

Meta-Analysis on the Clinical Efficacy of Supplementing the Qi-Dispelling, Wind-Eliminating, and Blood-Activating Method in the Treatment of IgA Nephropathy

Franz K. Müller^{1*}, Lucia F. Romano¹, Tesfaye M. Bekele¹

¹Department of Medical and Clinical Sciences, University of Vienna, Vienna, Austria.

Abstract

IgA nephropathy (IgAN) ranks among the most prevalent primary glomerular diseases. In traditional Chinese medicine, therapies aimed at supplementing qi, dispelling wind, and promoting blood circulation are frequently employed to manage this condition. Nevertheless, prior research is limited by small sample sizes, making it challenging to draw firm conclusions. This study performed a meta-analysis to systematically evaluate the clinical effectiveness of this approach and provide comprehensive evidence supporting its use. A systematic search for randomized controlled trials (RCTs) evaluating the use of qi-supplementing, wind-dispelling, and blood-activating interventions for IgAN was conducted across CNKI, Wanfang Data, Chongqing VIP, SinoMed, PubMed, EMBASE, and Web of Science databases from inception through January 2022. Studies were screened according to predefined inclusion and exclusion criteria, ultimately identifying 15 eligible trials. The quality of these studies was assessed using the Cochrane risk-of-bias tool (Cochrane Handbook 5.4). Outcome data were extracted, and meta-analysis was conducted using Review Manager 5.4 software.

Fifteen trials were included in the analysis. Pooled data revealed that interventions based on qi supplementation, wind dispelling, and blood activation significantly improved the total effective rate [odds ratio = 3.95, 95% CI 2.76–5.67] and reduced 24-hour urinary protein levels (mean difference = -0.35, 95% CI -0.54 to -0.16) as well as serum creatinine (mean difference = -15.41, 95% CI -28.39 to -2.44). These treatments did not negatively affect alanine transaminase, hemoglobin, or serum albumin levels, indicating a favorable safety profile. The YQH therapeutic approach demonstrates significant benefits for patients with IgAN, including improved renal function and decreased proteinuria, compared to conventional non-Chinese medicine treatments. These results provide strong support for incorporating this method into clinical practice for IgAN management.

Keywords: IgA nephropathy, Supplementing qi, Dispelling wind, Activating blood circulation, Chinese medicine, Meta-analysis

Corresponding author: Franz K. Müller
E-mail: franz.mueller@outlook.com

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Introduction

Globally, IgA nephropathy represents the most common primary glomerular disorder, accounting for approximately 47.5%–52.66% of all glomerulopathies, with incidence rising steadily [1]. Most patients

experience a slowly progressing, often asymptomatic course, with gradual GFR decline [2]. Within 10–20 years, up to 40% of patients may advance to end-stage renal disease [3]. Clinical evidence indicates that lower proteinuria correlates with reduced risk of renal failure [4–6]. According to the 2021 KDIGO guidelines, patients

excreting 0.75–1 g/day of proteinuria are at higher risk of renal function deterioration, and RAAS blockade remains the cornerstone of current therapy [7].

Long-term clinical practice has revealed that combining Chinese medicine with conventional treatments provides advantages, including reduced proteinuria, renal protection, and fewer adverse events [8–10]. Among these approaches, the YQH method—supplementing qi, dispelling wind, and activating blood—is commonly applied for IgAN. However, small sample sizes and varying study designs [11, 12] have hindered precise evaluation of its efficacy. To clarify its therapeutic impact, 15 RCTs investigating YQH prescriptions were selected for meta-analysis, offering an evidence-based foundation for its clinical application.

Materials and Methods

Literature search

Databases including PubMed, EMBASE, Web of Science, CBM, CNKI, VIP, and Wanfang Data were searched systematically. Keywords included “IgA Nephropathy” or “Berger’s Disease” combined with “Chinese Medicine” and “Clinical Trial.”

Inclusion and exclusion criteria

Inclusion criteria

- Participants with a confirmed clinicopathological diagnosis of IgAN.
- Control groups received standard non-Chinese medicine treatment, while treatment groups received YQH prescriptions in addition.
- RCTs were included regardless of blinding status.
- No restrictions on the dosage or composition of the YQH prescription.

