with categorical data were compared using the chi-square test (or Fisher's exact test, where applicable). The correlation coefficient test was designed to determine correlations between two variables using continuous data. The reliability (internal consistency) of the questionnaires used in the study was calculated. Statistical significance was determined at p < 0.05.

Results

Table socio-1 presents the of demographic characteristics the women. The highest percentage of 26-30 39.5% aged women years. Regarding education, highest the percentage had university or postgraduate (34.2%). Concerning occupation, the highest percentage were housewives, had sufficient monthly income, and live in urban. As for BMI, The highest percentage of women had a normal BMI (42.8%).

Table 2 presents the obstetric and medical history of the women. Most participants (70.4%)experienced menarche at 12 years or older. More than half (52.6%) reported menstrual irregularities before the age of 30, and 39.5% experienced menopausal symptoms such as hot flashes and night sweats. Regarding gravidity, 42.8% were nulligravida. In terms of living children, 47.4% had none. More than half (55.9%) had never undergone fertility treatment.

Among those who had undergone fertility treatment (n=67), 70.1% had one to two attempts. Regarding the duration of POI diagnosis, 42.8% had been diagnosed for 2–5 years. Additionally, 44.7% had a family history of infertility

or early menopause. In terms of associated medical conditions, 39.5% had chronic illnesses such as diabetes and hypertension.

Figure 1 illustrates the distribution of sources from which women obtained information about stem-cell-based ovarian regeneration. The majority (51%) reported relying on online articles or social media as their primary source of 27% received information. while information from healthcare providers. Family or friends accounted for 14.1%, and support groups were the least utilized source at 7.9%.

Figure 2 illustrates the frequency with which women seek information about stem-cell-based ovarian regeneration. The majority (37.8%) reported searching for information daily, followed closely by 36.2% who searched weekly. A smaller proportion (18.1%) sought information monthly, while only 7.9% reported searching rarely.

 Table 3 showed a comparison of the
 awareness assessment pre- and postintervention. It shows a high significant difference after intervention than before as evident in Basic Knowledge of Premature Ovarian Insufficiency, Knowledge of Stem Cells. Understanding the Mechanism of Stem-Cell Therapy, Awareness of Ovarian Regeneration, Awareness of Risks and Limitations. Perceived Benefits of Treatment, and trust in Healthcare Providers

Figure 3 reveals comparison of total level of awareness assessment Pre- and Post-Intervention. It shows a highly significant improvement (p < 0.001) in women's overall awareness of premature ovarian insufficiency (POI) and stemcell-based ovarian regeneration after the instructional intervention. These findings confirm the effectiveness of the instructional guidelines in enhancing awareness levels.

Figure 4 reveals the main barriers of accessing stem-cell-based ovarian regeneration. It shows the primary barriers that women identified in stem-cell-based accessing ovarian regeneration. The cost of the procedure was the most frequently reported barrier followed by the (36.2%), limited availability of treatment centers (29.6%). Additionally, 21.4% of participants cited a lack of sufficient information, while 12.8% expressed concerns about the safety and effectiveness of the treatment. These findings highlight the financial burden and limited access to specialized facilities are the most significant obstacles to adopting stem-cell therapy for premature ovarian insufficiency (POI).

Figure 5 displays distribution of women's expectations after intervention regarding the timeframe for seeing results from stem-cell therapy. It shows participants' expectations regarding how long it would take to see results from

stem-cell-based ovarian regeneration. The majority (41.1%) expected improvements within 6–12 months, while 29.6% believed it would take more than a year. Additionally, 18.8% of participants were unsure, and 10.5% stated that the duration would depend on the specific treatment plan.

These findings indicate that while most participants anticipate positive outcomes within a year, a considerable percentage remains uncertain about the expected timeframe. This highlights the need for enhanced patient education.

reveals Figure 6 participants' confidence in healthcare providers' recommendations regarding stem-cell therapy. The figure shows that most of the participants (46.1%) reported complete confidence, while 34.5% indicated they mostly trust their healthcare provider's guidance. A smaller proportion (14.5%) expressed somewhat trust, whereas only 4.9% had no confidence at all.

These findings highlight a generally high level of trust in healthcare professionals regarding stem-cell therapy for premature ovarian insufficiency (POI).

Table 4 displays comparison of theperception belief scale before and afterintervention. It shows a high significantdifference after intervention than beforeexcept for 2 items. First one, regarding

decision-making and accessibility, the preference for consulting multiple healthcare providers before deciding on stem-cell therapy showed no significant change (p = 0.122).

