Efficacy of Traditional Chinese Herbal Medicine in the management of female infertility: A systematic review

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Summary

Objectives: To assess the effect of Traditional Chinese Herbal Medicine (CHM) in the management of female infertility and on pregnancy rates compared with Western Medical (WM) treatment.

Methods: We searched the Medline and Cochrane databases and Google Scholar until February 2010 for abstracts in English of studies investigating infertility, menstrual health and Traditional Chinese Medicine (TCM). We undertook meta-analyses of (non-)randomised controlled trials (RCTs) or cohort studies, and compared clinical pregnancy rates achieved with CHM versus WM drug treatment or in vitro fertilisation (IVF). In addition, we collated common TCM pattern diagnosis in infertility in relation to the quality of the menstrual cycle and associated symptoms.

Results: Eight RCTs, 13 cohort studies, 3 case series and 6 case studies involving 1851 women with infertility were included in the systematic review. Meta-analysis of RCTs suggested a 3.5 greater likelihood of achieving a pregnancy with CHM therapy over a 4-month period compared with WM drug therapy alone (odds ratio = 3.5, 95% CI: 2.3, 5.2, p < 0.0001, n = 1005). Mean (SD) pregnancy rates were 60 ± 12.5% for CHM compared with 32 ± 10% using WM drug therapy. Meta-analysis of selected cohort studies (n = 616 women) suggested a mean clinical pregnancy rate of 50% using CHM compared with IVF (30%) (p < 0.0001).

Conclusions: Our review suggests that management of female infertility with Chinese Herbal Medicine can improve pregnancy rates 2-fold within a 4 month period compared with Western Medical fertility drug therapy or IVF. Assessment of the quality of the menstrual cycle, integral to TCM diagnosis, appears to be fundamental to successful treatment of female infertility.

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Abbreviations: ART, assisted reproductive technologies; BBT, basal body temperature; CHM, Chinese Herbal Medicine; IVF, in vitro fertilisation; RCT, randomised controlled trial; PCOS, polycystic Ovary Syndrome; TCM, Traditional Chinese Medicine; WM, Western Medicine.

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Introduction

Infertility affects 15% or 3 million of couples in Australia and is defined as the inability to conceive or achieve a viable pregnancy after one year of regular unprotected intercourse. While 80% of infertility might be related to conditions such as endometriosis or Polycystic Ovary Syndrome (PCOS), 20% are ‘unexplained’ in the Western Medicine model.1,2 However, diagnosis of a specific disease/condition and subsequent treatment with surgery, drugs, in vitro fertilisation (IVF) or other assisted reproductive technologies (ART) does not always result in a viable pregnancy and live birth. In 2008, for example, more than 61,900 ART cycles were recorded in Australia and New Zealand, and of these 22.6% resulted in clinical pregnancy, and 17.2% resulted in live births.3

IVF treatment is costly, emotionally and financially, for the treated couples and also for the public. The Australian Government’s expenditure on ART was about A$108 million in 2005 or A$210 million in 2008 due to increasing demand. Costs of one IVF treatment cycle in addition to medications and consultations are about A$6000–7000 with out-of-pocket costs estimated at A$3000–4000.4,5

Infertility causes emotional distress and grief for the affected couple.6,7 However, there is a dearth of recognition by organisations and the community for couples suffering infertility or recurrent miscarriages, and support services are inferior to those offered for a visible loss of pregnancy such as stillbirth.8–11

Alternative holistic therapies, such as Traditional Chinese Medicine, offer less invasive and less costly physical and emotional treatment compared with standard Western Medical treatment. However, awareness of TCM therapy for infertility is generally low and often not suggested by Western Medical practitioners.11,12 The first port of call for most couples experiencing infertility in Australia is General Practitioners, who routinely refer to infertility clinics for initial investigations and potential IVF treatment.13

Traditional Chinese Medicine searches for the individual’s underlying imbalances causing the infertility using diagnostic tools such as pulse, tongue, complexion, general physical and emotional wellbeing, and menstrual history. TCM pattern diagnosis determines the specific individual treatment including Chinese Herbal Medicine (CHM) and acupuncture. TCM pattern diagnosis refers to whole body systems such as meridians and involves the kidney, liver (blood), spleen, heart, and lung systems, excess or deficiency patterns, heat or cold patterns. The treatment principle in TCM is to balance any diagnosed imbalance.14–18

A thorough assessment of menstrual history is embedded in standard TCM pattern diagnosis in female infertility, providing a visible window into the woman’s (in-)fertility status. The combination of the basal body temperature (BBT) curve, menstrual flow, colour of the menstrual blood and clot formation, mucus changes, and any associated pain or distension are directly related to TCM pattern diagnosis and therefore therapy.16,19

This review summarises current evidence on the efficacy of TCM herbal therapy for the management of female infertility and compares pregnancy rates to those achieved with Western Medical treatment. A practical guide of TCM pattern diagnostic is provided featuring common imbalances underlying infertility in relation to quality of the menstrual cycle and associated symptoms.