Exclusion criteria

- Incomplete studies or missing outcome data.
- Animal studies.
- Studies without a clearly defined prescription composition.
- Studies with significant baseline imbalances between groups.

Screening process

Two reviewers independently screened titles, abstracts, and full texts based on the inclusion criteria. Discrepancies were resolved by a third expert to ensure consistency.

Data extraction

Relevant information was collected from each study, including the first author, publication year, participant demographics (age and gender), treatment protocols for both intervention and control groups, duration of therapy, outcome measures, and the specific components of the YQH prescriptions. All data were independently verified and then imported into Review Manager 5.4 for analysis.

Assessment of study quality

The risk of bias in the included studies was independently evaluated by two reviewers following the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions. The assessment covered seven domains: random sequence generation, allocation concealment, blinding of participants and study personnel, blinding of outcome assessment, completeness of outcome data, selective reporting, and other potential sources of bias. Each domain was categorized as having a low, high, or unclear risk of bias.

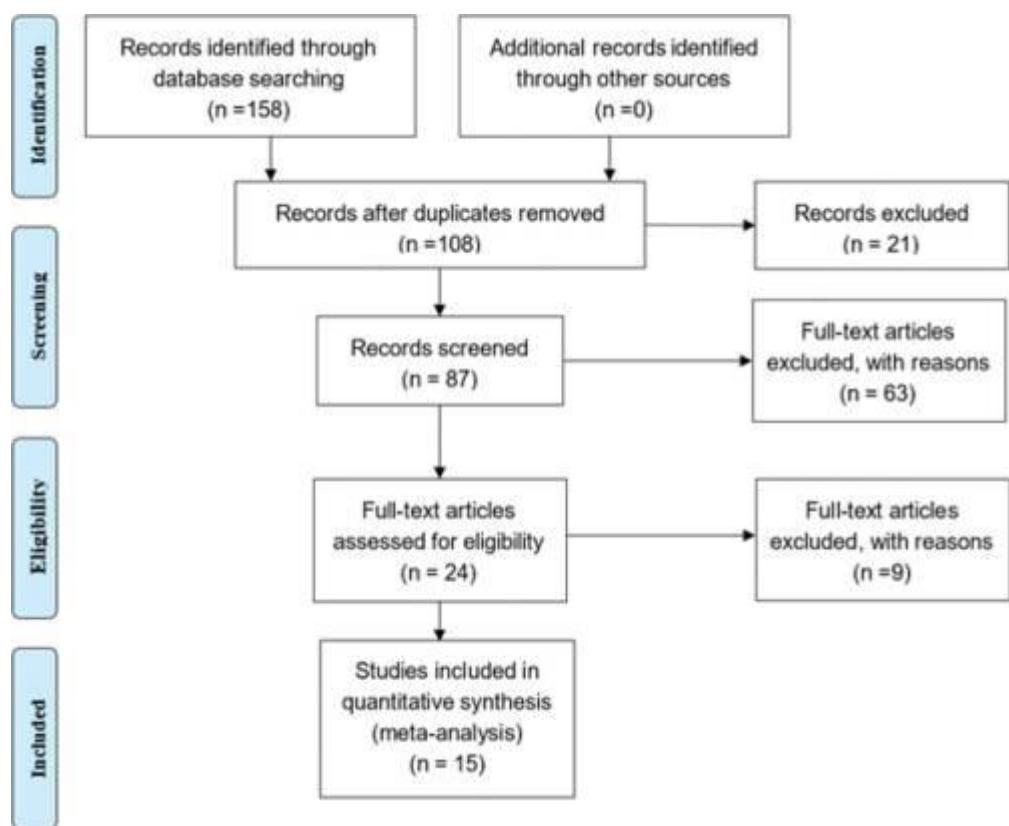
Statistical analysis

Statistical analyses were performed using Review Manager 5.4. Study heterogeneity was tested using the Chi-square statistic. When $P \leq 0.05$ or $I^2 \geq 50\%$, substantial heterogeneity was considered, and a random-effects model was applied; otherwise, a fixed-effect model was used for $P > 0.05$ or $I^2 < 50\%$. For outcomes including more than ten studies, funnel plots were generated to detect potential publication bias. Dichotomous variables were expressed as odds ratios (OR) with 95% confidence intervals (CI). Sensitivity analyses were performed to examine the robustness of the pooled estimates.