Second one, regarding ethical and emotional considerations, anxiety about trying experimental treatments remained unchanged (p = 0.450).

Finally, regarding belief in scientific advancements, confidence in scientific Advancement as a motivator for considering stem-cell therapy increased significantly (p < 0.001), reinforcing growing trust in medical advancements as a key influence in decision-making.

illustrates Figure 7 а highly significant improvement (p < 0.001) in participants' perception of stem-cellbased ovarian regeneration following the instructional intervention. The proportion of participants with low perception declined notably from 27.6% 9.2% pre-intervention to postintervention, while those with moderate perception decreased from 38.8% to 16.4%. Conversely, the percentage of participants high perception with increased substantially from 33.6% to 74.3%, indicating a strong shift toward greater awareness, confidence, and acceptance of the therapy.

These results indicate a significant improvement in overall perception levels.

Table 1. Distribution of Socio-demographic Data and Birl of Women (152)											
Variables	Freq.	%									
Age (Years)											
19 – 25	40	26.3									
26-30	60	39.5									
31-39	52	34.2									
Level of Education											
Illiterate	15	9.9									
Primary Education	35	23.0									
Secondary Education	50	32.9									
University or postgraduate Education	52	34.2									
Occupation											
Employed	65	42.8									
Housewife	87	57.2									
Monthly Income											
Insufficient	50	32.9									
Sufficient	102	67.1									
Residence											
Urban	85	55.9									
Rural	67	44.1									
Body Mass Index (BMI)											
Underweight (<18.5 kg/m ²)	25	16.4									
Normal (18.5–24.9 kg/m ²)	65	42.8									
Overweight (25–29.9 kg/m ²)	40	26.3									
Obese ($\geq 30 \text{ kg/m}^2$)	22	14.5									

Table 1 Distributio of Socia da hia Data d DML of Wo (152)

Table 2. Distribution of Obstetric & Medical History of the Women (152)

Variables		. (
	n	%
Age of menarche (Years)		
<12	45	29.6
≥12	107	70.4
Age at onset of menstrual irregularities (Years)		
< 30	80	52.6
\geq 30	72	47.4
Presence of menopausal symptoms (hot flashes, night sweats)		
Present	60	39.5
Absent	92	60.5
Gravidity		
Nulligravida	65	42.8
Primigravida	60	39.5
Multigravida	27	17.8
Number of Living Children		
None	72	47.4
One	55	36.2
Two or more	25	16.4

Previous infertility treatments		
No fertility treatment	85	55.9
IVF/ICSI	40	26.3
Hormone therapy	27	17.8
Number of trials of IVF or ICSI (n=67)		
1–2	47	70.1
≥3	20	29.9
Duration of POI Diagnosis (Years)		
Less than 2	55	36.2
2-5	65	42.8
More than 5	32	21.1
Family History of Infertility or Early Menopause		
Yes	68	44.7
No	84	55.3
Associated Medical Conditions		
None	42	27.6
Autoimmune diseases (Thyroid disorders, lupus)	50	32.9
Chronic illnesses (diabetes, hypertension)	60	39.5



