

# Spontaneous Pregnancy Following 6-Month Herbal Medicine Treatment for the Subclinical Stage of Premature Ovarian Insufficiency: A Case Report

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ARTICLE INFO	ABSTRACT
Article type: Case report	<b>Background &amp; aim:</b> Premature ovarian insufficiency (POI) in women under 40 leads to infertility and psychological distress. Timely diagnosis of POI is vital to prevent progression to ovarian failure. Chinese herbal medicine has shown efficacy in treating the subclinical stage of POI, aligning with the preventive approach of Chinese medicine.
Article History: Received: 22-Mar-2023 Accepted: 12-December-2023	<b>Case report:</b> A 29-year-old with subclinical POI received exclusive herbal medicine treatment. After six months, she achieved spontaneous conception, with an anti-mullerian hormone level of 0.41 ng/mL and follicle-stimulating hormone of 14.96 mIU/mL. Ultrasound revealed increased antral follicle count post-treatment. The patient delivered a healthy full-term baby without assisted reproductive technology.
Key words: Premature Ovarian Insufficiency Herbal Medicine Traditional Chinese Medicine Complementary Therapies Case Reports	<b>Conclusion:</b> Successful subclinical POI treatment with Chinese herbal medicine resulted in a safe, spontaneous pregnancy. This case underscores diagnostic challenges in POI, emphasising the necessity of adhering to criteria. Despite the lack of guidelines, Chinese herbal medicine shows promise for follicular growth in POI. Valuable insights contribute to learning points, emphasising the potential for natural conception without assisted reproductive technology as an indication of the efficacy of integrative approaches in subclinical POI management.

► Please cite this paper as:

Suan Sin Y, Chen M, Zhang J. Spontaneous Pregnancy Following 6-Month Herbal Medicine Treatment for the Subclinical Stage of Premature Ovarian Insufficiency: A Case Report. *Journal of Midwifery and Reproductive Health*. 2024; 12(4): 4505-4509. DOI: 10.22038/JMRH.2023.71336.2094

## Introduction

Premature ovarian insufficiency (POI) is defined as an irreversible reduction of ovarian function before reaching the age of 40 and mainly characterised by menstrual disorder such as amenorrhoea or oligomenorrhoea. The diagnosis of POI is based on an elevated serum follicle-stimulating hormone (FSH) level >25 IU/L on two separate occasions at least 1 month

apart and decreased oestradiol (E<sub>2</sub>) level <50 pg/mL (1). Serum FSH level between 15-25 IU/L is classified as a subclinical stage of POI, which belongs to high-risk population for POI (2). Conventional treatment for this condition is hormone replacement therapy (HRT) (3). However, it was suggested that HRT might increase the risk of other complications. This

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case report revealed the result of implementing Chinese herbal medicine in helping a POI patient at subclinical stage to conceive naturally without conventional intervention and successfully achieve a full-term live birth.

### Case presentation

A 29-year-old woman visited an outpatient clinic at Shandong University of Traditional Chinese Medicine (SDUTCM) affiliated hospital to seek medical assistance to conceive on 15<sup>th</sup> March 2021. She has been getting married for 1 year and having normal frequency and quality of sexual intercourse in the past 6 months. Her gravidity and parity were 0. Her menarche was at the age of 14. Her menses were regular with cycle intervals of 26-30 days and menstrual bleeding lasted for 7 days, with profuse flow and no clot. Her last menstrual period (LMP) was on

the 2nd of March 2021, and her previous menstrual period (PMP) was on the 3rd of February 2021. Her leucorrhoea was normal with a moderate amount, slightly yellowish, and no abnormal odor or vaginal itching.

On March 8, 2021, her blood test result showed an AMH level of 0.41 ng/mL. Transvaginal ultrasound on 15<sup>th</sup> March 2021 (Figure 1) showed an anteverted uterus, enlarged right and left ovaries with multiple peripherally enlarged follicles, and a measurement of 5.62x4.76x4.21 cm above the cervix. The cervical length was about 3.10 cm, with a homogenous echo. Her endometrium on day 14 of her menstrual cycle showed a thickness of 1.39 cm with non-homogenous intermediate signal intensity.