Results and Discussion

Study selection

The initial search identified 158 records across seven databases in English and Chinese (Figure 1). After removing duplicates, 108 records remained. Screening titles and abstracts narrowed the pool to 87 studies for full-text review. Following detailed examination, 63 studies were excluded due to duplication, incomplete data, or unavailable full texts. Of the 24 remaining RCTs, nine were further excluded because they either lacked detailed prescription compositions or had unsuitable control group designs. Ultimately, 15 RCTs met the inclusion criteria for meta-analysis. Study characteristics are summarized in Table 1.

**Figure 1.** Flowchart of the literature selection process.**Table 1.** Characteristics of the Included Studies

First Author	Outcome Measures	Year	Sample Size (Experimental/Control)	Mean Age (E/C)	Control	Intervention	Treatment Duration
Han [13]	1/2/3/4	2012	26/26	37.04/35.33	Conventional therapy	TCM + conventional therapy	3 mo
Luo [14]	1/2/4	2008	30/30	31.3/29.6	Conventional therapy	TCM + conventional therapy	6 mo
Meng [15]	2	2011	68/56	28.3/26.6	Conventional therapy	TCM + conventional therapy	6 mo
Pan [16]	2/3/5/6	2014	30/30	30.67±1.51/33.9±1.99	Conventional therapy	TCM + conventional therapy	3 mo
Wu [17]	1/2/3/5/7	2015	30/30	35.7/35.7	Conventional therapy	TCM + conventional therapy	6 mo
Dong [18]	2/3/6/7/8	2019	34/34	39±12/38±13	Conventional therapy	TCM + conventional therapy	12 mo
Chen [19]	2/3/7	2008	32/32	30±21.33/28±20.24	Conventional therapy	TCM + conventional therapy	6 mo
Chu [20]	1/2	2014	34/34	28.71±8.99/29.2±10.0	Conventional therapy	TCM + conventional therapy	1 mo
Xiang [21]	2	2011	28/26	29.3±4.95/29.57±6.17	Conventional therapy	TCM + conventional therapy	8 wk

Yang [22]	2/3/4/5	2016	30/29	33.4/31.7	Conventional therapy	TCM + conventional therapy	8 wk
Cai [23]	2/3	2020	64/63	39.41 ± 2.14/39.72 ± 2.31	Conventional therapy	TCM + conventional therapy	12 mo
Chang [24]	2/3/6/7/8	2020	29/29	37.34 ± 6.77/39.03 ± 9.14	Conventional therapy	TCM + conventional therapy	16 wk
Wang [25]	2/3/5/6/7/8	2021	25/27	37.84 ± 6.55/39.96 ± 9.29	Conventional therapy	TCM + conventional therapy	24 wk
Yu [26]	5/6/7/8	2021	25/27	38.56 ± 6.25/40.74 ± 9.2	Conventional therapy	TCM + conventional therapy	24 wk
Zhang [27]	1/2	2011	29/29	33.9 ± 8.16/31.9 ± 8.31	Conventional therapy	TCM + conventional therapy	8 wk

Outcome measures

1. Urine sediment erythrocyte count (RBC-M) (HPF)
2. 24-hour urine protein quantification (24hPRO) (g/24 h)
3. Serum creatinine (SCr) (μmol/L)
4. Endogenous creatinine clearance (CCr) (mL/min/1.73m²)
5. Blood urea nitrogen (BUN) (mmol/L)
6. Alanine transaminase (ALT) (U/L)
7. Serum albumin (Alb) (g/L)
8. Hemoglobin (Hb) (g/L)

Abbreviations

24hPRO: 24-hour urine protein; Alb: serum albumin; ALT: alanine transaminase; BUN: blood urea nitrogen; CCr: endogenous creatinine clearance; Hb: hemoglobin; RBC-M: urine sediment erythrocyte count; SCr: serum creatinine; TCM: traditional Chinese medicine