Methods

Search strategy

We searched the Medline and Cochrane databases and Google Scholar until February 2010 for abstracts in English.
Efficacy and diagnosis.

Types of studies
We included randomised controlled trials (RCTs), controlled trials (CTs), cohort studies (C), case series (CS) and case studies (Case) that investigated treatment of infertility with TCM herbal therapy.

Types of participants
Women of reproductive age with primary or secondary infertility were included. Infertility may have been associated with endometriosis, PCOS, amenorrhoea, advanced maternal age, or unexplained infertility. This review excluded studies of male infertility.

Types of interventions
Chinese Herbal Medicine (CHM) treatment defined as treatment with Chinese Herbs according to TCM pattern diagnosis. We included studies which used CHM alone, or in combination with acupuncture (Acu) or Western Medicine (WM) in the form of drugs or surgery. The control group in (R)CTs received WM pharmacological treatment only. In this review we excluded studies using acupuncture alone or TCM therapy (CHM ± Acu) in combination with assisted reproductive technologies (ART).

Types of outcome measures
The primary outcome was clinical pregnancy. We also assessed infertility status (number of years unsuccessful in achieving viable pregnancy), maternal age, CHM treatment duration, WM condition, and TCM pattern diagnosis, and — if available — live birth rate. In addition, we related common TCM pattern diagnosis in infertility to the quality of the menstrual cycle (colour, consistency and flow of blood, frequency, BBT, and associated symptoms including pain), and tongue and pulse appearance.

Study selection

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Data abstraction and quality assessment
Identified studies were assessed against the inclusion criteria and data abstracted independently by two authors, and consensus was reached by discussion. Reporting of study quality of RCTs was assessed using the risk of bias tool described in the Cochrane handbook for systematic reviews of interventions, and the Newcastle-Ottawa Quality Assessment Scheme was used to assess quality of cohort studies. We included case series and case studies in this review for further illustration and reference.

Data analysis
Meta-analysis of RCTs was conducted using the Cochrane Program Review Manager version 5.0.25. A random effects model and the inverse variance method were used for comparison of odds ratios between trials while accounting for heterogeneity between trials. We explored robustness of results by sensitivity analysis excluding selected trials with potential risk of bias.

Meta-analysis of cohort studies was conducted using the program Stata version 11. A pooled pregnancy rate of all studies was determined using a fixed model in the 'metan' package in Stata, with weighting of studies by sample size. Heterogeneity was explored by meta-regression analysis of the following variables: mean maternal age, mean length of infertility, mean CHM treatment duration and follow-up. We conducted sensitivity analysis excluding selected studies with potential risk of bias, and used this adjusted pooled estimate for comparison with the pregnancy rates of a cohort of women undergoing IVF.

Publication bias and small study effect for RCTs and cohort studies was assessed by funnel plot and Egger’s test.

Case study data were analysed descriptively. Additionally, information on the menstrual cycle and associated symptoms was systematically summarised in relation to TCM pattern diagnosis in infertility.

Results

Study description
A total of 24 articles and 6 books were included in the review featuring 8 RCTs, 13 cohort studies, 3 case series and 6 cases (Fig. 1). The eight RCTs studied 1005 participants, and the 13 cohort studies involved 793 participants. An additional 53 cases are described in the case series and case studies.

Characteristics of included studies are summarised in Table 1. Four of the eight RCTs investigated the effect of CHM alone in comparison to WM medication and four RCTs compared CHM plus WM medication with WM treatment alone. Ten cohort studies used CHM therapy alone, one combined CHM with acupuncture treatment, and two cohort studies combined CHM with either antibiotics, steroids or standard medication for hyperprolactinaemia. CHM alone or in combination with acupuncture was used in the treatment of infertility in the case studies.

Women who participated in the studies were between 18 and 45 years old, with a mean of 30 years. Infertility was experienced on average 4.5 years (range 1–20 years). Treatment duration with CHM was on average 4 months in the RCTs and cohort studies, and 5–6 months in the case studies, ranging from one up to 18 months for some individuals.

