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STUDY PROTOCOL

Efficacy of Acupuncture for Diminished Ovarian Reserve: A Randomized Controlled Trial Protocol

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Background: With diminished ovarian reserve (DOR) becoming increasingly younger in women, age-related fertility decline in females is gradually becoming one of the most important factors affecting female fertility. The purpose of the study is to assess whether acupuncture can successfully relieve the age-related decline in female fertility. This will provide substantial proof in support of the therapeutic effectiveness of acupuncture.

Methods: This is a randomized, double-blind, controlled trial. There will be 108 participants diagnosed with DOR recruited in China. Participants will be randomly assigned in a 1:1 ratio to two groups, including acupuncture and sham acupuncture groups. The participants will receive acupuncture treatments three times a week, each lasting 30 minutes, for 36 weeks. The primary outcome was the change in ovarian function modeling as assessed by four metrics: age, ovarian reserve markers such as follicle-stimulating hormone (FSH) and anti-Müllerian hormone (AMH) in the Ovarian Reserve Function Prediction Tool (OvaRePred). Secondary outcomes will include changes in the antral follicle count (AFC), serum sex hormone levels, Zung's Self-rating Anxiety Scale (SAS), and the Self-rating Depression Scale (SDS). Adverse events (AEs) associated with acupuncture will be documented following each treatment session. AEs will be monitored and reported to ensure patient safety throughout the trial.

Expected Results and Conclusion: We will be able to measure the effectiveness of acupuncture for patients with DOR and whether acupuncture is superior to sham acupuncture. The proposed acupuncture treatment might provide an alternative option for those patients.

Trial Registration Number: ChiCTR2400086376.

Keywords: acupuncture, female age-related fertility decline, randomized controlled trial, diminished ovarian reserve

Introduction

Diminished ovarian reserve (DOR) refers to a decline in both the quantity and quality of oocytes, resulting in hormonal abnormalities and compromised fertility among women.[1] Reproductive dysfunction has emerged as a prominent factor in the aging female population, significantly impacting their reproductive capacity.[2] DOR affects approximately 26% of women of reproductive age worldwide.[3,4] The increasing trend of delayed childbearing, combined with poor lifestyle habits and psychological stress, has led to a rising incidence of DOR among young women.[5] This troubling trend creates a negative cycle, where DOR not only reduces reproductive potential but also worsens physical and psychological stress, potentially further impairing ovarian function. If left untreated, DOR may lead to premature ovarian failure (POF), which can have significant implications for reproductive health.[6,7] DOR affects younger women more commonly, and its prevalence in the infertile population increases with age as a result of most women deferring childbearing due to changes in lifestyle and rising social pressures.[8–10] Therefore, the current objective is to actively involve patients with DOR in adopting lifestyle modifications, hormone replacement therapy (HRT), or assisted reproductive technology (ART)

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interventions to optimize their ovarian function and enhance fertility outcomes.[11,12] However, long-term HRT exhibits limited efficacy in enhancing clinical pregnancy rates and is associated with potential risks such as an elevated susceptibility to cardiovascular disease and endometrial thinning.[13–15]

Acupuncture is a therapeutic modality frequently employed in the realm of complementary and alternative medicine (CAM) with the aim of enhancing ovarian functionality.[16] Extensive clinical evidence indicates that acupuncture significantly improves ovarian function by modulating serum sex hormone levels and alleviating anxiety and depression.[17,18] This therapeutic approach has been associated with enhanced reproductive outcomes, including increased oocyte yield, improved embryo quality, higher implantation rates, and improved clinical pregnancy rates, with optimal efficacy typically observed after 1–3 menstrual cycles of treatment.[19] Nonetheless, the effectiveness of acupuncture is in doubt due to the small number of studies, poor quality, and limited outcome indicators, despite some clinical trials indicating promising results.[20–23] Currently, the evaluation of ovarian function changes often relies on a combination of biomarkers such as luteinizing hormone (LH) and anti-Müllerian hormone (AMH).[24] It is difficult to accurately and effectively assess the efficacy of various treatments because these indicators are numerous and complex and may be interpreted differently by clinicians, which may lead to different results.[25]

To address this, our tool utilizes the fixed-interval theory of reproductive patterns to estimate age at menopause. OvaRePred is the development of a comprehensive tool that not only assesses an individual's current ovarian reserve, but also predicts important fertility time points. The tool uses the fixed-interval theory of the reproductive pattern to estimate age at menopause and gives three predictive models (AA, AFA, and AAFA) that divide ovarian reserve function into four classes that correspond to different levels of ovarian function.[25] This comprehensive tool will allow for a more precise and personalized assessment of ovarian function, surpassing traditional methods of ovarian reserve assessment that rely heavily on clinician expertise.

Consequently, OvaRePred scores and grading were employed as the primary outcome measures in this study to assess the efficacy of acupuncture in mitigating age-related fertility decline, thereby providing robust and definitive scientific evidence supporting the effectiveness of acupuncture. Moreover, OvaRePred was utilized for predicting menopausal age among fertile women, offering a reliable reference timeframe for determining optimal conception timing. Although evidence suggests the therapeutic potential of acupuncture, its superiority over sham acupuncture in improving ovarian function and pregnancy outcomes remains controversial. Several randomized trials have reported comparable efficacy between verum acupuncture and sham acupuncture,[22,23] highlighting challenges in designing appropriate control groups. To address these issues, this study utilized standardized sham acupuncture as a placebo control to minimize placebo effects and preserve blinding, thereby enhancing methodological rigor and the reliability of the findings.