Figure 1. Source of Information about Stem-Cell-Based Ovarian Regeneration



Figure 2. Frequency of Searching for Information about POI and Its Treatments

Table 3. Comparison of the Awareness Assessment Pre- and Post-Intervention

Variables	Pre –	interve	ntion		Post	– interv	ention	Chi – Square		
	Inco	rect	Corr	ect	Incor	rect	Corr	ect	/Fisher's	s exact test
	n	%	n	%	n	%	n	%	X ²	Р
Basic Knowledge of Premature Ovarian Insufficiency										
At what age is ovarian function considered										0.00111
premature?	92	60.5	60	39.5	22	14.5	130	85.5	68.772	<0.001**
Which of the following is a characteristic of POI?	97	63.8	55	36.2	27	17.8	125	82.2	66.738	<0.001**
Which of the following is a common symptom of POI?	82	53.9	70	46.1	20	13.2	132	86.8	56.716	<0.001**
Which of the following is a scientifically supported risk factor for developing POI?	102	67.1	50	32.9	32	21.1	120	78.9	65.391	<0.001**
Which medical condition is commonly linked to POI?	87	57.2	65	42.8	17	11.2	135	88.8	71.615	<0.001**
What is a possible complication of untreated POI?	107	70.4	45	29.6	30	19.7	122	80.3	78.780	< 0.001**
Which lifestyle factors are beneficial for ovarian health?	94	61.8	58	38.2	24	15.8	128	84 2	67 870	<0.001**
Knowledge of Stem Cells		01.0	50	30.2	21	15.0	120	01.2	07.070	(0.001
What is the primary function of stem cells in medical treatments?	87	57.2	65	42.8	22	14.5	130	85.5	60.428	<0.001**
Which type of stem cells is primarily researched for ovarian regeneration?	102	67.1	50	32.0	27	17.8	125	82.2	75 748	~0.001**
What is the most common method for introducing	102	07.1	50	52.7	21	17.0	125	02.2	75.740	<0.001
stem cells into the body for ovarian regeneration?	97	63.8	55	36.2	32	21.1	120	78.9	56.895	< 0.001**
How are induced pluripotent stem cells (iPSCs)										
created?	92	60.5	60	39.5	42	27.6	110	72.4	33.363	< 0.001**
Understanding the Mechanism of Stem-Cell Therapy										
What role do stem cells play in ovarian										
regeneration?	58	38.2	94	61.8	38	25.0	114	75.0	6.090	0.013*
From which parts of the body can stem cells be							100			0.00.44
harvested for ovarian regeneration?	67	44.1	85	55.9	43	28.3	109	/1./	8.205	0.004*
what is a key goal of ovarian regeneration using stem cells?	77	50.7	75	10.3	52	34.2	100	65.8	8/16	0.00/*
Awareness of Ovarian Regeneration	11	50.7	15	47.5	52	54.2	100	05.8	0.410	0.004
What is the primary goal of stem-cell-based ovarian	_									
regeneration?	94	61.8	58	38.2	26	17.1	126	82.9	63.664	< 0.001**
What are the potential benefits of stem-cell-based										
ovarian regeneration?	92	60.5	60	39.5	32	21.1	120	78.9	49.032	< 0.001**
Which of the following statements is true about	07	63 0			24		110		50 0 40	0.001.00
stem-cell therapy for POI?	97	63.8	55	36.2	34	22.4	118	77.6	53.240	<0.001**
Awareness of Risks and Limitations										
based therapies?	48	31.6	104	68.4	27	17.8	125	82.2	7.806	0.005*
Why is stem-cell-based ovarian regeneration not widely accessible?	52	34.2	100	65.8	34	22.4	118	77.6	5.254	0.021*
What percentage of stem-cell therapy success has	117	77.0	25	00.0	02	(1.2	50	20.0	0.071	0.002:
been reported in early clinical trials?	117	//.0	35	23.0	93	61.2	59	38.8	8.8/1	0.003*
success of stem-cell-based ovarian regeneration?	130	85.5	22	14.5	108	71.1	44	28.9	9.367	0.002*

Egyptian Journal of Health Care, December 2024 EJHC Vol. 15 No. 4

Perceived Benefits of Treatment										
Which of the following outcomes would you										
consider the greatest benefit of stem-cell-based										
ovarian regeneration?	130	85.5	22	14.5	147	96.7	5	3.3	11.747	< 0.001**
Trust in Healthcare Providers										
What kind of support do you prefer from your										
healthcare provider during the treatment process?	92	60.5	60	39.5	52	34.2	100	65.8	21.111	< 0.001**



Figure 3. Comparison of the Awareness Assessment Total Level



Figure 4. Distribution of the Most Significant Barriers Preventing Pursuing of Stem-Cell Therapy





Figure 5. Distribution of Participants' Expectations after Intervention regarding the Timeframe for Seeing Results from Stem-Cell Therapy



Figure 6. Distribution of the Participants' Confidence in Healthcare Providers' Recommendations Regarding Stem-Cell Therapy.