Methodological quality
RCTs were considered of sufficient quality to be included in the review if they reported detailed information on the
Table 1  Management of infertility and pregnancy rates using Chinese Herbal Medicine (CHM) therapy.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design, treatment groups</th>
<th>Age</th>
<th>Infertility</th>
<th>Treatment duration</th>
<th>N</th>
<th>WM condition</th>
<th>TCM pattern diagnosis</th>
<th>Pregnancy outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RCT</td>
<td>18–37 yrs (m25.5)</td>
<td>1–20 yrs (m7)</td>
<td>6 mths</td>
<td>107</td>
<td>PCOS</td>
<td>Spleen-Shen-Yang deficiency</td>
<td>TCM: 50/76 (66%) Cont: 8/31 (26%)</td>
</tr>
<tr>
<td>2</td>
<td>RCT</td>
<td>23–45 yrs (m30)</td>
<td>–</td>
<td>3 mths</td>
<td>24 mths follow-up</td>
<td>100</td>
<td>Endometriosis, surgery on all before trial</td>
<td>TCM: 32/48 (67%), m7 mths Cont: 29/52 (56%), m9.5 mths Cont: no side effects Cont: 13/52 (25%), acne, 19 (36.5%) increase in glutamic alanine transaminase, 31 (60%) oligomenorrhea</td>
</tr>
<tr>
<td>3</td>
<td>RCT</td>
<td>20–40 yrs</td>
<td>1–8 yrs</td>
<td>3–6 mths</td>
<td>90</td>
<td>PCOS, oligomenorrhea, amenorrhea</td>
<td>Blood stasis, Damp</td>
<td>TCM: 34/48 (71%) Cont: 12/42 (28.5%)</td>
</tr>
<tr>
<td>4</td>
<td>RCT</td>
<td>18–36 yrs (m29)</td>
<td>1–10 yrs</td>
<td>CHM 2 mths + CC 1 mth</td>
<td>86</td>
<td>PCOS</td>
<td>–</td>
<td>TCM: 24/46 (52.2%) Cont: 9/40 (22.5%)</td>
</tr>
<tr>
<td>5</td>
<td>RCT</td>
<td>25–30 yrs (n = 31)</td>
<td>≥2 yrs</td>
<td>1–3 mths</td>
<td>85</td>
<td>Immunological infertility</td>
<td>Kidney Yin def</td>
<td>TCM: 19/60 (32%) Cont: 6/25 (24%)</td>
</tr>
<tr>
<td>6</td>
<td>RCT</td>
<td>23–38 yrs (m28)</td>
<td>2–10 yrs (m3.5)</td>
<td>CHM 15 days + CC 5 days</td>
<td>62</td>
<td>PCOS, Stein–Leventhal syndrome, amenorrhea</td>
<td>Blood stasis</td>
<td>TCM: 21/32 (65.5%) Cont: 11/30 (36.6%) Side effects lower in TCM group</td>
</tr>
<tr>
<td>7</td>
<td>RCT</td>
<td>25–35 yrs (m27.8)</td>
<td>2–10 yrs (m3.5)</td>
<td>CHM 2–3 mths; all treated with CC for 6 mths prior</td>
<td>58</td>
<td>PCOS</td>
<td>–</td>
<td>TCM: 18/28 (64%) Cont: 11/30 (36%)</td>
</tr>
<tr>
<td>8</td>
<td>Non-randomised controlled trial</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>417</td>
<td>Endometriosis</td>
<td>Kidney def and Blood stasis</td>
<td>TCM: 182/298 (61%) Cont: 26/119 (22%) Side effects with Danazol: weight gain, acne and elevated liver enzymes</td>
</tr>
<tr>
<td>C1</td>
<td>Cohort study</td>
<td>&lt;30 yrs (n = 164)</td>
<td>3–11 yrs (m6.6)</td>
<td>3 mths</td>
<td>343 incl. a–d: 253 a. 90 b. 17 c. 8 d. 4</td>
<td>1a. Function of primary infertility 1b. Blood stasis 2. Menses problems 1c. Phlegm-Damp 2a. Irregular menses, 2b. Dysmenorrhea 2c. Amenorrhea 3. Thin endometrial lining, underdeveloped follicles 4. Cervicitis 5. Vaginitis 6. Endometritis 7. Fallopian tube blockage (Adnexitis) 8. Ovarian mass</td>
<td>Total: 136/343 (40.5%) 1a. d. 93/239 (69.9%) 1a. d. 42/61 (68.7%) 1b. 8/17 (47.13%) 1c. 7/28 (25%) 1d. 1/4 (25%) 2a. 488/75 (64.6%) 2b. 2/6 (33.3%) 2c. 2/6 (33.3%) 2c. 3/9 (33.3%) 2e. 3/20 (45.5%) 3. 457/73 (64%) 4. 3/7 (43%) 5. 1/7 (14%)</td>
<td></td>
</tr>
<tr>
<td>#</td>
<td>Authors</td>
<td>Cohort</td>
<td>Duration</td>
<td>Follow-up</td>
<td>Details</td>
<td>Results</td>
<td></td>
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<tr>
<td>C2</td>
<td>Zhang 01</td>
<td>24–38 yrs</td>
<td>2–10 yrs</td>
<td>3 mths Follow-up 6–12 mths</td>
<td>Endometriosis, dysmenorrhea, antibodies against endometrium</td>
<td>Qi def, Blood def 55/94 (58%) 6–12 mths after conclusion of treatment; improvement: no antibodies (86%), no menses pain (72%) a. 18/32 (56%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>Fang 91</td>
<td>25–37 yrs (m31)</td>
<td>1.5–8 yrs</td>