Assessment of study quality

Regarding randomization, seven out of the fifteen included studies were rated as having an unclear risk because they only mentioned “random” without specifying the method [13–19], while two studies were deemed high risk [20, 21]. Allocation concealment was properly reported in only four studies, which were therefore classified as low risk [22–25]. A blinded process was documented in three studies, all of which were rated low risk [22–24]. All studies provided complete outcome data, resulting in a low-risk rating for this domain across all trials. Only three studies explicitly reported other biases, which were considered high risk [14, 18, 24], and the remaining studies were judged as unclear due to insufficient information. Overall, the quality assessment showed a predominance of low-risk ratings; however, the proportion of unclear-risk items and the presence of high-risk domains—primarily in allocation concealment and selective reporting—indicate that the overall methodological quality of the included studies was not optimal (Figures 2 and 3).

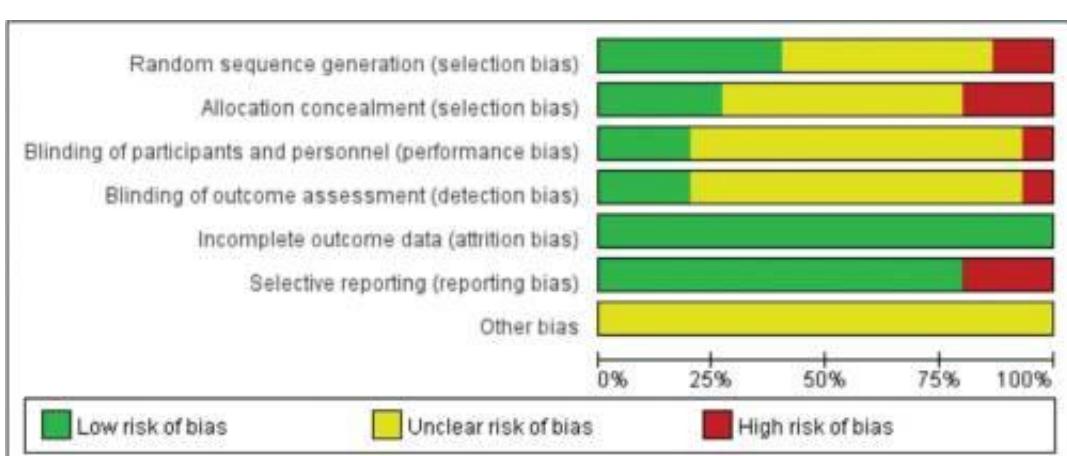


Figure 2. Bar chart summarizing the risk of bias assessment for the included studies.