Table 4. Comparison of the Perception Belief Scale before and after Intervention

Variables	iables Pre – intervention Post – intervention								Chi –	Square				
	Disagree		Neutral		Agree		Disa	gree	Neu	tral	Agree		/Fisher's exact test	
	n	%	n	%	n	%	n	%	n	%	n	%	X ²	Р
Stem-CellTherapyPerceptionandBeliefScale														
I would consider stem- cell therapy as a treatment for premature ovarian insufficiency (POI).	6	3.9	40	26.3	106	69.7	4	2.6	22	14.5	126	82.9	7.350	0.025*
Stem-cell therapies will become standard POI treatment in the future.	34	22.4	55	36.2	63	41.4	6	3.9	25	16.4	121	79.6	49.133	<0.001**
I believe the potential risks of stem-cell-based treatments are well understood.	34	22.4	60	39.5	58	38.2	7	4.6	30	19.7	115	75.7	46.561	<0.001**
I trust stem-cell therapy as a safe and effective option for fertility treatment.	34	22.4	58	38.2	60	39.5	6	3.9	28	18.4	118	77.6	48.964	<0.001**
Stem-cell therapy gives hope to patients with limited fertility options.	30	19.7	52	34.2	70	46.1	4	2.6	18	11.8	130	85.5	54.397	<0.001**
Accessibility														
I am confident in my ability to make an informed decision about stem-cell-based ovarian regeneration.	20	13.2	57	37.5	75	49.3	17	11.2	35	23.0	100	65.8	9.076	0.010*
Stem-cell therapy will be accessible and affordable for most patients in the future.	37	24.3	60	39.5	55	36.2	12	7.9	30	19.7	110	72.4	41.088	<0.001**
Insurance should cover stem-cell therapy as a standard fertility treatment.	32	21.1	52	34.2	68	44.7	6	3.9	18	11.8	128	84.2	52.671	<0.001**
Geographic location is a barrier to access advanced fertility treatments like stem- cell therapy.	42	27.6	60	39.5	50	32.9	19	12.5	35	23.0	98	64.5	30.819	<0.001**
I would consult multiple healthcare providers before deciding on stem-cell therapy.	10	6.6	20	13.2	122	80.3	4	2.6	14	9.2	134	88.2	4.193	0.122

Support and Social Factors														
Having a strong support system is essential during fertility treatments.	12	7.9	25	16.4	115	75.7	5	3.3	12	7.9	135	88.8	9.050	0.010*
Friends and family influence my decision to pursue stem-cell therapy.	17	11.2	35	23.0	100	65.8	10	6.6	22	14.5	120	78.9	6.598	0.036*
Relationship with my partner impacts my perception of treatment success.	17	11.2	29	19.1	106	69.7	7	4.6	20	13.2	125	82.2	7.382	0.024*
Social stigma affects my willingness to pursue advanced fertility treatments.	37	24.3	55	36.2	60	39.5	22	14.5	40	26.3	90	59.2	12.182	0.002*
Ethical and Emotional Considerations														
I feel comfortable with the ethical implications of using stem-cell therapy in fertility treatments.	32	21.1	50	32.9	70	46.1	10	6.6	27	17.8	115	75.7	29.340	<0.001**
I feel anxious about trying experimental treatments like stem- cell therapy.	32	21.1	40	26.3	80	52.6	30	19.7	50	32.9	72	47.4	1.597	0.450
Belief in Scientific Advancements														
My belief in scientific advancements motivates me to consider stem-cell therapy.	25	16.4	52	34.2	75	49.3	5	3.3	15	9.9	132	86.8	49.462	<0.001**



Figure 7. Comparison of the Perception Belief Scale Total Level

Discussion

suffering POI Women from (premature ovarian insufficiency) often experience a lack of awareness regarding emerging therapies like stem cell-based ovarian regeneration. Recent studies suggest that mesenchymal stem cell (MSC)-based treatments show promise for POI, highlighting a need for greater dissemination of information to improve women's understanding and perception of these innovative treatments. Continuous education and awareness campaigns could help bridge this gap (Hammond & Marczak, 2025). Therefore, the present study intended to investigate the effectiveness of instructional guidelines and perception on awareness of premature ovarian insufficiency women regarding stem cell- based ovarian regeneration.

Regarding the studied women's personal traits, it has been determined as the majority of participants were under 40 between (26 - 30)aged years, had secondary or university education, were housewives and maintained a normal BMI with a smaller percentage being overweight or obese. In this regard, Yuk & Kim (2021) who studied "Incidence and prevalence of primary ovarian insufficiency in South Korea "reported that the average age of newly diagnosed women with POI was 22.2 ± 0.6 years before the age of 40 and the majority had normal BMI. Also, a study conducted by **Alqersh & Ahmed, (2022)** reported that the majority of participants had completed secondary or university education and were housewives.

Concerning obstetric and medical history, the current study findings indicated that most participants experienced menarche at the age of 12 years or older, with more than half reporting menstrual irregularities before the age of 30. Moreover, over a third of participants experienced menopausal symptoms like hot flashes and night sweats. Additionally, the majority did not have children, and more than half had never undergone fertility treatment while lower than third had IVF/ICSI trial. The duration of POI diagnosis varied, with less than half diagnosing for 2-5 years. Nearly half of the studied women reported a family history of infertility or early menopause, while also presenting with associated medical conditions such as chronic illnesses and autoimmune diseases or having no medical conditions at all.