<td>3–6 mths</td>
<td>Luteal phase defect a. Simple b. With complications fallopian tube, sperm antibodies</td>
<td>Kidney def</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C4</td>
<td>Wing 06</td>
<td>&lt;35 yrs (n = 18) &gt;35 yrs (n = 32)</td>
<td>—</td>
<td>6 mths &gt;6 mths if not pregnant, follow-up 12 mths</td>
<td>Unexplained infertility</td>
<td>No pattern given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5</td>
<td>Tan 01</td>
<td>25–30 yrs (n = 28) 31–40 yrs (n = 13)</td>
<td>5–9 yrs (m6); 5 yrs (n = 26); 6–9 yrs (n = 15)</td>
<td>3–12 mths</td>
<td>Primary Inf (n = 34, 83%); secondary Inf (n = 7, 17%) Anovulation</td>
<td>Qi def, Blood def, Yin def, vacuity cold 30/41 (73%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C6</td>
<td>Tian 98</td>
<td>21–41 yrs (m29)</td>
<td>—</td>
<td>1–3 mths</td>
<td>Hyperprolactinaemia, with serum prolactin 30–50ng/ml (n = 18) Amenorrhea (n = 6)</td>
<td>Kidney def 21/29 (72%); improved ovulation rate (89%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C7</td>
<td>Usuki 89</td>
<td>24–38 yrs (m29)</td>
<td>0.5–2 yrs</td>
<td>≥3 mths</td>
<td>PCOS, oligomen (n = 22), amenorrhea (n = 24) (Artificial periodic therapy)</td>
<td>Qi def, Blood def, Yin def</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C8</td>
<td>He 04</td>
<td>16–35 yrs (m26)</td>
<td>—</td>
<td>1 mth</td>
<td>Recurrent miscarriage (n = 31), endometriosis, pelvic inflammation, ovarian cyst.</td>
<td>34/41 (83%) ongoing pregnancy rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C9</td>
<td>Jiang 97</td>
<td>25–40 yrs; &gt;30 (n = 27), &gt;30 (n = 14)</td>
<td>1–2 mths (m1.5)</td>
<td>41</td>
<td>Blood stasis due to Qi def, Qi stagnation, Cold or Heat</td>
<td>37/40 (92.5%) Pregnant after 1 mth; 8; 2 mths: 10; 3 mths: 9; 4–6 mths: 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C10</td>
<td>Guo 04</td>
<td>25–38 yrs</td>
<td>2–14 yrs</td>
<td>3–6 mths</td>
<td>Mild to medium fallopian tube blockage (21), uterine dysplasia (5), adnexitis = inflammation of ovaries (28)</td>
<td>Blood def, Qi stagnation, Kidney Yang def, Cold accumulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Study design, treatment groups</td>
<td>Age</td>
<td>Infertility</td>
<td>Treatment duration</td>
<td>N</td>
<td>WA condition</td>
<td>TCM pattern diagnosis</td>
<td>Pregnancy outcome</td>
</tr>
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</tr>
<tr>
<td>C11</td>
<td>Wang 91*</td>
<td>Cohort CHN</td>
<td>21–44 yrs (m3⑥)</td>
<td>1–10 yrs (m3)</td>
<td>3 mths</td>
<td>22 of 76 infertile, trying for pregnancy</td>
<td>Endometriosis, dysmenorrhea, nodules/cysts, dyspareunia</td>
<td>Blood stasis</td>
</tr>
<tr>
<td>C12</td>
<td>Dingling 82*</td>
<td>Cohort CHN</td>
<td>24–34 yrs (m2⑧)</td>
<td>1–10 yrs (m2.2) (n①5)</td>
<td>1–16 mths (m9)</td>
<td>18</td>
<td>a. Secondary amenorrhea (n=⑨), b. anovulation (n=③), c. luteal insufficiency (n=⑥)</td>
<td>Kidney Yin and Yang def</td>
</tr>
<tr>
<td>C13</td>
<td>Liu 94*</td>
<td>Cohort CHN</td>
<td>20–29 yrs (n=①2); 30–39 yrs (n=①21); ≥40 yrs (n=①3)</td>
<td>3–13 yrs (m3.⑤)</td>
<td>6–9 mths</td>
<td>10 of 46 infertile, trying for pregnancy</td>
<td>Endometriosis, dysmenorrhea, nodules, dyspareunia, anal tenesmus</td>
<td>Blood stasis</td>
</tr>
<tr>
<td>CS2</td>
<td>Lewis 04*</td>
<td>Case series CHN + Acu</td>
<td>28–①3 yrs (m3⑥)</td>
<td>1–9 yrs (m4)</td>
<td>2–18 mths (m6)</td>
<td>14</td>
<td>e.g. 1. advanced age/premature ovarian failure 2. unexplained, dysmenorrhea, endometriosis, 3. PCOS, 4. anovulation, thin endometrium</td>
<td>1. Spleen and Kidney Jing def, 2. Liver Qi stagn, Blood stasis, 3. Spleen def, Phlegm-Damp, 4. Liver Qi Excess and heat</td>
</tr>
</tbody>
</table>
**Efficacy of Traditional Chinese Herbal Medicine in the management of female infertility: A systematic review**

