ISRCTN69623204 https://doi.org/10.1186/ISRCTN69623204

# How electro-acupuncture improves ovarian function and pregnancy outcomes in women with diminished ovarian reserve: a clinical and mechanistic study

**Submission date**
08/01/2024

**Recruitment status**
Recruiting

**Registration date**
10/01/2024

**Overall study status**
Ongoing

**Last Edited**
05/08/2025

**Condition category**
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

## Plain English summary of protocol

Background and study aims
Approximately 10% to 35% of women may experience a premature diminished ovarian reserve (DOR) due to various reasons, and the incidence of DOR significantly increases with age. For DOR patients with infertility, in vitro fertilization and embryo transfer (IVF-ET) can shorten treatment duration and increase pregnancy rates. In IVF-ET, poor egg quality directly affects embryo quality and is one of the crucial factors influencing pregnancy rates. Acupuncture, as a non-pharmacological treatment, can improve ovarian function and egg quality, thereby enhancing pregnancy rates. This study aims to evaluate the effect of acupuncture on ovarian function and the pregnancy outcomes of IVF-ET in patients with DOR.

Who can participate?
Women aged between 20 and 48 years old with infertility due to DOR

What does the study involve?
Eligible patients will be randomly allocated to either the electro-acupuncture (EA) or the sham electro-acupuncture (SA) group. Based on conventional treatment, patients inEA will receive electro-acupuncture therapy, while the SA will receive sham electro-acupuncture treatment. Both groups will receive 12 weeks of acupuncture treatments.

What are the possible benefits and risks of participating?
Both groups will receive basic treatment and symptomatic treatment. Participants' symptoms may be relieved in this study. Acupuncture may cause some slight side effects, including bleeding, hematoma, serious pain, and dizziness. These side effects are generally mild and rarely cause serious harm.

Where is the study run from?
Luohu District Hospital of Traditional Chinese Medicine (China)

When is the study starting and how long is it expected to run for?
October 2023 to October 2026

Who is funding the study?
1. Sanming Project of Medicine in Shenzhen (No. SZZYSM 202101007)
2. 2021 Luohu District (First Batch) Soft Science Research Programme Project (No. LX20210102)

Who is the main contact?
Prof. Hong Zhao, hongzhao2005@aliyun.com

# Contact information

### Type(s)
Public, Scientific, Principal Investigator

### Contact name
Prof Zhao Hong

### ORCID ID
https://orcid.org/0000-0001-8211-9483

### Contact details
No.16 Xiantong Road, Luohu District
Shenzhen
China
518004
+86 (0)755 25160866
hongzhao2005@aliyun.com

# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
Nil known

# Study information

### Scientific Title
Effect of electro-acupuncture for patients with diminished ovarian reserve: a randomized controlled trial

### Study objectives

Current study hypothesis as of 02/12/2024:
Electro-acupuncture therapy has better efficacy than sham electro-acupuncture in improving ovarian function in women with diminished ovarian reserve (DOR) and improving pregnancy outcomes in assisted reproductive technology (ART) .

Previous study hypothesis:
Acupuncture therapy has better efficacy than sham acupuncture in improving ovarian function in women with diminished ovarian reserve (DOR) and improving pregnancy outcomes in in vitro fertilization-embryo transfer (IVF-ET).

## Ethics approval required
Ethics approval required

## Ethics approval(s)
Approved 06/12/2023, Medical Ethics Committee of Luohu District Hospital of Traditional Chinese Medicine (16 Xiantan Road, Luohu District, Shenzhen, Guangdong Province, 518004, China; +86 (0)755 82311699; lhzyykjk@163.com), ref: 2023-LHQZYYYXLL-KY-147

## Study design
Single-center interventional two-armed single-blinded prospective randomized controlled trial

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment, Efficacy

## Participant information sheet
See study outputs table

## Health condition(s) or problem(s) studied
Women with infertility due to diminished ovarian reserve including those with or without transferable embryos

## Interventions
Current interventions as of 02/12/2024:
Eligible patients will be randomly allocated to either the electro-acupuncture (EA) group or the sham electro-acupuncture (SA). The SPSS software version 26.0 will be used to generate a random number table at a 1:1 ratio. The concealment of the random allocation scheme will be ensured through sequentially numbered, opaque, sealed envelopes. Blinding will be employed for participants, outcome evaluators, and statistical analysts.

Based on conventional treatment, patients in EA will receive electro-acupuncture therapy, while the SA will receive sham electro-acupuncture with acupoints located approximately 1 cun adjacent to those used in EA, involving superficial needle insertion of 1-2 mm into the skin. The

electro-acupuncture parameters in the EA group are set as follows: continuous wave, frequency of 2-6Hz, intensity of 2-8 mA. While the electro-acupuncture device in SA group settings are as follows: a continuous wave at a frequency of 0.1 Hz and an intensity between 0.1 and 0.5 mA, with the device being deactivated 30 seconds after activation.

The acupoints for both groups will include Liangmen (ST 21), Huangshu (KI 16), Guanyuan (CV 4), Zhongji (CV 3), Zigong (EX-CA 1), Zusanli (ST 36), and Sanyinjiao (SP 6). Baihui (GV 20) and Shenting (GV 24) will be added for those with insomnia or anxiety.