This piece of result agreed on by **Guzel et al., (2017)** who researched "Menstrual cycle characteristics of young females with occult primary ovarian insufficiency at initial diagnosis and one-

year follow-up" and noted that the average age of menarche was 13.1 ± 1.2 , More participants with occult POI stated that their mothers and/or sisters had an early menopausal family history that is positive than those without occult POI. Also, another study reported by Shestakova et al., (2016) named " Occult form of premature ovarian insufficiency" revealed that participants who have an unidentified occult form of may present with menstrual POI irregularities, unexplained infertility or repeated IVF failures. Additionally, Vignali (2022)studied "Successful menstrual regularity and spontaneous pregnancies with a resveratrol-based multivitamin supplement in women with idiopathic premature ovarian insufficiency" noted that before successful treatment the studied women had infertility, anovulation, and irregular menstruation. They had never received chemotherapy, radiation therapy, or ovarian surgery.

Finally, a study carried out by **Izhar** et al., (2017) named "Occult form of premature ovarian insufficiency in womenwith infertility and oligomenorrhea as assessed by poor ovarian response criteria" reported that the participants' infertility lasted an average of three years, ranging from two to seven years. Menstrual irregularity lasted between two and nine years, with a median of five years. Notably, the diagnosis of premature ovarian insufficiency had been made for about three years, and the irregular menstruation happened a median of two years before infertility.

The study findings indicate that most accessed information participants regarding stem-cell-based ovarian regeneration predominantly from online articles or social media, with much fewer consulting healthcare providers. around two-thirds Additionally, of participants actively seek this information on a daily or weekly basis, while only a small fraction do so monthly. These findings agreed with Takashima et al. (2023) who studied "Hope for the best but prepare for the worst: Social media posted by participants in stem cell clinical trials" and reported that daily social media posts from participants can offer valuable insights and enhance the research environment by displaying patient perspectives and enhancing the clinical trial experience. They might offer information about the involvement that members of the study team and other stakeholders might not otherwise notice.

Awareness of premature ovarian insufficiency has been growing, particularly regarding its implications, such as decline of ovarian function at an early age. Recent studies highlight the potential of stem-cell therapy for treating POI, focusing on the biological characteristics and mechanisms of action of mesenchymal stem cells (MSCs) in ovarian regeneration. Educational interventions can enhance understanding of these treatments and their benefits for women experiencing POI (Aboalola et al., 2022).

The findings of the present study proved that instructional intervention resulted in a highly significant enhancement in participants' awareness of premature ovarian insufficiency (POI) and stem-cell-based ovarian regeneration, with (P < 0.001) indicating improvement the was statistically significant. Before the intervention 69.1% of participants had low awareness, which decreased to 4.6% after the intervention. This reflects a substantial improvement in knowledge regarding POI and related treatments and highlights the effectiveness of the instructional guidelines in significantly enhancing awareness levels.

This result was in harmony with Eldesouky (2019) who studied "Impact of an educational program on patients' awareness and attitudes regarding importance of stem cell in their treatment program for patients about importance of stem cell" and noted that immediately following the program's implementation,

there was a statistically significant improvement. Also, a study conducted by (2022) named Aboalola et al.. "infodemic of misinformation on stem cell therapy among the population of Saudi Arabia" presented that, there is a troubling inclination and desire among the Saudi population to pursue stem cell therapies, as well as lack а of understanding and awareness of the potential negative health consequences of such experimental treatments. It emphasizes the importance of educational programs that provide the public with current knowledge about the state of stem cell research.

The study findings highlight that the financial burden and limited access to specialized facilities are the most significant obstacles to adopting stemcell therapy for premature ovarian insufficiency (POI). Additionally fewer participants cited a lack of sufficient information and expressed concerns about the safety and effectiveness of the treatment. This piece of result agreed on by Kim & Kim (2024) who revealed that the widespread clinical use of stem cells is hampered by technological and ethical challenges. Furthermore, the constraints and chances of clinically implementing stem cell therapy for POI are discussed. Moreover, a study conducted by Poulos (2018) who researched "The limited application of stem cells in medicine" and reported that the failure of stem cell therapies in clinical translation is due to the polarizing ethical debate, with legislators restricting certain therapies and favouring less controversial ones, leading to limited clinical significance.

Regarding participants' expectations for seeing results from stem-cell therapy, the study findings pointed to expectations for improvements from stem-cell therapy vary among participants, with most anticipating results within 6-12 months, while nearly one-third expect benefits to take over a year. Some participants expressed uncertainty or indicated that results might depend on the specific treatment plan. These findings indicate that while most participants anticipate positive outcomes within a year, a considerable percentage remains uncertain about the expected timeframe. This highlights the need for enhanced women education.