The odds of achieving a pregnancy with CHM therapy over a 4-month period were 3.5 times higher (95% CI: 2.34, 5.24, \( p < 0.0001 \); \( I^2 = 42\% \)) than with WM drug therapy in women with infertility \( (n=1005 \text{ in 8 RCTs}; \text{ Fig. 2a}) \). Mean (SD) pregnancy rates in the CHM group were 60% (59.9 ± 12.5) compared with 32% (31.6 ± 9.9) in the WM group.

Sensitivity analysis including seven trials of women diagnosed with PCOS or endometriosis revealed a mean pregnancy rate of 64% (63.9 ± 5.9) in the CHM group versus 33% (32.6 ± 10.3) in the WM group, and an odds ratio of 3.9 (95% CI: 2.65, 5.72, \( p < 0.0001 \); \( I^2 = 31\% \)), excluding the trial by Chen 95 of women with immunological infertility.\(^{30}\) Sensitivity analysis of 7 RCTs excluding the non-randomised trial by Zhang 06\(^{31}\) resulted in an odds ratio of 3.08 (95% CI: 2.01, 4.72, \( p < 0.0001 \); \( I^2 = 28\% \)).

Funnel plots and Egger’s test of RCTs investigating the effect of CHM on women’s infertility indicated no publication bias or small study effect (asymmetric coefficient = −2.28, \( p = 0.187 \)).

**Meta-analysis of cohort studies**

Most women participating in the cohort studies had primary infertility and had been diagnosed with a range of WM conditions including PCOS, endometriosis, oligomenorrhea, amenorrhea, dysmenorrhea, luteal phase defect, fallopian tube blockage, pelvic inflammation, hyperprolactinaemia, or unexplained infertility (Table 1).

The pooled pregnancy rate of all 13 cohort studies included in the systematic review involving 793 women treated with CHM therapy for 4.2 ± 2.5 months was 49.1% (95% CI: 45.7, 52.4, \( I^2 = 93.5\% \)).

Meta-regression analyses of mean maternal age \( (\rho = 0.69) \), mean length of infertility \( (\rho = 0.15) \), and mean CHM treatment duration \( (\rho = 0.86) \) did not explain heterogeneity amongst studies.

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### Table: Characteristics of included trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of treatment</th>
<th>Duration (months)</th>
<th>Pregnancy rate</th>
<th>Participants</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHM</td>
<td>Traditional Chinese Medicine</td>
<td>3-12</td>
<td>3.5</td>
<td>1005</td>
<td>12</td>
</tr>
<tr>
<td>WM</td>
<td>Western Medicine</td>
<td>3-12</td>
<td>1.5</td>
<td>1005</td>
<td>12</td>
</tr>
</tbody>
</table>

---

### Meta-analysis of RCTs

1. **Egger’s test**: Cochrane 06
2. **Heterogeneity**: \( I^2 = 31\% \)
3. **Pregnancy rates**: CHM > WM (95% CI: 2.65, 5.72)
4. **Odds ratio**: 3.9 (95% CI: 2.01, 4.72)
5. **Publication bias**: No
6. **Small study effect**: No

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### Meta-analysis of cohort studies

1. **Pregnancy rate**: 49.1% (95% CI: 45.7, 52.4)
2. **Heterogeneity**: \( I^2 = 93.5\% \)
3. **Meta-regression**: Age, infertility duration, CHM duration

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**Eggs:**

- CHM (Acupuncture, herbal medicine, etc.)
- WM (Conventional medicine, etc.)

**Notes:**

- CHM vs WM: 3.5 times higher
- Sensitivity analysis: 64% vs 33% (95% CI: 2.65, 5.72)
- Publication bias: No
- Small study effect: No

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**Table 1: Characteristics of included trials**

<table>
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<tr>
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<td>3-12</td>
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<td>3-12</td>
<td>1.5</td>
<td>1005</td>
<td>12</td>
</tr>
</tbody>
</table>
In the sensitivity analysis we excluded the following six studies with potential risk of bias: pregnancy was a secondary outcome measurement in three studies, one study had a very short follow-up of 1 month, all participants received biomedical treatment for tubal patency before CHM therapy, and participants received treatment to avoid miscarriage.