This study aims to explore the role of acupuncture as an adjunctive therapy for improving ovarian function, providing valuable insights into its clinical application for managing ovarian dysfunction. Additionally, it seeks to establish a foundation for future research on integrating modern predictive tools, such as OvaRePred, with CAM therapies to promote a multidisciplinary approach in fertility.

Methods

Study Design

This is a double-blind randomized controlled trial aimed at comparing the efficacy of acupuncture versus sham acupuncture in addressing ovarian function among 108 participants diagnosed with diminished ovarian reserve (DOR). The study protocol adheres to the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) checklist (Appendix 1). Prior to commencing the study, comprehensive information regarding the study objectives, methods, potential benefits, and risks will be provided to participants by a research assistant. Participants have autonomy in deciding whether or not to participate or withdraw from the study after gaining a thorough understanding of its overall design; those who choose to participate will be required to sign an informed consent form. The ethics committee of Sichuan Jinxin Sinan Women's and Children's Hospital has reviewed this study. Registration for this trial has been completed on Clinicaltrials.gov (ChiCTR2400086376). Figure 1 visually represents the flow of the study, while Table 1 presents a detailed timeline.

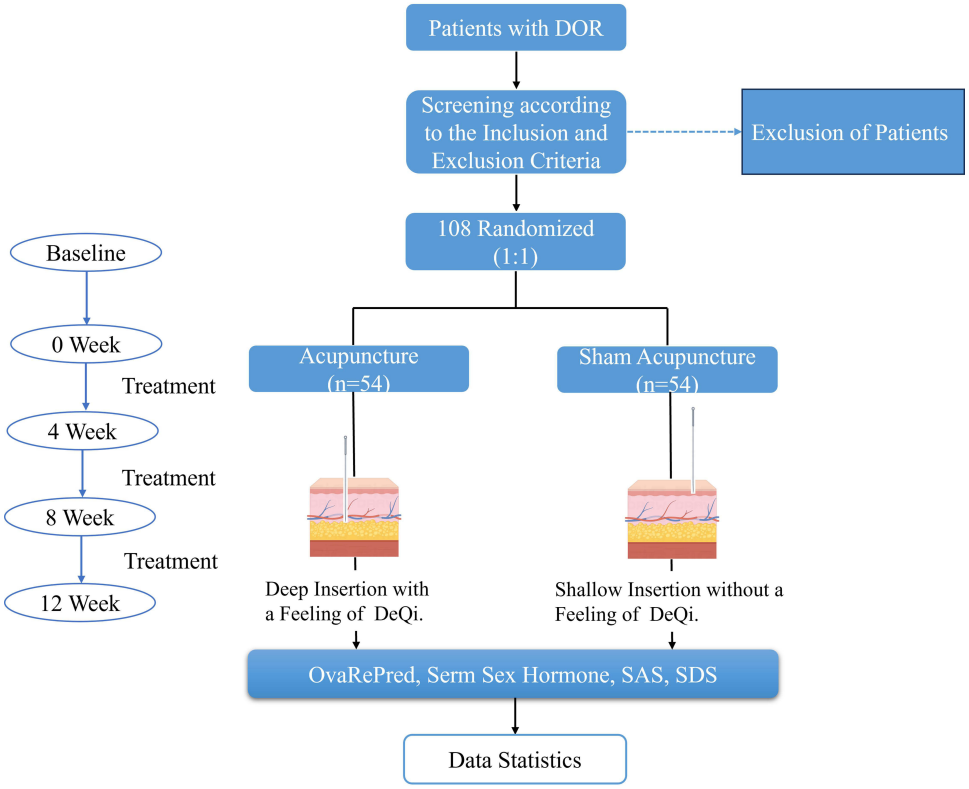

Figure 1 The Research Flowchart.

Study Population

Diagnostic Criteria

We enrolled participants who had received a confirmed diagnosis of DOR and evaluated their ovarian function using OvaRePred. The eligibility for the diagnosis of DOR was determined by the *Guidelines Outlined in the Expert Consensus on the Clinical Diagnosis and Management of Diminished Ovarian Reserve 2022* published by the Expert Consensus Panel on the Clinical Diagnosis and Management of DOR.[20] Each participating physician was responsible for the screening and identification of patients based on these criteria.

Table 1 Trial Processes Chart

Period	**Baseline**		**Treatment**		
Week	**−4**	**0**	**4**	**8**	**12**
Recruitment					
Medical history	○				
AFC	○				
AMH	○				
Informed consent	○				
Randomization		○			
Intervention					
Acupuncture			○	○	○
Sham acupuncture			○	○	○

(*Continued*)

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Table 1 (Continued).