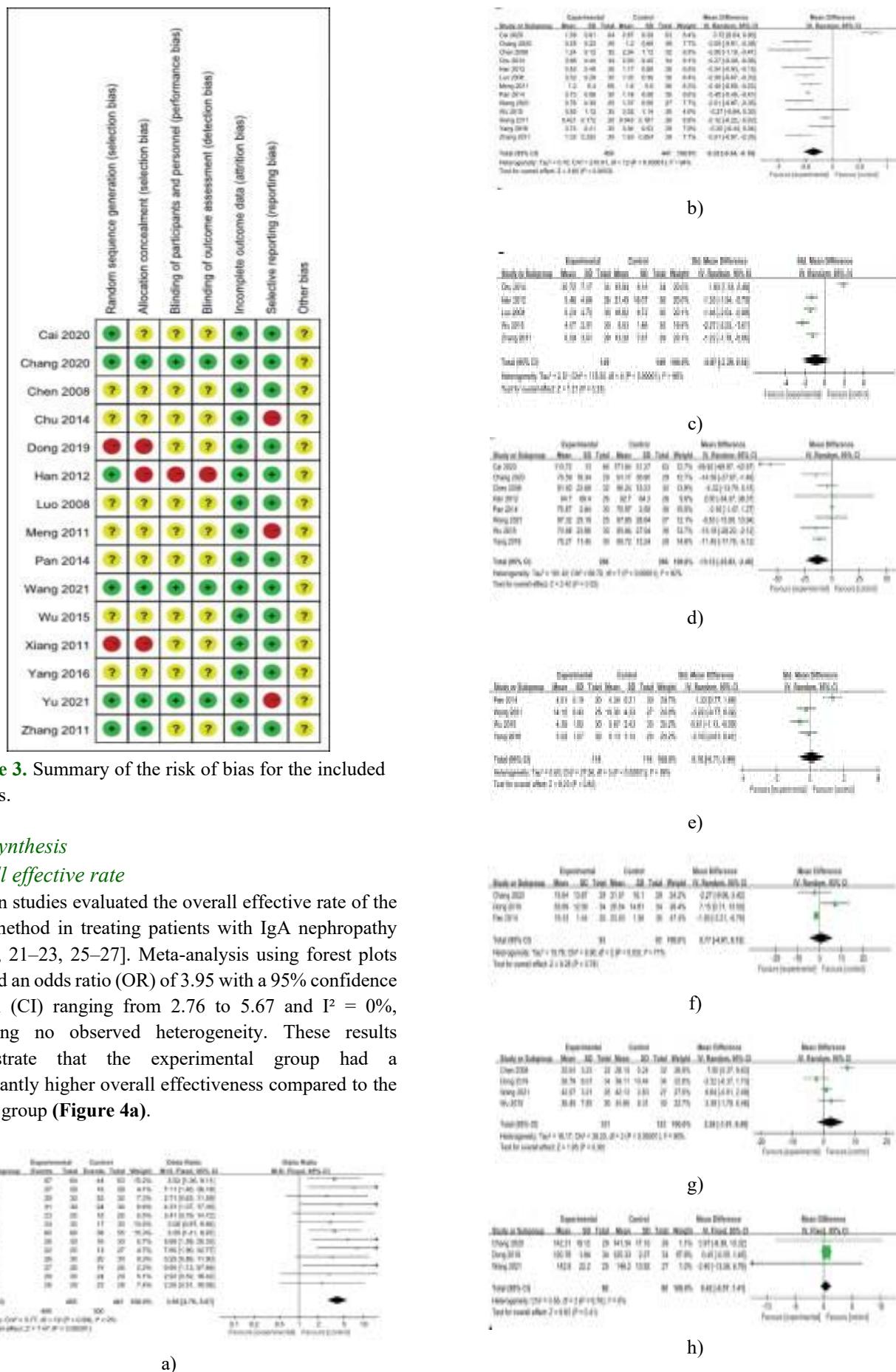


Figure 3. Summary of the risk of bias for the included studies.

Data synthesis

Overall effective rate

Thirteen studies evaluated the overall effective rate of the YQH method in treating patients with IgA nephropathy [13–19, 21–23, 25–27]. Meta-analysis using forest plots revealed an odds ratio (OR) of 3.95 with a 95% confidence interval (CI) ranging from 2.76 to 5.67 and $I^2 = 0\%$, indicating no observed heterogeneity. These results demonstrate that the experimental group had a significantly higher overall effectiveness compared to the control group (Figure 4a).

Experimental YQH method; **Control** placebo; **Data Points** Odds Ratio; **W.H. Forest Plot** (95% CI)

a)

Study	Experimental	Control	Odds Ratio	95% CI
Cai 2020	0.7	0.6	1.12	0.26, 3.18
Chang 2020	0.7	0.5	1.40	0.45, 3.95
Chen 2008	0.7	0.5	1.40	0.25, 2.65
Chu 2014	0.7	0.5	1.40	0.25, 2.65
Dong 2019	0.6	0.3	2.00	0.60, 6.00
Han 2012	0.6	0.3	2.00	0.60, 6.00
Luo 2008	0.7	0.5	1.40	0.25, 2.65
Meng 2011	0.7	0.5	1.40	0.25, 2.65
Pan 2014	0.7	0.5	1.40	0.25, 2.65
Wang 2021	0.7	0.5	1.40	0.25, 2.65
Wu 2015	0.7	0.5	1.40	0.25, 2.65
Xiang 2011	0.6	0.3	2.00	0.60, 6.00
Yang 2016	0.7	0.5	1.40	0.25, 2.65
Yu 2021	0.6	0.5	1.12	0.26, 3.18
Zhang 2011	0.7	0.5	1.40	0.25, 2.65

b)