The pooled pregnancy rate of seven cohort studies included in the adjusted meta-analysis involving 616 women treated with CHM therapy was 48.7% (95% CI: 44.7, 52.7, $I^2 = 82.8\%$, Fig. 2b), similar to the pooled pregnancy rate of 13 cohort studies with slightly lower heterogeneity.

The adjusted odds of achieving a pregnancy with CHM therapy ranging between 1 and 12 months were 2.3 higher (95% CI: 1.6, 3.4, $p < 0.0001$) compared with the pregnancy rate of 30.4% a cohort of women ($n = 7439$) undergoing IVF in Australia in one year (2008/2009).

**Case series and case studies**

Case studies listed in Table 1 illustrate that individual infertility can often be associated with multiple TCM pattern. While there might be a dominating pattern, TCM treatment is dependent on the underlying combination of imbalances. In addition, Table 1 illustrates that a specific condition in WM, such as PCOS, might be associated with different TCM patterns in different individuals. While WM standardises the treatment to a specific illness/condition, TCM aligns the treatment with the underlying imbalance causing the condition.

**TCM pattern diagnosis and the menstrual cycle**

Common TCM pattern in infertility include Kidney Jing deficiency, Kidney Yin or Yang deficiency, Spleen deficiency, Blood deficiency, Liver Qi stagnation, Blood stasis, Heat, Cold or Dampness (Tables 1 and 2). Imbalances underlying infertility are visible by observing the characteristics of the menstrual cycle, and are integrated with pulse and tongue diagnosis, and physical and emotional wellbeing (Table 2). The quality of the menstrual cycle is assessed by the appearance (colour, clots) and flow of the menstrual blood, the basal body temperature (BBT) curve, and the length and frequency of the menstrual cycle.

**Discussion**

Our meta-analyses of RCTs and cohort studies of 1621 women with infertility suggest that the odds of achieving pregnancy with Chinese Herbal Medicine (CHM) are about three times greater than with conventional WM treatment using standard medication or IVF.

Clinical pregnancy rates of about 60% were achieved with Chinese Herbal Medicine therapy over 4 months compared with 30% using WM fertility drug treatment, or IVF over 12 months.

Our review included English-only articles which might have introduced some bias. However, Juni et al. argue that generally there is little effect on summary treatment effect if non-English studies were included in meta-analyses, with effect size changes expected to be less than 5%. Therefore the effect sizes in our meta-analyses are likely to be reasonably good estimates.

Here we compared approaches to diagnosis and treatment of infertility of two different medical systems (TCM versus WM). Available data did not allow meaningful direct comparison of specific interventions (e.g. a specific herbal formula versus a specific drug), due to fundamentally different diagnostic approaches.

In addition to pulse and tongue diagnosis, TCM uses the characteristics of the menstrual cycle as an essential
Table 2  Common TCM pattern in infertility and manifestations.

<table>
<thead>
<tr>
<th>TCM pattern</th>
<th>BBT</th>
<th>Quality of menses</th>
<th>Tongue</th>
<th>Pulse</th>
<th>Other symptoms</th>
<th>WM condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Color</td>
<td>Clots</td>
<td>Flow</td>
<td>Frequency</td>
</tr>
<tr>
<td>Kidney Jing Deficiency</td>
<td>Long follicular phase, low temp luteal phase; unstable; monophasic, little fertile mucus</td>
<td>Pink, watery</td>
<td>No</td>
<td>Scanty</td>
<td>Delayed</td>
<td>Lower back</td>
</tr>
<tr>
<td>Kidney Yin deficiency</td>
<td>Bright red, Short follicular phase, with higher temp (&gt;36.5 °C)</td>
<td>No</td>
<td>Scanty</td>
<td>Irregular, shortened</td>
<td>Lower back, knees</td>
<td>Red with little coat, cracked</td>
</tr>
<tr>
<td>Kidney Yang deficiency</td>
<td>Long follicular phase, low temp (&lt;36.2 °C); short luteal phase with low temp</td>
<td>Some times</td>
<td>Scanty</td>
<td>Irregular, delayed</td>
<td>Lower back, knees, legs</td>
<td>Pal, swollen</td>
</tr>
<tr>
<td>Spleen Qi deficiency</td>
<td>Slow-rise luteal phase (&gt;3 days, not usual 1–2 days); short luteal phase</td>
<td>No</td>
<td>Scanty</td>
<td>Short</td>
<td>Mid-cycle pain</td>
<td>Swollen with white fur</td>
</tr>
<tr>
<td>Blood deficiency</td>
<td>Bright red, Long follicular phase</td>
<td>No</td>
<td>Scanty</td>
<td>Delayed</td>
<td>Mild lower abdominal, pressure relieves pain</td>
<td>Abdominal cramps</td>
</tr>
<tr>
<td>Liver Qi Stagnation</td>
<td>Dark red/purple, Slow-rise unstable luteal phase</td>
<td>Yes</td>
<td>Scanty</td>
<td>Irregular</td>
<td>Dark red with purple spots</td>
<td>Deep</td>
</tr>
<tr>
<td>Heat, Kidney Yin deficiency</td>
<td>Follicular phase too short and temp too high</td>
<td>Often</td>
<td>Heavy</td>
<td>Irregular, mid-cycle bleeding</td>
<td>Thick itchy leukorrhea</td>
<td>Red, peeled (sides, tip) with yellow coating</td>
</tr>
<tr>
<td>Liver or Heart Fire</td>
<td>Unstable follicular luteal phase, sawtooth or saddle pattern</td>
<td>Some times</td>
<td>Thick, excessive</td>
<td>Shortened, intermittent bleeding</td>
<td>Abdominal</td>
<td>Red tip</td>
</tr>
<tr>
<td>Damp-heat</td>
<td>Monophasic, little fertile mucus</td>
<td>No</td>
<td>Scanty, sticky</td>
<td>Irregular</td>
<td>Lower abdomen, loins, bloating</td>
<td>Red with thick, greasy yellow fur</td>
</tr>
<tr>
<td>Phlegm-Damp or Cold-Damp</td>
<td>Long follicular phase, monophasic temp chart</td>
<td>Yes</td>
<td>Scanty</td>
<td>Delayed</td>
<td>Abdominal distension, pain</td>
<td>Pale with white fur</td>
</tr>
<tr>
<td>Blood stasis and Dampness</td>
<td>Slow fall of temp at start of cycle</td>
<td>Yes</td>
<td>Heavy</td>
<td>Irregular</td>
<td>Lower abdominal</td>
<td>Purple swollen, sticky coating</td>
</tr>
<tr>
<td>Cold uterus</td>
<td>Low temp, Dark brown spotting</td>
<td>Some times</td>
<td>Scanty</td>
<td>Irregular</td>
<td>Painful periods</td>
<td>Pale, or purplish</td>
</tr>
</tbody>
</table>