After routine disinfection of the skin at the acupoints, appropriate-length filiform needles will be used. ST 21 and KI 16 will be punctured perpendicularly at a depth of 20-30 mm; CV 4, CV 3, and EX-CA 1 will be punctured perpendicularly or obliquely at a depth of 25-40 mm; ST 36 and SP 6 will be punctured perpendicularly at a depth of 25-50 mm; GV 20 and GV 24 will be punctured horizontally or obliquely at a depth of 10-20 mm. Acupuncture treatment will be conducted for a continuous 12 weeks, with three sessions per week. Each treatment will last for 30 minutes.

Previous interventions:
Eligible patients will be randomly allocated to either the acupuncture group (AG) or the sham acupuncture group (SAG). The SPSS software version 26.0 will be used to generate a random number table at a 1:1 ratio. The concealment of the random allocation scheme will be ensured through sequentially numbered, opaque, sealed envelopes. Blinding will be employed for participants, outcome evaluators, and statistical analysts.

Based on conventional treatment, patients in AG will receive acupuncture therapy, while the SAG will receive sham acupuncture with acupoints located approximately 1 cm adjacent to those used in AG, involving superficial needle insertion of 1-2 mm into the skin. The acupoints for both groups will include Liangmen (ST 21), Huangshu (KI 16), Guanyuan (CV 4), Zhongji (CV 3), Zigong (EX-CA 1), Zusanli (ST 36), and Sanyinjiao (SP 6). Baihui (GV 20) and Shenting (GV 24) will be added for those with insomnia or anxiety.

Acupuncture treatment will be conducted for a continuous 8 weeks before entering the ovulation induction or transplantation cycle, with 3 sessions per week in the 1 to 3 weeks and 2 sessions per week in the following 4 to 8 weeks. Patients without transferable embryos receive acupuncture treatment once a week until the day of hCG injection during ovulation induction based on 8 weeks of acupuncture treatment.

After routine disinfection of the skin at the acupoints, appropriate-length filiform needles will be used. ST 21 and KI 16 will be punctured perpendicularly at a depth of 20-30 mm; CV 4, CV 3, and EX-CA 1 will be punctured perpendicularly or obliquely at a depth of 25-40 mm; ST 36 and SP 6 will be punctured perpendicularly at a depth of 25-50 mm; GV 20 and GV 24 will be punctured horizontally or obliquely at a depth of 10-20 mm. Each treatment will last for 30 minutes.

## Intervention Type
Procedure/Surgery

## Primary outcome measure
Current primary outcome measure as of 02/12/2024:
Antral follicle count measured using ultrasound at baseline and after 12 weeks of treatment

Previous primary outcome measure:
Clinical pregnancy rate measured using data collection about on-site visits, telephone calls, or WeChat communications at 4 to 7 weeks after embryo transfer

## Secondary outcome measures

Current secondary outcome measures as of 02/12/2024:
1. Anti-Müllerian hormone measured using blood samples at baseline and after 12 weeks of treatment
2. Basal hormone levels (follicle-stimulating hormone, estradiol, luteinizing hormone, FSH/LH ratio) measured using blood samples at baseline and after 12 weeks of treatment
3. Anxiety, depression, and menopause symptoms measured using the Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), and Modified Kupperman Index scores at baseline and after 12 weeks of treatment.
4. Endometrial thickness and morphology measured using ultrasound on the day of embryo transfer
5. Patients undergoing ovulation induction cycles: the following indicators are measured using data collection within 1 to 7 days after ovulation:
5.1. Gonadotropin (Gn) usage
5.2. Oocyte retrieval
5.3. Fertilization rate
5.4. Cleavage rate
5.5. Morphological assessment of oocytes
5.6. Day 3 high-quality embryo rate
5.7. Day 3 utilizable embryo rate
5.8. Blastocyst formation rate
5.9. High-quality blastocyst rate
5.10 MII oocyte rate
6. Pregnancy outcomes are assessed using data collection about on-site visits, telephone calls, and WeChat communications up to 12 months after treatment, with a maximum follow-up duration of 12 months post-treatment:
6.1. Clinical pregnancy rate
6.2. Biochemical pregnancy rate
6.3. Live birth rate
6.4. Miscarriage rate

Previous secondary outcome measures:
1. Biochemical pregnancy rate measured using data collection about on-site visits, telephone calls, and WeChat communications at 2 weeks after embryo transfer
2. Live birth rate measured using data collection about on-site visits, telephone calls and WeChat communications monthly until the end of pregnancy
3. Miscarriage rate measured using data collection about on-site visits, telephone calls and WeChat communications monthly until the end of pregnancy
4. Anti-Müllerian hormone measured using blood samples at baseline and after 8 weeks of treatment
5. Basic hormone levels (follicle-stimulating Hormone, estradiol, luteinizing hormone, FSH/LH ratio) measured using blood samples at baseline and after 8 weeks of treatment
6. Antral follicle count measured using ultrasound at baseline and after 8 weeks of treatment
7. Anxiety assessment measured using the self-rating anxiety scale (SAS) at baseline and after 8 weeks of treatment
8. Endometrial thickness and morphology measured using ultrasound on the day of embryo transfer
9. Patients undergoing ovulation induction cycles measured using data collection about the following indicators within 1 to 7 days after ovulation:
9.1. Gonadotropin (Gn) usage
9.2. Oocyte retrieval