Study	Experimental	Control	Mean Difference	95% CI
Cai 2020	0.7	0.6	0.10	-0.14, 0.34
Chang 2020	0.7	0.5	0.20	-0.14, 0.54
Chen 2008	0.7	0.5	0.20	-0.14, 0.54
Chu 2014	0.7	0.5	0.20	-0.14, 0.54
Dong 2019	0.6	0.3	0.30	0.04, 0.56
Han 2012	0.6	0.3	0.30	0.04, 0.56
Luo 2008	0.7	0.5	0.20	-0.14, 0.54
Meng 2011	0.7	0.5	0.20	-0.14, 0.54
Pan 2014	0.7	0.5	0.20	-0.14, 0.54
Wang 2021	0.7	0.5	0.20	-0.14, 0.54
Wu 2015	0.7	0.5	0.20	-0.14, 0.54
Xiang 2011	0.6	0.3	0.30	0.04, 0.56
Yang 2016	0.7	0.5	0.20	-0.14, 0.54
Yu 2021	0.6	0.5	0.10	-0.14, 0.34
Zhang 2011	0.7	0.5	0.20	-0.14, 0.54

c)

Study	Experimental	Control	Mean Difference	95% CI
Cai 2020	0.7	0.5	0.20	-0.14, 0.54
Chang 2020	0.7	0.5	0.20	-0.14, 0.54
Chen 2008	0.7	0.5	0.20	-0.14, 0.54
Chu 2014	0.7	0.5	0.20	-0.14, 0.54
Dong 2019	0.6	0.4	0.20	-0.14, 0.54
Han 2012	0.6	0.4	0.20	-0.14, 0.54
Luo 2008	0.7	0.5	0.20	-0.14, 0.54
Meng 2011	0.7	0.5	0.20	-0.14, 0.54
Pan 2014	0.7	0.5	0.20	-0.14, 0.54
Wang 2021	0.7	0.5	0.20	-0.14, 0.54
Wu 2015	0.7	0.5	0.20	-0.14, 0.54
Xiang 2011	0.6	0.4	0.20	-0.14, 0.54



i)

Figure 4. Forest plots illustrating the effects of the YQH method in IgA nephropathy. (a) Overall effective rate; (b) 24-hour urinary protein (24hPRO); (c) urine sediment erythrocyte count (RBC-M); (d) serum creatinine (SCr); (e) blood urea nitrogen (BUN); (f) alanine transaminase (ALT); (g) serum albumin (ALB); (h) hemoglobin (Hb); (i) endogenous creatinine clearance (CCr). Abbreviations: 24hPRO = 24-hour urinary protein, BUN = blood urea nitrogen, CCr = endogenous creatinine clearance, Hb = hemoglobin, RBC-M = urine sediment erythrocyte count, SCr = serum creatinine, YQH method = supplementing qi, dispelling wind, and activating blood method.

24-hour urinary protein (24hPRO)

Thirteen studies reported 24hPRO outcomes [13–19, 21–23, 25–27]. Meta-analysis revealed a mean difference (MD) of -0.35 (95% CI: -0.54 to -0.16), with a Z-value of 3.65 ($P = .0003$). High heterogeneity was observed among the studies ($P < .00001$, $I^2 = 94\%$), necessitating the use of a random-effects model. Overall, the pooled data indicate that YQH therapy significantly reduced 24hPRO levels in patients with IgAN (Figure 4b).

Urine sediment erythrocyte count (RBC-M)

Five trials [13, 16, 18, 25, 26] evaluated RBC-M. The pooled effect size was $MD = -0.87$ (95% CI: -2.29 to 0.54), with $Z = 1.21$ ($P = .23$). Heterogeneity was substantial ($P < .00001$, $I^2 = 96\%$), and a random-effects model was applied. These results suggest no significant difference in RBC-M between the YQH and control groups ($P > .05$) (Figure 4c).

Serum creatinine (SCr)

Eight studies [15–17, 19, 22, 23, 26, 27] reported SCr. The meta-analysis showed $MD = -13.12$ (95% CI: -23.83 to -2.40), $Z = 2.4$ ($P = .02$), with high heterogeneity ($P < .00001$, $I^2 = 92\%$). A random-effects model was applied, and the pooled results indicate that YQH treatment effectively reduced serum creatinine levels (Figure 4d).