Refs. 14—18, 36.
(A) Meta-analysis of RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>TCM</th>
<th>Control</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>N</td>
<td>n</td>
</tr>
<tr>
<td>Hua o3</td>
<td>50</td>
<td>76</td>
<td>8</td>
</tr>
<tr>
<td>Wu o6</td>
<td>32</td>
<td>48</td>
<td>29</td>
</tr>
<tr>
<td>Lin o5</td>
<td>34</td>
<td>48</td>
<td>12</td>
</tr>
<tr>
<td>Xia o4</td>
<td>24</td>
<td>46</td>
<td>9</td>
</tr>
<tr>
<td>Chen 95</td>
<td>19</td>
<td>60</td>
<td>6</td>
</tr>
<tr>
<td>Shao o4</td>
<td>21</td>
<td>32</td>
<td>11</td>
</tr>
<tr>
<td>Ren 02</td>
<td>17</td>
<td>28</td>
<td>11</td>
</tr>
<tr>
<td>Zhang o6</td>
<td>182</td>
<td>298</td>
<td>26</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>636</td>
<td>369</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total events</td>
<td>379</td>
<td>112</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.14; Chi² = 12.03, df = 7 (P = 0.10); I² = 42%
Test for overall effect: Z = 6.09 (P < 0.00001)

(B) Adjusted meta-analysis of cohort studies

<table>
<thead>
<tr>
<th>Study</th>
<th>n/N</th>
<th>Effect Size (95% CI)</th>
<th>ES (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luolan</td>
<td>86</td>
<td>0.40 (0.34, 0.45)</td>
<td>55.68</td>
<td></td>
</tr>
<tr>
<td>Zhang</td>
<td>01</td>
<td>0.59 (0.48, 0.69)</td>
<td>15.26</td>
<td></td>
</tr>
<tr>
<td>Fang</td>
<td>91</td>
<td>0.56 (0.38, 0.74)</td>
<td>5.19</td>
<td></td>
</tr>
<tr>
<td>Wing</td>
<td>06</td>
<td>0.56 (0.41, 0.70)</td>
<td>8.12</td>
<td></td>
</tr>
<tr>
<td>Tan</td>
<td>01</td>
<td>0.73 (0.57, 0.86)</td>
<td>6.66</td>
<td></td>
</tr>
<tr>
<td>Tian</td>
<td>98</td>
<td>0.72 (0.53, 0.87)</td>
<td>4.71</td>
<td></td>
</tr>
<tr>
<td>Usuki</td>
<td>89</td>
<td>0.44 (0.25, 0.65)</td>
<td>4.38</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>300/616</td>
<td>0.49 (0.45, 0.53)</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

Overall effect: I² = 82.8%, p < 0.0001

Figure 2  (a) Meta-analysis of RCTs investigating pregnancy rates of infertile women treated with Chinese Herbal Medicine (CHM) compared with WM fertility medications. (b) Adjusted meta-analysis of cohort studies investigating pregnancy rates of infertile women treated with CHM. TCM, Traditional Chinese Medicine; CI, confidence interval; n, number of pregnancies; N, number of women; ES, effect size.

diagnostic tool to ascertain underlying imbalances causing infertility. We have summarised common TCM pattern diagnosis in infertility in relation to the quality of the menstrual cycle and associated symptoms, providing a practical guide to a woman’s fertility status for health professionals but also women and couples experiencing infertility.