**Figure 1.** Ultrasound on 15<sup>th</sup> March 2021 showed an anteverted uterus and enlarged right and left ovaries with multiple peripherally enlarged follicles

A slightly strong echo was reported at the upper right edge of the uterine cavity, measuring 0.70x0.54x0.53 cm with an unclear border and no significant ovarian stromal blood flow. The right ovary measuring 3.09x2.39 cm was seen with 1 enlarged follicle sized 2.20 cm which was poorly developed, and another 2 small follicles. The left ovary measuring 2.53x1.15 cm was seen with 1 small follicle. The ultrasound screening suggested further investigation after menstrual bleeding on the strong echogenicity in the uterine cavity.

In her medical history, there was no recent trauma, no previous surgical history, no familial infertility issue, no bleeding disorder, or no anticoagulation treatment. Her tongue was light red with a thin white coating. Her pulse was deep and threadlike.

Her hormonal test on 17<sup>th</sup> May 2021, which was the second day of her menstrual bleeding (LMP: 16<sup>th</sup> May 2021), showed a result of LH level at 2.68 mIU/ml, FSH level at 14.96 mIU/ml, progesterone level at 1.34 ng/ml, prolactin level at 23.64 ng/ml, estradiol level at 26.96 pg/ml and testosterone level at 0.51 ng/ml. Her FSH level met the diagnostic criteria for the subclinical stage of POI.

A revisit ultrasound screening was performed during her second visit on 22<sup>nd</sup> May 2021. Her endometrium had a thickness of 0.52 cm. Ultrasound scan on the right ovary revealed an enlarged follicle with diameter of 0.95 cm and another 2 small follicles, as well as a 1.73x0.83 cm anechoic area with low tension. An ultrasound scan of the left ovary revealed only one to two small follicles.

On 28<sup>th</sup> May 2021, the patient's ultrasound screening revealed a type B endometrium with

1.0 cm thickness. Three enlarged follicles with diameters of 1.40 cm, 1.0 cm, and 0.8 cm were seen in the right ovary. There were 1 to 2 small follicles in the left ovary.

On 4<sup>th</sup> June 2021, the ultrasound screening showed a type A-B endometrium with 1.3 cm thickness. Approximately 5 small follicles and fluid within the cavity of a corpus luteum were observed in the right ovary. An antral follicle with diameter of 0.8 cm and another 2 small follicles were observed in the left ovary.

At the first visit, the patient underwent a comprehensive consultation with a renowned specialist in the Department of Reproductive Medicine at the SDUTCM-affiliated hospital, well-versed in the use of Chinese herbal medicine. The specialized consultations involved a detailed medical history review, a thorough examination, and relevant diagnostic tests. Based on the findings and the patient's specific health needs, a modified formulation of Shen Qi Shou Tai Wan was prescribed for a duration of 7 days. The prescription consisted of the following ingredients: DangShen 15 g, ZhiHuangQi 15 g, TuSiZi 30 g, SangJiSheng 15 g, XuDuan 15 g, CuXiangFu 12 g, ChaoBaiShao 15 g, FuChaoBaiZhu 12 g, YanDuZhong 15g, HuangQin 12 g and ZhiGanCao 6g. Additionally, the patient was advised to monitor her basal body temperature and supplement her diet with folic acid.

The patient received a prescription for Gui Shen Wan with ChenPi 9g for 6 days on May 22, 2021. The ingredients of Gui Shen Wan include GouQiZi 12 g, TuSiZi 12 g, ZhuYuRou 9 g, DuZhong 9 g, ShuDiHuang 9 g, DangGui 9 g, ShanYao 12 g, FuLing 9 g and ZhiGanCao 6g.

During her third visit on 28<sup>th</sup> May 2021, patient was prescribed the same herbal medicine as previous visit for the following 3 days. From 31<sup>st</sup> May 2021 onwards, a patent oral medication named DangGui Blood Nourishing Oral Decoction (DangGui Yi Xue Kou Fu Ye) was given to be taken 10ml orally twice a day for a period of 5 days. The patient was advised to revisit for follow-up treatment on 5<sup>th</sup> June 2021.

On 4<sup>th</sup> June 2021, the patient was prescribed with modification of Shen Qi Shou Tai Wan (eliminate E Jiao) for 7 days. A patent medicine, named Gu Shen An Tai Wan was also prescribed

to be taken 6g orally twice a day for a period of 7 days. The patient was advised to carry out a pregnancy test on the 14<sup>th</sup> day after ovulation. If the test kit shows positive, the patient was advised to revisit immediately. If the result turns out negative, a follow-up treatment was suggested on 18<sup>th</sup> June 2022.