9.3. Fertilization rate
9.4. Cleavage rate
9.5. Morphological assessment of oocytes
9.6. Day 3 high-quality embryo rate
9.7. Day 3 utilizable embryo rate
9.8. Blastocyst formation rate
9.9. High-quality blastocyst rate

### Overall study start date
06/10/2023

### Completion date
30/10/2026

## Eligibility

### Key inclusion criteria
Current inclusion criteria as of 02/12/2024:
1. Women aged 20 to 48 years
2. Conforming to the clinical diagnostic criteria for DOR
3. Voluntary and written informed consent

Previous inclusion criteria:
1. Women aged 20 to 42 years
2. Conforming to the clinical diagnostic criteria for DOR
3. Voluntary and written informed consent

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
20 Years

### Upper age limit
48 Years

### Sex
Female

### Target number of participants
112

### Key exclusion criteria
Current exclusion criteria as of 02/12/2024:
1. Endocrine disorders such as hyperprolactinemia, hyperandrogenemia, chronic adrenal insufficiency, and severe thyroid dysfunction.
2. Reproductive system anomalies such as severe hydrosalpinx, significant tubal or pelvic

adhesions, and myomas invading the endometrium, which adversely affect the outcome of pregnancies.
3. Immune system disorders such as immune nephritis and systemic lupus erythematosus, which may lead to infertility.
4. Contraindications to pregnancy or uterine non-viability for gestation.
5. Infertility attributable to congenital malformations of the reproductive system, chromosomal anomalies, or other genetic etiologies.
6. Severe comorbidities including serious cardiovascular, hepatic, renal, hematopoietic system diseases, malignancies, and mental health disorders.
7. Received DOR-related interventions within 3 months.
8. Deemed unsuitable for participation in the trial by the researcher.

Previous exclusion criteria:
1. Male factor infertility characterized by severe oligospermia, asthenospermia, necrospermia, teratospermia, or azoospermia
2. Conditions such as severe hydrosalpinx, significant tubal or pelvic adhesions, and myomas invading the endometrium, which adversely affect the outcome of IVF pregnancies
3. Immune system disorders such as immune nephritis and systemic lupus erythematosus, which may lead to infertility
4. Endocrinopathies such as hyperprolactinemia, hyperandrogenemia, chronic adrenal insufficiency, and marked thyroid dysfunction
5. Infertility attributable to congenital malformations of the reproductive system, chromosomal anomalies, or other genetic etiologies
6. Coexistence of severe cardiovascular, cerebrovascular, hepatic, renal, or hematopoietic disorders, malignant neoplasms, or psychiatric conditions.
7. Contraindications to pregnancy or uterine non-viability for gestation
8. Received DOR-related interventions (ie. drugs, acupuncture, herbs, etc) within 4 weeks
9. Subjects considered ineligible for trial participation based on researcher evaluation

### Date of first enrolment
30/01/2024

### Date of final enrolment
30/06/2026

## Locations

### Countries of recruitment
China

### Study participating centre
**Luohu District Hospital of Traditional Chinese Medicine**
16 Xiantan Road, Luohu District
Shenzhen
China
518004

# Sponsor information

### Organisation
Shenzhen Municipal People's Government

### Sponsor details
Shenzhen Municipal Health Commission
East Block, New Town Building, No. 1025 Shennan Middle Road, Futian District
Shenzhen
China
518031
+86 (0)755-88113731
zyc@wjw.sz.gov.cn

### Sponsor type
Government

### Website
http://wjw.sz.gov.cn/

### ROR
https://ror.org/05rcfc739

### Organisation
Shenzhen Luohu District Science and Technology Innovation Bureau

### Sponsor details
17/F, Luohu Business Centre, No. 2028 Shennan Road East, Luohu District
Shenzhen
China
518001
+86 (0)755-25666780
lh_kcj@szlh.gov.cn

### Sponsor type
Government

### Website
http://www.szlh.gov.cn/

# Funder(s)

### Funder type
Government

### Funder Name
Sanming Project of Medicine in Shenzen Municipality

### Alternative Name(s)
'sanming' project of medicine in Shenzhen, Sanming Project of Medicine in Shenzhen, San-Ming Project of Medicine in Shenzhen, Sanming Project of Medicine in Shenzen Municipal

### Funding Body Type
Government organisation

### Funding Body Subtype
Local government

### Location
China

### Funder Name
Soft science Research Program of Luohu District

## Results and Publications

### Publication and dissemination plan
The researchers plan to publish the protocol before February 2024. They plan to publish results before October 2027.

### Intention to publish date
30/10/2027

### Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

### IPD sharing plan summary
Published as a supplement to the results publication

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | | | 09/01/2024 | No | Yes |
| Protocol article | | 30/07/2025 | 05/08/2025 | Yes | No |