Period	Baseline		Treatment		
Week	**−4**	**0**	**4**	**8**	**12**
Assessment					
OvaRePred		○			○
FSH		○			○
LH		○			○
E_2		○			○
P		○			○
SAS		○			○
SDS		○			○
Adverse events					○

Abbreviations: AFC, Antral follicle count; AMH, Anti-Müllerian hormone; OvaRePred, Ovarian Reserve Function Prediction Tool; FSH, Follicle-stimulating hormone; LH, Luteinizing hormone; E_2, Estradiol; P, Progesterone; SAS, Zung Self-Rating Anxiety Scale; SDS, Zung Self-Rating Depression Scale.

Diagnostic Criteria

1. AMH <1.1ng/mL, suggesting a diminish in ovarian reserve function;
2. Antral follicle count (AFC) <5-7 follicles, suggesting a diminish in ovarian reserve function;
3. FSH ≥10 IU/L in two consecutive menstrual cycles indicate diminished ovarian function.

Inclusion Criteria

1. Female participants aged between 30 and 45 years.
2. Participants diagnosed with DOR and classified as having poor ovarian reserve (≤75 points) according to the AAFA model used by OvaRePred.
3. Participants with regular menstrual cycles, specifically within a range of 28±7 days.
4. Participants who are not currently enrolled in any other ongoing clinical study and have not undergone acupuncture treatment for infertility in the past three months.
5. The participant must personally provide her informed consent.

Exclusion Criteria

1. Participants with DOR resulting from congenital factors such as pelvic surgery, radiotherapy, chemotherapy, uterine artery embolization, hormonal or immunosuppressive treatments.
2. Participants who also present comorbid endocrine disorders affecting reproductive function, including polycystic ovary syndrome, hyperprolactinemia, hyperandrogenemia, thyroid disease, and diabetes mellitus.
3. Participants with severe cardiovascular, cerebrovascular, hepatic or renal diseases or malignant hematologic conditions.
4. Participants with any psychiatric illness.
5. Participants or their partners exhibiting chromosomal abnormalities.
6. Participants contraindicated for acupuncture due to bleeding tendencies, susceptibility to infection, severe allergic diseases or presence of skin ulcers or scars.
7. Participants planning to undergo ART within 3 months of enrollment.

Patient and Public Involvement

Due to the implementation of a double-blind experimental design, it was not appropriate or feasible to involve patients or the public in the design, conduct, reporting, or dissemination plans of our research.

OvaRePred Scores and Status

During the initial phase of the study, each participant will provide demographic data, medical history, menstrual and reproductive history, serological indicators, and details of any current medical therapy. The OvaRePred assessment will be completed by participants during the screening period (baseline week) using the online tool. The scoring criteria for ovarian reserve status are as follows:

1. Excellent Ovarian Reserve (90–100 points): Indicates a robust availability of healthy oocytes, suggesting optimal fertility potential.
2. Good Ovarian Reserve (75–90 points): Reflects a satisfactory quantity of viable oocytes, with potential fertility impact.
3. Fair Ovarian Reserve (50–75 points): Indicates a limited reserve of oocytes, which may require ART for conception.
4. Poor Ovarian Reserve (≤ 50 points): Suggests very few viable oocytes, indicating a significantly reduced ovarian reserve and potential challenges in natural concept.

In this study, low ovarian reserve is defined as a score of ≤ 75 points, which encompasses both "Fair" and "Poor" ovarian reserve classifications.

Blinding and Randomization

The random assignment of participants was conducted using SAS® 9.4 software (SAS Institute Inc). The order of random assignment will be documented in sealed nontransparent envelopes containing two sets of randomized numbers. Furthermore, these envelopes will be sequentially opened by an independent research assistant, separate from the investigator and evaluator.[26] Additionally, the research assistant will randomly assign participants in a 1:1 ratio to either the acupuncture or sham acupuncture groups.

Sample Size Calculation

The primary outcome measure of this study is the ovarian reserve score, which is calculated using the OvaRePred algorithm.[25] Although not previously utilized as a primary outcome measure, the reliability of AMH as a predictor of ovarian reserve is well-established and it serves as an independent variable in the OvaRePred study.[27] Therefore, the selection of AMH was made for conducting sample size calculation in this study.

According to the randomized controlled trial conducted by Wang Ling et al,[28] both the acupuncture and placebo groups exhibited a significant increase in AMH levels of 0.3 μg/L after a 3-month treatment period (pre-treatment: 0.44 ± 0.29 μg/L, post-treatment: 0.66 ± 0.38 μg/L). The sham acupuncture group exhibited no statistically significant alteration in AMH levels following a 3-month intervention (pre-treatment: 0.49 ± 0.29 μg/L, post-treatment: 0.50 ± 0.30 μg/L). Based on the research findings of Wang Ling et al, assuming similar results, we postulate that the AMH level in the acupuncture group will increase by 0.3 μg/L compared to the sham acupuncture group, with a variance of 0.4 μg/L. The sample size for each group was determined using PASS (version 2021) software, with a bilateral α of 0.05 and a power of 90% (1-β). Based on these calculations, a minimum sample size of 43 participants per group was required. Considering a potential dropout rate of 20%, we aimed to recruit 54 participants per group, resulting in a total sample size of 108.