These findings aligned with Lee et al., (2020) who studied "Mid-to longterm efficacy and safety of stem cell therapy for acute myocardial infarction" and noted that when compared to the control group, the intervention group had slight gains at 6, 12, 24, and 36 months. Additionally, individuals who received MSC injections showed greater gains. Prior systematic reviews have only documented stem cell therapy's shortterm (about six to twelve months) efficacy (Xu et al., 2016).

According to the findings of the present study, there was a significant level of confidence in healthcare providers regarding recommendations for stem-cell therapy to treat premature ovarian insufficiency (POI), with most of participants showing most confidence level. One third expressed somewhat confidence level, while fewer reported having no confidence in these recommendations. This overall indicates a high level of confidence in healthcare professionals regarding stem-cell therapy for premature ovarian insufficiency (POI).

This result was consistent with **Banu** et al., (2023) who studied "Effects of autologous stem cell therapy for fertility enhancement among with women premature ovarian insufficiency" and reported that the fertility and ovarian function of women can be significantly impacted by autologous stem cell treatment. The results indicated that autologous stem cells ovarian transplant can increase levels of anti-mullerian hormone (AMH) and number of antral follicle count (AFC) and decrease level of follicle stimulating hormone (FSH) in patients with POI, with a total pregnancy rate of 4% after the third cycle follow-up. These findings increased the likelihood and confidence that autologous stem cell injection, which promotes ovarian function, may be a different strategy for enhancing follicular development in women with POI.

Stem cell therapy is being considered probable treatment for women with premature ovarian insufficiency (POI). Research indicates that various types of stem cells may offer protective properties and could help restore ovarian function (Gupta et al., 2018).

The study findings reported that women's acceptance of stem-cell therapy for POI increased significantly, with greater trust in their safety, effectiveness, and future standardization. The belief that stem-cell therapy provides hope for women with limited fertility options also increased. Confidence in making informed decisions improved, with more participants believing insurance should cover the therapy and it will become affordable and accessible. Social support systems were recognized as essential, and concerns about social stigma decreased. Ethical and emotional considerations improved, with increased confidence in the morality and appropriateness of stemcell therapy. Confidence in scientific advancements also increased, reinforcing trust in medical advancements. indicating a strong shift toward greater awareness, confidence, and acceptance of the therapy. Finally, the study findings

revealed highly significant а improvement (p < 0.001) in participants' overall perception levels of stem-cellbased ovarian regeneration following the instructional intervention indicating instructional effectiveness of the guidelines improving in women perception level.

In this regard a study conducted by Kim & Kim (2024) studied "current status and future prospects of stem cell therapy for infertile patients with premature ovarian insufficiency" and revealed that stem-cell therapy (SCT) is being explored for its potential in treating infertility, particularly in patients with POI. Nevertheless. an extensive awareness of stem cells mechanisms is essential to their extensive use in clinical settings. Social support systems, family, friends, and partners' influence on decision-making has increased, and stigma have concerns about social decreased. Ethical and emotional considerations improved, have but anxiety about experimental treatments remains unchanged. Confidence in scientific advancements has also increased, reinforcing trust in medical advancements as a key influence in decision-making.

Considering these results, the importance of stem cells in treating premature ovarian insufficiency should indeed be emphasized in health education

efforts in outpatient clinics, hospitals, and communities. This can enhance public awareness of the possible benefits of stem cell therapy, which offers hope for repairing and regenerating diseased tissues. Future studies ought to emphasize the applicability of stem cell therapy in various diseases, employing larger sample sizes for more robust findings.

Conclusion

The results of this study displayed the that application of nursing instructional guidelines was effective in improving awareness and perception among women with premature ovarian insufficiency (POI) regarding stem-cellbased ovarian regeneration. This supports all previously mentioned research hypotheses.

Recommendations

The following recommendations are made in light of the study's findings:

- Implement structured nursing instructional programs to improve awareness and perception of POI and stem-cell therapy in gynecological and fertility care settings.
- Conduct larger-scale studies with more diverse populations to further

validate the effectiveness of educational guidelines.

- Integrate educational programs on reproductive health, POI management, and emerging therapies into nursing curricula and healthcare training programs.

References

- Aboalola, D., Badraiq, H., Alsiary, R.,
 Zakri, S., Aboulola, N., Haneef, L.,
 ... & Alsayegh, K. (2022). An infodemic of misinformation on stem cell therapy among the population of Saudi Arabia: a cross-sectional study. Frontiers in Medicine, 9, 789695.
- Alqersh, A., & Ahmed, M. (2022). Effect of Nursing Instructional Program on Genitourinary Syndrome and Stress Level Among Premature Ovarian Insufficiency Women. International Egyptian Journal of Nursing Sciences and Research, 2(2), 592-605.
- Banu, J., Jahan, N., Anwary, A.,
 Tarique, M., Aziz, I., Laskar, N., ...
 & Darmini, M. (2023). Effects of autologous stem cell therapy for fertility enhancement among women with premature ovarian insufficiency. International Journal of Reproduction, Contraception,

Obstetrics and Gynecology, 12(2), 311.