Blood urea nitrogen (BUN)

Four trials [15, 16, 19, 23] assessed BUN. The effect size was $MD = 0.10$ (95% CI: -0.71 to 0.90), $Z = 0.23$ ($P = .82$), with significant heterogeneity ($P < .00001$, $I^2 = 89\%$). A random-effects model was used, and results indicate no

significant difference between experimental and control groups (Figure 4e).

Alanine transaminase (ALT)

Three studies [15, 20, 22] reported ALT. The pooled MD was 0.77 (95% CI: -4.61 to 6.15), $Z = 0.28$ ($P = .78$), with moderate heterogeneity ($P < .03$, $I^2 = 71\%$), analyzed using a random-effects model. No significant difference in ALT was observed between groups (Figure 4f).

Serum albumin (ALB)

Four studies [16, 17, 20, 23] reported ALB changes. The combined effect size was $MD = 2.26$ (95% CI: -1.97 to 6.49), $Z = 1.05$ ($P = .30$), with high heterogeneity ($P < .00001$, $I^2 = 90\%$), analyzed using a random-effects model. No significant difference was found between the YQH and control groups (Figure 4g).

Hemoglobin (Hb)

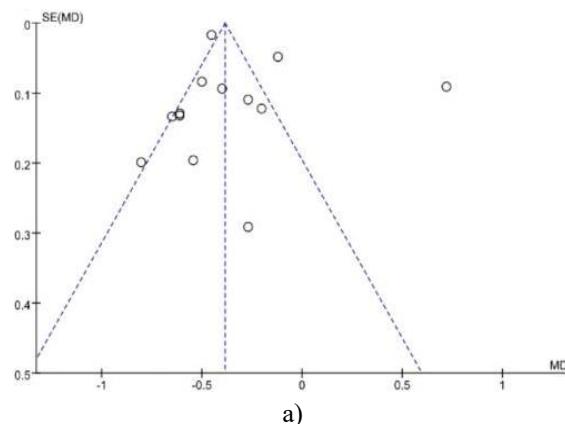
Three studies [20, 22, 23] reported Hb levels. The pooled effect size was $MD = 0.42$ (95% CI: -0.57 to 1.41), $Z = 0.83$ ($P = .41$), with no observed heterogeneity ($P = .76$, $I^2 = 0\%$). A fixed-effects model was used, indicating no significant difference between groups (Figure 4h).

Endogenous creatinine clearance (CCr)

Three studies [13, 19, 26] reported CCr. The pooled MD was -0.28 (95% CI: -4.50 to 3.93), $Z = 0.13$ ($P = .90$), with no heterogeneity ($P = .43$, $I^2 = 0\%$), analyzed using a fixed-effects model. No significant difference was observed between the YQH and control groups (Figure 4i).

Publication bias

Funnel plots were generated for outcomes with more than 10 studies, including 24hPRO and overall effective rate. The asymmetric distribution of these plots suggests the possibility of publication bias (Figure 5).



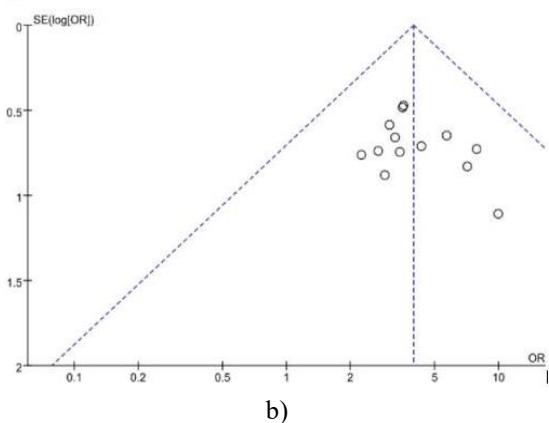


Figure 5. Funnel plots assessing publication bias. (a) 24hPRO; (b) Total effective rate. Abbreviations: 24hPRO = 24-hour urinary protein quantity, ALT = alanine transaminase.