The sample size formula used is:

$$N1 = N2 = \frac{2(t\alpha/2 + t\beta)^2 \times \sigma^2}{\delta^2}$$

Acupuncture and Sham Acupuncture

Acupuncture Group

We have selected common acupoints used to improve ovarian function in women based on our clinical experience. Each participant will be treated with acupuncture in a private treatment room to assure privacy and prevent communication between participants.

According to the standardized location of *Nomenclature and location of meridian points* in 2021 (GB/T 12346–2021), acupoints can be divided into two categories.[29] In Acupoint Group 1, the acupoints on the frontal region that were treated while the participants were in the prone position included Shenting (GV24), Baihui (DU20), Benshen (GB13), Zhongwan (CV12), Huangshan (KI16), Daimai (GB26), Qihai (CV6), Guanyuan (CV4), Dahe (KI12), Zigong (EX-CA1), Zusanli (ST36), Sanyinjiao (SP6) and Taichong (LR3). The backside acupoints treated in the prone position of the patient in Acupoint Group 2 consisted of Shenshu (BL23), Dachangshu (BL25), Ciliao (BL32) and Taixi (KI3). Participants alternated between the two groups of acupoints during treatment, starting first with the acupoints in Group 1. Figure 2 illustrates the precise locations of these points, and Appendix 2 lists them accordingly.

The patient's skin and the acupuncturist's fingers will be disinfected using 75% ethanol before inserting sterile, disposable acupuncture needles (0.25 mm in diameter, lengths of 25 mm, 40 mm, or 75 mm, Hua Tuo, Suzhou, China) into the designated acupoints. The needles will be manipulated to elicit the De Qi sensation, characterized by sensations such as soreness, numbness, heaviness, fullness, and pain.[30] A total of 36 acupuncture treatment will be administered over a 12-week period, with each session lasting 30 minutes. No manual manipulation will be performed during the acupuncture retention phase. Treatments will be conducted every other day, with three sessions per week. The acupuncture interventions will be handled by licensed acupuncturists with more than five years of experience. The acupuncture treatments will begin on the second day of the menstrual cycle and continue uninterrupted for the duration of the menstrual period.

Sham Acupuncture Group

The sham acupuncture procedure was meticulously standardized using 0.25 mm × 25 mm disposable sterile needles inserted to a depth of 0.1 cun (approximately 3 mm) at predetermined non-acupoint locations. These control points were selected based on established sham acupuncture protocols, anatomically corresponding to but not overlapping with the acupuncture points (see Figure 2 and Appendix 2 for detailed locations). All practitioners underwent rigorous training to ensure consistent shallow needle insertion without eliciting De Qi sensation, maintain proper needle manipulation techniques to preserve participant blinding, and adhere to standardized sterilization procedures. In addition, the treatment duration and course are exactly the same as those of the acupuncture group. Moreover, subjects in the sham acupuncture group will be treated individually in a separate room to prevent unblinding caused by interference from other factors. The intervention protocol strictly followed the STRICTA guidelines for sham acupuncture reporting, with detailed quality control measures documented in Appendix 3.

Outcome Measurement

Primary Outcomes

Primary efficacy outcomes will be assessed using ovarian reserve assessment scores and status derived from the OvaRePred, including scores from the AAFA model, AFA model, and AA model. These assessments will be performed at baseline and on days 2–5 of the participant's menstrual cycle after 12 weeks of treatment.

Secondary Outcomes

Serum levels of AMH, FSH, Estradiol (E_2), LH, and Progesterone (P) will be measured at baseline, after 4 weeks, 8 weeks, and 12 weeks of treatment (during days 2–5 of the menstrual cycle).

Zung's Self-rating Anxiety Scale (SAS) and the Self-rating Depression Scale (SDS), which are instruments that screen for anxiety and depression, will be used to assess changes in the psychological status of the participant before treatment and at the end of the 12-week treatment period, on days 2–5 of the participant's menstrual cycle.[31,32]

Safety Outcomes

At each visit, clinicians will inquire about and document any adverse events (AEs) reported by the participants. Common AEs associated with acupuncture include intolerable pain, localized hematoma, and infection. All AEs will be recorded in the Case Report Form (CRF), detailing the event name, onset and resolution dates, severity, causality,