- Eldesouky, I. (2019). Impact of an educational program on patients' awareness and attitudes regarding importance of stem cell in their treatment—program for patients about importance of stem cell. Int J Novel Res Healthcare Nurs, 6, 480-8.
- Elfayomy, K., Almasry, M., El-Tarhouny, A., & Eldomiaty, A. (2016). Human umbilical cord bloodmesenchymal stem cells transplantation renovates the ovarian surface epithelium in a rat model of premature ovarian failure: possible direct and indirect effects. Tissue and Cell, 48(4), 370-382.
- Evangelinakis, N.. Geladari, V., Geladari, V., Kontogeorgi, A., K., Peppa, M., & Papaioannou, Kalantaridou. S. (2024). The influence of environmental factors on premature ovarian insufficiency and ovarian aging. Maturitas, 179, 107871.
- Fenton, J. (2015). Premature ovarian insufficiency: Pathogenesis and management. Journal of mid-life health, 6(4), 147.
- Golezar, S., Keshavarz, Z., Tehrani, F. R., & Ebadi, A. (2020). An

exploration of factors affecting the quality of life of women with primary ovarian insufficiency: a qualitative study. BMC women's health, 20(1), 1-9.

- Golezar, S., Ramezani Tehrani, F., Khazaei, S., Ebadi, A., & Keshavarz, Z. (2019). The global prevalence of primary ovarian insufficiency and early menopause: a meta-analysis. Climacteric, 22(4), 403-411.
- Gupta, S., Lodha, P., Karthick, S., & Tandulwadkar, R. (2018). Role of autologous bone marrow-derived stem cell therapy for follicular recruitment in premature ovarian insufficiency: review of literature and a case report of world's first baby with ovarian autologous stem cell therapy in a perimenopausal woman of age 45 year. Journal of human reproductive sciences, 11(2), 125-130.
- Guzel, Y., Aba, A., Yakin, K., & Oktem, O. (2017). Menstrual cycle characteristics of young females with occult primary ovarian insufficiency at initial diagnosis and one-year follow-up with serum amh level and antral follicle count. PLoS One, 12(11), e0188334.
- Hammond, J., & Marczak, M. (2025). Women's experiences of premature

ovarian insufficiency: a thematic synthesis. Psychology & Health, 40(2), 192-216.

- Herraiz, S., Buigues, A., Díaz-García,
 C., Romeu, M., Martínez, S.,
 Gómez-Seguí, I., ... & Pellicer, A.
 (2018). Fertility rescue and ovarian follicle growth promotion by bone marrow stem cell infusion. Fertility and sterility, 109(5), 908-918.
- Hu, Q., Xin, Y., Zhu, T., Fan, W.,
 Zhang, L., Ye, Y., & Li, D. (2024).
 Application of mesenchymal stem cell therapy for premature ovarian insufficiency: Recent advances from mechanisms to therapeutics. *World Journal of Stem Cells*, 16(1), 1.
- Huang, Y., Chen, R., Chen, JM., Shi,
 Y., & Lin, S. (2023). Correction: Therapeutic options for premature ovarian insufficiency: An updated review. Reproductive Biology and Endocrinology: RB&E, 21, 81.
- Ishizuka. **B**. (2021). Current understanding of etiology, the symptomatology, and treatment options in premature ovarian insufficiency (POI). Frontiers in endocrinology, 12, 626924.
- Izhar, R., Husain, S., Tahir, S., & Husain, S. (2017). Occult form of premature ovarian insufficiency in women with infertility and

oligomenorrhea as assessed by poor ovarian response criteria. Journal of reproduction & infertility, 18(4), 361.