After undergoing pure Chinese herbal medicine treatment and taking folic acid as a supplement for 6 months, the patient came back on 18<sup>th</sup> June 2022 with a positive pregnancy test result. Throughout the pregnancy period, she received regular prenatal checkups to monitor the progress of the pregnancy and ensure the well-being of both the mother and the baby. The pregnancy proceeded without any reported complications, and in February 2023, she successfully delivered a healthy full-term baby girl via vaginal birth with the assistance of an epidural.

## Discussion

Women with POI often have fewer or lower-quality eggs, leading to fertility challenges. It can only happen to women younger than the age of 40 and more common among women in their 30s. The pregnancy rate for women with POI is low. It can be treated in different ways depending on the patient's underlying health problem and diagnosis by the gynecologist who specialised in reproductive endocrinology. The HRT commonly implements oestrogen and progesterone.

Numerous studies supports the effectiveness of Chinese medicine for POI, which views it as a pathological condition mainly caused by kidney deficiency, leading to depletion of Tian Gui and disharmony between Yin and Yang. Pathogenesis of POI in Chinese medicine is also related to liver Qi stagnation and spleen deficiency (5). Tian Gui is the basic substance to form kidney essence. Prolonged Kidney deficiency can affect the normal flow of Qi and blood, thus causing dysfunction in the thoroughfare and conception vessels, which then affects the maturation of ovary function. Having said that, in general, the treatment principles should include tonifying kidney, regulating liver Qi, and regulating thoroughfare and conception vessels (6-7). Herbal medicine is effective in treating women with POI and most

importantly, it only causes very few side effects (8).

A 2020 systematic review reported that herbal medicine, which tonifies kidneys and activates blood, is effective and safe for POI (9). A clinical study revealed that Chinese medicine can promote spontaneous ovulation and increase fertility rate among POI patients (10). Based on the pharmacological perspective, herbal medicine can improve the serum AMH level and decrease serum FSH and LH in POI mice experiment. It also improves endometrial thickness, volume of the ovary and uterus, as well as the hormonal and INHB levels by reducing the AZpAb, IL-6, and IL-7. Moreover, a recent study revealed that herbal medicine significantly upregulates the GDF-9 and Smad2 protein expression in mice with POF having autoimmune disorders. Thus, it can promote the growth and development of follicles and increase the ratio of egg maturation via regulation of the GDF-9/Smad2 signaling pathway. The root cause of POI occurrence is related to the follicular atresia due to abnormal apoptosis of the granulosa cells. Several laboratory studies have shown that herbal medicine can suppress the apoptosis of granulosa cells by downregulating Bax and upregulating Bcl-2 expression.

In our case, the patient did not have any abnormal menstrual disorder or any past medical history that would affect her ovarian function. Despite abnormal AMH and ToRCH profile results preoperatively, the patient achieved a successful pregnancy and delivered a healthy baby boy at a gestation age of 38 weeks and 5 days through spontaneous vaginal delivery.

### Conclusion

In this case, Chinese medicine appeared to improve ovarian function in a POI patient with fewer side effects, suggesting potential benefits for conception, though further studies are needed to validate these findings. The treatment of Chinese medicine emphasises its holism concept; thus, it comes with diversification in the herb prescription based on syndrome differentiation. This case report provides a new insight into the treatment of the subclinical stage of POI by using Chinese medicine only and successfully helped the patient to conceive and

give birth without other intervention. This case has not shown any adverse effects, indicating the safety of using Chinese medicine on POI patients.

### Declarations

### Acknowledgements

We thank the Department of Reproductive Medicine at the SDUTCM-affiliated hospital for their support and contributions to this study. We also extend our gratitude to the patient involved for her participation.

### Conflicts of interest

The authors declared no conflicts of interest.

### Ethical considerations

Informed consent was obtained from the patient for the use of her medical information in this publication. All personal identifiers were removed to ensure the patient's privacy and confidentiality. The treatment provided was consistent with the standards of care in Traditional Chinese Medicine, and no invasive procedures were conducted during the course of treatment.

### Ethical approval

No formal ethical approval was obtained from the institution, as it involves the retrospective description of a single patient's clinical course and treatment outcomes. Informed consent was obtained from the patient, ensuring confidentiality and adherence to ethical guidelines.

### Funding

No financial support was received for this study.

### Authors' contribution

Yen Suan Sin was primarily responsible for drafting the manuscript, including the synthesis of clinical details and conceptual framework. Min Chen conducted patient interviews and collected relevant clinical data. Jianwei Zhang provided mentorship throughout the project and served as the attending physician responsible for the patient's treatment. All authors critically reviewed the manuscript and approved the final version for publication.

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