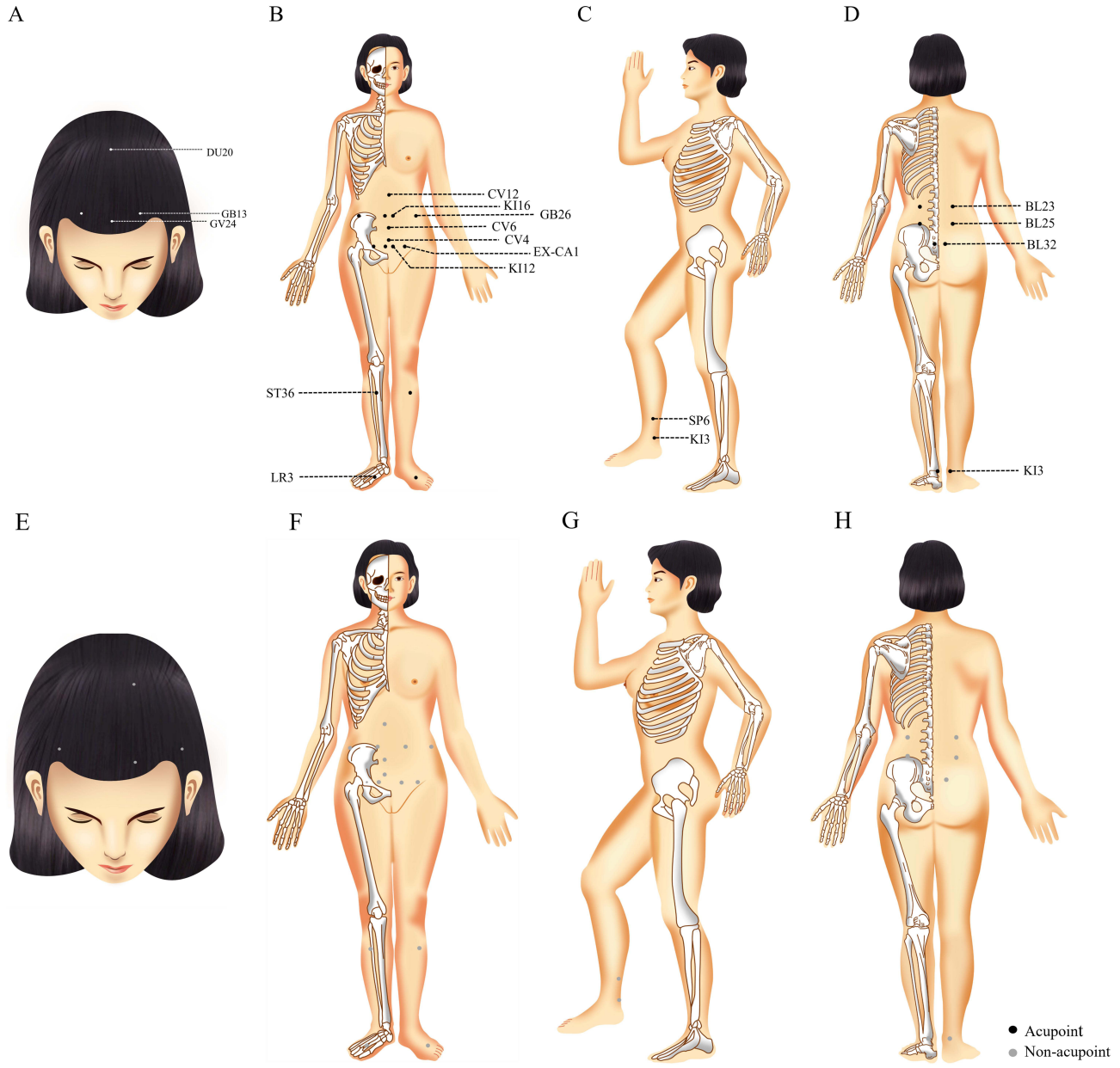

Figure 2 Schematic Representation of Acupuncture Point Localization. (**A**) Acupuncture group head acupuncture point localization; (**B**) Acupuncture group front acupuncture point localization; (**C**) Acupuncture group lateral acupuncture point localization; (**D**) Acupuncture group back non-acupuncture point localization; (**E**) Sham acupuncture group head non-acupuncture point localization; (**F**) Sham acupuncture group front non-acupuncture point localization; (**G**) Sham acupuncture group lateral non-acupuncture point localization; (**H**) Sham acupuncture group back non-acupuncture point localization. The black dots represent the acupuncture points for the acupuncture group; the gray dots represent the non-acupuncture points for the sham acupuncture group.

impact on the intervention, and outcome.[33] AEs will be analyzed and reported according to a predefined protocol, which includes the calculation of incidence rates and comparison of severity between the treatment and control groups. Severity will be classified as follows: mild AEs are transient, do not interfere with normal activities, and require no medical intervention; moderate AEs cause discomfort, limit normal activities, and require medical treatment; severe AEs significantly impair health, necessitate urgent medical intervention, and may lead to hospitalization or long-term rehabilitation. Statistical analyses will be performed to compare the incidence rates and severity of AEs between the treatment and control groups.

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Co-Medication

During the whole period of acupuncture treatment, it was strictly forbidden for participants to self-medicate with Chinese herbs or any other complementary medications without the reproductive medicine specialist's explicit approval. Non-reproductive medicine specialists are not allowed to prescribe any medications to participants during the study. If additional medication is required, participants must notify the researchers promptly or the study may be terminated.

Statistical Analysis

Statistical analyses will be performed using SAS version 9.1.3. Both intention-to-treat (ITT) and per-protocol (PP) analyses will be conducted to ensure the robustness of the results. For the primary outcomes, linear regression models with baseline adjustment will be applied for continuous variables, while repeated-measures ANOVA or mixed-effects models will be used for longitudinal data to account for within-subject correlations. Missing data will be handled using multiple imputation (MI) under the missing-at-random (MAR) assumption, with sensitivity analyses performed to compare imputed and complete-case results. Normality and homogeneity of variance will be tested using Shapiro–Wilk and Levene's tests, guiding the selection of appropriate statistical methods. Depending on data distribution, the following tests will be used: independent or paired t-tests for normally distributed data, Mann–Whitney *U*-tests for non-parametric comparisons, and chi-square tests or Fisher's exact tests for categorical variables. Exploratory subgroup analyses will investigate treatment response variations based on baseline characteristics, including age (30–40 vs 40–45 years) and baseline OvaRePred scores (50–75 vs ≤50), using interaction terms in regression models. Results will be reported as mean ± SD for normally distributed continuous variables or median (interquartile range, IQR) for non-normally distributed data. Statistical significance will be set at $P < 0.05$ for all two-sided tests, with corrections for multiple comparisons applied where appropriate.