The fundamental principle of TCM therapy is to restore balance within the body, which affects hormonal regulation of the menstrual cycle, and provides a physiological environment to facilitate conception, implantation, and maintenance of a viable pregnancy. The quality of the environment in the body is considered as important as the quality of eggs, sperm and embryo. TCM practitioners often refer to the environment, including the endometrium, as the ‘soil’ and eggs/embryo as the ‘seed’ (Chinese proverb: ‘Cultivate the soil before planting the seed’). Any irregularities in the menstrual cycle and general wellbeing,
often seen in conditions associated with infertility, including advanced maternal age and unexplained infertility, are fundamental factors which can be optimised before conception is attempted.\textsuperscript{16,17,51}

While the approach to infertility treatment might differ between the TCM and WM model, the desired outcome in both is the achievement of a viable pregnancy. In TCM, the diagnostic and treatment approach to conditions such as PCOS and endometriosis is not any different than to amenorrhea, dysmenorrhea, irregular menses or unexplained infertility.

PCOS, for example, is one of the most common female endocrine disorders affecting approximately 5–10\% of women of reproductive age and is thought to be one of the leading causes of female subfertility.\textsuperscript{55} PCOS is associated with amenorrhea or oligomenorrhea, irregular menses, hirsutism, obesity, insulin resistance, acne, hair loss, and infertility. The treatment of PCOS in the WM model involves prescription of the contraceptive pill, anti-diabetic drugs, gonadotropin (glycoprotein hormone), clomiphene (estrogen receptor modulator), sometimes surgery to destroy excess antral follicles, and IVF.\textsuperscript{55} In contrast, TCM therapy uses herbal formulae or acupuncture treatment to restore, nourish, and resolve underlying imbalances associated with PCOS such as Kidney Jing deficiency, Phlegm-Damp accumulation, Liver Qi stagnation, Blood stasis, or Liver fire.\textsuperscript{14–16}

Additionally, 20–30\% of women with fertility problems are diagnosed with endometriosis, which is associated with dispersed uterine tissue in the abdominal cavity causing inflammation and adhesions, and can lead to fallopian tube blockage, ovarian cysts and abdominal pain during bowel movements, urination, or sexual intercourse. WM therapy can involve invasive laparoscopy and removal of excess tissue or cysts.\textsuperscript{56} There is no word for ‘endometriosis’ in TCM classical texts.\textsuperscript{14,33} Instead, the clinical picture is described as dysmenorrhea or abdominal masses. TCM therapy involves the treatment of Liver Qi stagnation, Blood stasis, accumulation of Phlegm, and other potential underlying imbalances.\textsuperscript{14–16}

Women and couples experiencing infertility may benefit from a holistic approach, inclusion of the menstrual cycle as a diagnostic tool, and integration of therapies such as TCM to improve fertility and pregnancy outcomes, shorten treatment time frames, and reduce the emotional and financial burden.

In 2010, a 3-month treatment period with TCM including diagnosis, consultation, herbal formulae and acupuncture cost about $600–800 (personal communication with TCM practitioners and TCM practice websites in Australia), whereas an IVF treatment cycle incurred an estimated fee of $6000–7000.\textsuperscript{5} Health fund rebates are available for TCM consultations and acupuncture, but not for herbal formulae.\textsuperscript{55} TCM practice in Australia will become more transparent and consistent with the introduction of mandatory registration nationally in July 2012, as currently practiced in Victoria only.\textsuperscript{56}

Conclusions

Our meta-analyses suggest Traditional Chinese Herbal Medicine to be more effective in the treatment of female infertility achieving on average a 60\% pregnancy rate over 4 months compared with 30\% achieved with standard Western Medical drug treatment, or IVF over 12 months.

The TCM approach to infertility treatment integrates the menstrual cycle as a simple, non-invasive, sensitive, motivational, diagnostic tool to understanding a women’s fertility status.

Our findings suggest that the integration of TCM diagnostic tools and therapy in the current WM model of infertility treatment could improve pregnancy rates while reducing treatment time frames and emotional and financial burden.

In this review we focused on the TCM approach and diagnosis of infertility, a review of herbal formulae used in TCM therapy, and comparison of therapies combining TCM and ART/IVF were outside the scope of this review.

Author’s contributions

KR conceptualised the study, and undertook data collection, extraction and quality assessment with KS. KR undertook data analysis and interpretation, and prepared the manuscript with contributions from KS. All authors approved the final version.

Acknowledgements

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