IgA nephropathy is a primary glomerular disorder mediated by immune complexes, characterized by IgA deposition in the mesangial region and mesangial cell proliferation. It represents the most prevalent form of chronic nephritis and typically presents with mild to moderate proteinuria and microscopic hematuria [28]. Around 40% of patients progress to end-stage renal disease following diagnosis [3], and sustained proteinuria is a key risk factor for renal function decline [4–6]. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend foundational therapies such as RAAS blockade, including angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, for patients with IgA nephropathy whose 24-hour urine protein exceeds 1 g [7]. However, in practice, these medications often achieve only limited reductions in proteinuria [7, 29], and many patients fail to reach complete remission. Consequently, combining conventional therapy with Chinese medicine to further reduce proteinuria and prevent renal damage has become a clinical priority [10].

From the perspective of traditional Chinese medicine, IgA nephropathy develops under conditions of Qi deficiency, blood stasis, and wind invasion [30–33]. The primary pathogenesis is spleen and kidney Qi deficiency, considered the main internal factor [34, 35], while wind acts as the initiating external factor by disturbing the collaterals [33], and blood stasis exacerbates disease progression in later stages [36]. Proper functioning of the spleen and kidneys is essential for the circulation of nutrients and fluids through the veins and channels; dysfunction leads to leakage of essence in the urine, manifesting as proteinuria and hematuria [37]. As described in the Inner Canon of Huangdi, wind is a guiding pathogenic factor characterized by dispersing, migrating, and variable properties [38]. Early in IgA nephropathy, patients often experience conditions such as cold or

tonsillitis [39, 40]. Since kidney meridians connect to the throat and tongue, wind can enter the kidney via these channels, disrupting renal function and producing symptoms like foamy urine and proteinuria [41].

Wind is frequently accompanied by other pathogenic factors such as heat and dampness, which further impair kidney function, contributing to recurrent, persistent, and difficult-to-treat IgA nephropathy. Structurally, the kidney's glomeruli and tubules coordinate its essential functions, with the tubules surrounded by vessels; the collaterals mirror the glomerular structure and function [42, 43]. Blood stasis in these collaterals can lead to proteinuria and renal hypofunction, prolonging disease duration and complicating treatment [44].

In this meta-analysis, we aimed to evaluate the clinical efficacy of the YQH method in treating IgA nephropathy, a topic not previously examined in a systematic manner. Data from the 15 included studies were analyzed using RevMan, assessing outcomes such as 24-hour urinary protein (24hPRO), serum creatinine (SCr), blood urea nitrogen (BUN), liver function, and serum albumin (ALB). The pooled results showed that the odds ratio (OR) for the overall effective rate was 3.95 (95% CI: 2.76–5.67). The mean difference (MD) for 24hPRO was -0.35 (95% CI: -0.54 to -0.16), and for SCr, MD = -13.12 (95% CI: -23.83 to -2.4), indicating that YQH therapy combined with conventional treatment achieved greater clinical efficacy than conventional therapy alone. No significant changes were observed for BUN or endogenous creatinine clearance (CCr). Additionally, the YQH method did not adversely affect ALT, Hb, or ALB levels, suggesting it is safe for patients with IgA nephropathy.

Heterogeneity was noted for 24hPRO and SCr outcomes, which may be attributed to several factors: variations in treatment duration, baseline patient characteristics, differences in drugs used in control groups, variability in Chinese medicine compositions in the YQH prescription, and inconsistencies in measurement methods. Despite these limitations, the study supports that YQH therapy effectively reduces 24hPRO and SCr while maintaining normal ALT, Hb, and ALB levels. Limitations include small sample sizes, overall low methodological quality of the included RCTs, and the fact that all studies were conducted in China, predominantly involving Asian populations. Future research should involve multicenter, large-sample RCTs across different regions and improved experimental designs for traditional Chinese medicine interventions.

Conclusion

This meta-analysis demonstrates that the YQH method, when combined with conventional therapy, provides superior clinical outcomes for patients with IgA nephropathy compared with conventional treatment alone.

The method effectively reduces urinary protein and preserves renal function without adversely affecting serum ALT, Hb, or ALB levels, supporting its use as a complementary therapy alongside standard treatments.

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Conflict of interest: None

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Ethics statement: As it is a systematic review and meta-analysis based on previously published literature, ethical approval and informed consent from patients are not required. This review has been registered, CRD42022332207.

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