Discussion

Female fertility declines with age due to physiological DOR.[34] Concurrently, changes in lifestyle habits have resulted in a shift towards younger occurrences of DOR.[35] Patients with DOR typically present with reduced follicle numbers and ovarian volume, impairing their ability to produce high-quality embryos.[12] Therefore, enhancing ovarian reserve is considered crucial in reversing DOR, although the exact pathogenesis of DOR remains incompletely understood.[36] This study aimed to investigate the efficacy of acupuncture in clinical practice by evaluating the effects of acupuncture on ovarian reserve function, AFC, and serum sex hormones in patients with DOR at different ages in a clinical randomized controlled trial.

Sham acupuncture is often considered a placebo control in clinical randomized controlled trials.[37] The therapeutic effects of acupuncture are based on the stimulation of specific acupoints using precise manipulation techniques. Due to the inherent nature of acupuncture, achieving double-blind conditions is challenging, particularly with respect to acupoint selection and the method of stimulation. Consequently, a sham acupuncture protocol was implemented in the control group to minimize the potential therapeutic effects associated with the placebo. While some placebo responses are inevitable, efforts were made to reduce their influence. Participants in the sham acupuncture group were treated in a separate room to prevent unintentional unblinding, ensuring that treatment allocation remained concealed throughout the study.

The OvaRePred serves as an online assessment tool that evaluates ovarian reserve status in reproductive-aged women based on age and sex hormone indicators, aiding in optimizing conception timing and managing ovarian diseases.[17] OvaRePred is a validated tool developed by Xuhuiyu et al based on extensive and long-term clinical data, demonstrating high reliability in predicting ovarian reserve and menopause timing.[38–40] DOR is closely linked with age, with approximately 10% of women experiencing premature ovarian aging leading to early menopause.[41] OvaRePred is an online clinical model prediction tool that predicts the present state and future outcome of a disease.[42,43] In this study, the OvaRePred score and grade were selected as the primary outcome indicators to objectively evaluate the therapeutic effect of acupuncture on age-related decline in female fertility. The tool's capacity to forecast the participant's future age at perimenopause will be helpful in a more accurate assessment of the short- and long-term effectiveness of acupuncture.

The SAS and SDS are widely used to assess anxiety and depression in clinical trials. However, it is important to acknowledge that these self-reported measures may be subject to biases, as participants may underreport or overreport their symptoms due to personal or social factors, which could affect the accuracy of the results. To mitigate these biases, we ensured the anonymity and confidentiality of participants during the assessment process. Additionally, the scales were administered by trained clinicians, and participants were instructed to respond as honestly and accurately as possible, thus minimizing response bias. However, future studies could benefit from incorporating objective psychometric measures to complement the self-reported data and further enhance the reliability of psychological assessments.

This study implemented a 12-week intervention period corresponding to the typical human follicular development cycle of 2–3 months.[44] The duration enabled comprehensive assessment of acupuncture-induced modifications in ovarian function markers throughout a complete follicular growth phase. While the study design did not incorporate a follow-up period for evaluating longitudinal reproductive outcomes, we employed the validated OvaRePred prediction tool to estimate future reproductive potential. This analytical instrument calculated projected menopausal age and optimal fertility windows through quantitative analysis of established biomarkers including chronological age, AMH, FSH and AFC. Although clinical trial registration parameters necessitated restriction of the observation period to the twelve-week intervention phase, the acquired data provide essential baseline measurements for subsequent longitudinal investigations. These future studies will be crucial for validating potential correlations between short-term improvements in ovarian reserve markers and long-term reproductive outcomes.

Strengths and Limitations of this Study

In this study, a novel online tool was used to replace the complex and laborious observational indicators commonly used in the past to observe the effect of acupuncture on ovarian function in patients with age-related reduced fertility. The online tool also allowed for further prediction of the effect of acupuncture on future patients' perimenopausal ages. This study employed a standardized shallow-needling sham acupuncture protocol, maintaining procedural consistency with the acupuncture group. This rigorous control design ensured adequate blinding and facilitated the evaluation of specific therapeutic effects attributable to acupuncture. Furthermore, the insufficient visiting time is the limitation of this study.

Ethics and Dissemination

This trial will be conducted in accordance with the *Declaration of Helsinki*. The study protocol has been approved by the Medical Ethics Committee of Sichuan Jinxin Sinan Women's and Children's Hospital (No. (2023) Reproductive Ethics Review No. (041)). It was registered in the Clinical Trial Registry on May 31, 2022 (No. ChiCTR2400086376). Written informed consent will be obtained before randomization. Study results will be presented in academic meetings and peer-reviewed academic journals.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no potential conflicts of interest or financial relationships in this study.