- Jiao, X., Meng, T., Zhai, Y., Zhao, L., Luo, W., Liu, P., & Qin, Y. (2021). Ovarian reserve markers in premature ovarian insufficiency: within different clinical stages and different etiologies. Front Endocrinol 12: 601752.
- Kim, K., & Kim, J. (2024). Current
 Status and Future Prospects of Stem
 Cell Therapy for Infertile Patients
 with Premature Ovarian
 Insufficiency. Biomolecules, 14(2),
 242.
- Lagergren, K., Hammar, M., Nedstrand, E., Bladh, M., & Sydsjö,
 G. (2018). The prevalence of primary ovarian insufficiency in Sweden; a national register study. BMC women's health, 18(1), 1-4.
- Lambrinoudaki, I., Paschou, A., Lumsden, A., Faubion, S., Makrakis, E., Kalantaridou, S., & Panay, N. (2021). Premature ovarian insufficiency: a toolkit for the primary care physician. *Maturitas*, 147, 53-63.
- Lee, H., Cho, J., Han, Y., & Lee, H. (2024). Mid-to long-term efficacy and safety of stem cell therapy for acute myocardial infarction: a systematic

review and meta-analysis. Stem Cell Research & Therapy, 15(1), 290.

- Liesveld, L., Sharma, N., & Aljitawi, O. S. (2020). Stem cell homing: From physiology to therapeutics. Stem cells, 38(10), 1241-1253.
- Ling, L., Feng, X., Wei, T., Wang, Y., Wang, Y., Wang, Z., ... & Xiong, Z. Human amnion-derived (2019). mesenchymal stem cell (hAD-MSC) transplantation improves ovarian function in rats with premature ovarian insufficiency (POI) at least partly through а paracrine mechanism. Stem cell research & therapy, 10, 1-18.
- Mahla, S. (2016). Stem cells applications in regenerative medicine and disease therapeutics. International journal of cell biology, 2016(1), 6940283.
- Munoz-Torres. **R..** Martínez-González, B., Lozano-Luján, D., Martínez-Vázquez, C., Velasco-Elizondo, P., Garza-Veloz, I., & Martinez-Fierro, M. L. (2023). Biological properties and surgical applications of the human membrane. Frontiers amniotic in Bioengineering and Biotechnology, 10, 1067480.
- Park, S., Chugh, M., Elsharoud, A., Ulin, M., Esfandyari, S.,

Aboalsoud, A., ... & Al-Hendy, A. (2021). Safety of intraovarian injection of human mesenchymal stem cells in a premature ovarian insufficiency mouse model. Cell Transplantation, 30, 963689720988502.

- Paschou, A., Augoulea, A., & Lambrinoudaki, I. (2020).
 Premature ovarian insufficiency. Eur Gynecol Obstet; 2:5–9.
- Petrou, P., Kassis, I., Levin, N., Paul, F., Backner, Y., Benoliel, T., ... & Karussis, D. (2020). Beneficial effects of autologous mesenchymal stem cell transplantation in active progressive multiple sclerosis. Brain, 143(12), 3574-3588.
- **Poulos, J. (2018).** The limited application of stem cells in medicine: a review. Stem cell research & therapy, 9, 1-11.
- Shelling, N., & Ahmed N. (2023). The role of lifestyle and dietary factors in the development of premature ovarian insufficiency. Antioxidants, 12(8), 1601.
- Shestakova, G., Radzinsky, E., & Khamoshina, B. (2016). Occult form of premature ovarian insufficiency. Gynecological Endocrinology, 32(sup2), 30-32.

- Stuenkel, A., & Gompel, A. (2023). Primary ovarian insufficiency. New England Journal of Medicine, 388(2), 154-163.
- Takashima, K., Minari, J., Chan, S., & Muto, K. (2023). Hope for the best, but prepare for the worst: Social media posted by participants in stem cell clinical trials. Regenerative Therapy, 24, 294-297.
- Torrealday, S., Kodaman, P., & Pal, L. (2017). Premature Ovarian Insufficiency-an update on recent advances in understanding and manage-ment. F1000Research, 6, 2069.
- Vignali, M. (2022). Successful Mestrual Regularity and Spontaneous Pregnancies with a Resveratrol-Based Multivitamin Supplement in Women with Idiopathic Premature Ovarian Insufficiency. The EuroBiotech Journal, 6(1), 40-43.
- Webber, L., Davies, M., Anderson, R., Bartlett, J., Braat, D., ... & Vermeulen, N. (2016). ESHRE Guideline: management of women with premature ovarian insufficiency. Human Reproduction, 31(5), 926-937.
- Xu Y, Cai Y, Tian M, Liu D, Huang C.(2016). Stem cell transplantation dose in patients with acute myocardial

infarction: a meta-analysis. Chronic Dis Transl Med. 2016;2(2):92–101.

https://doi.org/10.1016/j.cdtm.2016.09.006.

Yuk, S., & Kim, M. (2021). Incidence and prevalence of primary ovarian insufficiency in South Korea: a population-based study. Archives of Gynecology and Obstetrics, 1-9.