References

1. Christodoulaki A, Boel A, Tang M, et al. Prospects of germline nuclear transfer in women with diminished ovarian reserve. *Front Endocrinol*. 2021:22635370. doi:10.3389/fendo.2021.635370.
2. Dong L, Teh DBL, Kennedy BK, et al. Unraveling female reproductive senescence to enhance healthy longevity. *Cell Res* 2023;33(1):11–29. doi:10.1038/s41422-022-00718-7
3. Devine K, Mumford SL, Wu M, et al. Diminished ovarian reserve in the United States assisted reproductive technology population: diagnostic trends among 181,536 cycles from the society for assisted reproductive technology clinic outcomes reporting system. *Fertil Sterility*. 2015;104 (3):612–619.e613. doi:10.1016/j.fertnstert.2015.05.017
4. Steiner AZ, Pritchard D, Stanczyk FZ, et al. Association between biomarkers of ovarian reserve and infertility among older women of reproductive age. *JAMA*. 2017;318(14):1367. doi:10.1001/jama.2017.14588
5. Hu Y, Wang W, Ma W, et al. Impact of psychological stress on ovarian function: insights, mechanisms and intervention strategies. *Int J Mol Med*. 2025;55(2). doi:10.3892/ijmm.2024.5475
6. Wang X, Wang L, Xiang W. Mechanisms of ovarian aging in women: a review. *J Ovarian Res*. 2023;16(1):67. doi:10.1186/s13048-023-01151-z
7. Chen L, Xia M, Duan H, et al. Research progress of Chinese medicine in treating decreased ovarian reserve function. *J Prac Chin Med*. 2024;40 (06):1238–1240.
8. Mills M, Rindfuss RR, McDonald P, et al. Why do people postpone parenthood? Reasons and social policy incentives. *Hum Reprod Update*. 2011;17(6):848–860. doi:10.1093/humupd/dmr026
9. Chen S, Lou Y, Xia R, et al. Female age and infertility and reduced fertility. *Inter J Reprod Health/Family Plan*. 2011;30(04):265–271.
10. Londero AP, Rossetti E, Pittini C, et al. Maternal age and the risk of adverse pregnancy outcomes: a retrospective cohort study. *BMC Pregnancy Childbirth*. 2019;19(1):261. doi:10.1186/s12884-019-2400-x
11. Tal R, Seifer DB. Ovarian reserve testing: a user's guide. *Am J Obstet Gynecol*. 2017;217(2):129–140. doi:10.1016/j.ajog.2017.02.027
12. Penzias A, Azziz R, Bendikson K, Practice Committee of the American Society for Reproductive Medicine. Electronic address aao, practice committee of the American society for reproductive M. Testing and interpreting measures of ovarian reserve: a committee opinion. *Fertil Steril*. 2020;114(6):1151–1157. doi:10.1016/j.fertnstert.2020.09.134
13. Wang Y, Huang R, Li X, et al. High concentration of chemerin caused by ovarian hyperandrogenism may lead to poor IVF outcome in polycystic ovary syndrome: a pilot study. *Gynecol Endocrinol*. 2019;35(12):1072–1077. doi:10.1080/09513590.2019.1622087
14. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the women's health initiative randomized controlled trial. *JAMA*. 2002;288321–288333.
15. Yang F, Yang Z. A prospective case-series study of acupuncture to regulate menstruation and promote pregnancy in the treatment of decreased ovarian reserve function. *Chin Acupunc Moxibus*. 2020;40(06):619–622. doi:10.13703/j.0255-2930.20190925-k0001
16. Fu Y, Ding DN, Shen Y, et al. Complementary and alternative medicine for premature ovarian insufficiency: a review of utilization and mechanisms. *Evid Based Complement Alternat Med*. 2022:20229053930. doi:10.1155/2022/9053930.
17. Zhao Y, Lan Y, Liu L, et al. Efficacy of acupuncture in animal models of various ovarian dysfunctions: a systematic review and meta-analysis. *Front Med*. 2024;11. doi:10.3389/fmed.2024.1348884
18. Huang S, Zhang D, Shi X, et al. Acupuncture and related therapies for anxiety and depression in patients with premature ovarian insufficiency and diminished ovarian reserve: a systematic review and meta-analysis. *Front Psychiatry*. 2024:151495418. doi:10.3389/fpsyt.2024.149541.
19. Zhang X, Sun H, Zhang N, et al. Conception vessel acupuncture research regularity in the treatment of diminished ovarian reserve: a multi-center, large-sample prospective cohort study protocol. *Front Endocrinol*. 2024;15. doi:10.3389/fendo.2024.1380444
20. Feng J, He H, Wang Y, et al. The efficacy and mechanism of acupuncture in the treatment of male infertility: a literature review. *Front Endocrinol*. 2022:131009537. doi:10.3389/fendo.2022.10095.
21. Feng J, Wang J, Zhang Y, et al. The efficacy of complementary and alternative medicine in the treatment of female infertility. *Evid Based Complement Alternat Med*. 2021;2021:6634309. doi:10.1155/2021/6634309
22. Xie Y, Shi W, Tan Y, et al. Acupuncture and moxibustion for diminished ovarian reserve: a scoping review. *Comple Ther Med*. 2023:77102973. doi:10.1016/j.ctim.2023.102973.
23. Cheong YC, Dix S, Hung Yu Ng E, et al. Acupuncture and assisted reproductive technology. *Cochrane Database Syst Rev*. 2013;7:CD006920. doi:10.1002/14651858.CD006920.pub3
24. Wang RR, Su MH, Liu LY, et al. Systematic review of acupuncture to improve ovarian function in women with poor ovarian response. *Front Endocrinol*. 2023:141028853. doi:10.3389/fendo.2023.1028853.
25. Xu H, Feng G, Yang R, et al. OvaRePred: online tool for predicting the age of fertility milestones. *Innovation*. 2023;4(5):100490. doi:10.1016/j.xinn.2023.100490
26. Clark L, Dean A, Mitchell A, et al. Envelope use and reporting in randomised controlled trials: a guide for researchers. *Res Methods Med Health Sci*. 2020;2(1):2–11. doi:10.1177/2632084320957204
27. Di Clemente N, Racine C, Pierre A, et al. Anti-mullerian hormone in female reproduction. *Endocr Rev*. 2021;42(6):753–782. doi:10.1210/endrev/bnab012
28. Wang L, Ma J, Xu J, et al. A randomized double-blind controlled study of he's nurturing nest granules combined with acupuncture in the treatment of ovarian reserve hypoplasia with infertility in patients with renal deficiency. *J Beijing Univ Trad Chin Med*. 2023;46(09):1218–1226.
29. Wu X, Huang L, Zhao J. Interpretation of the standard "nomenclature and location of meridian points (GB/T 12346-2021). *Chin Acupunc Moxibus*. 2021;42:579–582+584. doi:10.13703/j.0255-2930.20220117-k0001
30. Zhou K, Fang J, Wang X, et al. Characterization of de qi with electroacupuncture at acupoints with different properties. *J Altern Complement Med*. 2011;17(11):1007–1013. doi:10.1089/acm.2010.0652
31. Dunstan DA, Scott N. Norms for Zung's self-rating anxiety scale. *BMC Psychiatry*. 2020;20(1):90. doi:10.1186/s12888-019-2427-6
32. Dunstan DA, Scott N. Clarification of the cut-off score for Zung's self-rating depression scale. *BMC Psychiatry*. 2019;19(1):177. doi:10.1186/s12888-019-2161-0
33. Kawakami T, Kohsaka S, Sato Y, et al. Standards for assessing and reporting adverse events. *Lancet Respir Med*. 2022;10(12):e110–e111. doi:10.1016/S2213-2600(22)00444-1

34. American College of O, Gynecologists Committee on Gynecologic P, Practice C. Female age-related fertility decline. Committee opinion no. 589. *Fertil Steril*. 2014;101(3):633–634. doi:10.1016/j.fertnstert.2013.12.032.
35. Pastore LM, Christianson MS, Stelling J, et al. Reproductive ovarian testing and the alphabet soup of diagnoses: DOR, POI, POF, POR, and FOR. *J Assist Reprod Genet*. 2018;35(1):17–23. doi:10.1007/s10815-017-1058-4
36. Yin J, Chang H-M, Li R, et al. Recent progress in the treatment of women with diminished ovarian reserve. *Gynecol Obs Clin Med*. 2021;1(4):186–189. doi:10.1016/j.gocm.2021.10.004
37. Lim CED, Rwc N, Cheng NCL, et al. Acupuncture for polycystic ovarian syndrome. *Cochrane Database Syst Rev*. 2019;2019(7). doi:10.1002/14651858.CD007689.pub4
38. Han Y, Xu H, Feng G, et al. An online tool for predicting ovarian reserve based on AMH level and age: a retrospective cohort study. *Front Endocrinol*. 2022:13946123. doi:10.3389/fendo.2022.946123.
39. Xu H, Feng G, Wang H, et al. A novel mathematical model of true ovarian reserve assessment based on predicted probability of poor ovarian response: a retrospective cohort study. *J Assist Reprod Genet*. 2020;37(4):963–972. doi:10.1007/s10815-020-01700-1
40. Xu H, Shi L, Feng G, et al. An ovarian reserve assessment model based on anti-müllerian hormone levels, follicle-stimulating hormone levels, and age: retrospective cohort study. *J Med Internet Res*. 2020;22(9):e19096. doi:10.2196/19096
41. McCallie BR, Haywood M, Denomme MM, et al. Forecasting early onset diminished ovarian reserve for young reproductive age women. *J Assist Reprod Genet*. 2021;38(7):1853–1860. doi:10.1007/s10815-021-02155-8
42. van Smeden M, Reitsma JB, Riley RD, et al. Clinical prediction models: diagnosis versus prognosis. *J Clin Epidemiol*. 2021:132142–132145. doi:10.1016/j.jclinepi.2021.01.009.
43. Riley RD, Collins GS. Stability of clinical prediction models developed using statistical or machine learning methods. *Biom J*. 2023;65(8):e2200302. doi:10.1002/bimj.202200302
44. Homer HA. Understanding oocyte ageing: can we influence the process as clinicians? *Curr Opin Obstet Gynecol*. 2021;33(3):218–224. doi:10.1097/gco.0000000000000708