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Therapeutic effect of Corbrin (Bailing) capsule on patients with renal insufficiency: A meta-analysis

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ABSTRACT

Objective: At present, there remains controversy regarding the clinical efficacy of Corbrin (Bailing) capsules in the treatment of renal insufficiency (RI). A meta-analytic approach was adopted in this study to assess the clinical efficacy of Corbrin capsules for treating RI, aiming to provide a certain level of clinical evidence to guide the selection of RI therapeutic interventions.

Methods: The meta-analysis was conducted on databases containing PubMed, CNKI, Weipu Database, Cochrane Library and Wanfang until January 2023. The search for relevant studies was conducted without language restrictions. The study encompassed a randomized controlled trial that examined the efficacy of Corbrin capsules in treating RI. Blood urea nitrogen (BUN), serum creatinine (Scr), 24-h urine protein quantity (24 h UPQ), and estimated creatinine clearance (ECC) were amalgamated using standardized mean difference (SMD) and its corresponding 95 % confidence interval (CI). Meanwhile, the treatment effect (TE) outcome was aggregated using odds ratio (OR) and its corresponding 95 % CI. To evaluate heterogeneity, the Q test and I² statistics were employed within a random-effects model framework.

Results: A total of 11 engible articles were included, involving 1100 patients (594 in the Corbrin capsule group and 516 in the control group). Compared with control subjects, the SMD was-1.3532 for Ser (95 % CI: 2.0617 to -0.6448), -1.7868 for UPQ (95 % CI: 2.8901 to -0.6836), -1.3302 for BUN (95 % CI: 2.2428 to -0.4176), and 1.7842 for ECC (95 % CI: 0.6774–2.8910). TE had an OR of 1.9786 (95 % CI: 0.7153–5.4734), and publications were not found to be biased (t = 0.5627, *P* = 0.6738).

Conclusion: In RI patients, Corbrin capsule has a relatively good therapeutic effect.

1. Introduction

Renal insufficiency (RI) is a commonly encountered clinical disorder, characterized by the kidneys' inability to efficiently eliminate metabolic byproducts and waste from the body, resulting in disrupted metabolic processes and imbalances in electrolytes and fluids. In severe cases, it can even pose a life-threatening condition. In recent years, with the influence of factors such as aging populations, the rise in chronic diseases, and inappropriate medication use, the incidence of RI has gradually escalated, emerging as a significant facet of public health concern. While the prevalence of RI is relatively low in developed countries (approximately 0.15 %), its complex treatment and poor prognosis contribute to substantial impacts on both hospital and community resources [1,2]. The average mortality

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rate associated with RI is 45 %, which may exceed 80 % if dialysis is required [3,4]. Diseases such as diabetic nephropathy, hypertension, chronic glomerulonephritis, pyelonephritis, and polycystic kidney disease are all correlated with the occurrence of RI [5,6]. Clinically, RI often manifests through symptoms like reduced urine output, edema, hypertension, anemia, fatigue, and weakness [7]. When RI occurs, metabolic byproducts accumulate within the body, leading to toxic reactions that can be life-threatening in severe cases [8]. RI disrupts fluid and electrolyte balance in the body, giving rise to issues such as hypertension and edema, further exacerbating the strain on the heart and vasculature [9]. Additionally, RI may trigger anemia, skeletal problems, and neurological issues, consequently affecting patients' quality of life [10]. Hence, the exploration of effective pharmaceutical interventions for treating RI beyond dialysis is imperative.

In clinical practice, various approaches are employed for treating RI, including pharmacological therapy, dietary and lifestyle interventions, dialysis, and kidney transplantation. Pharmacological interventions primarily aim to manage symptoms, slow disease progression, and prevent complications, but these medications may lead to adverse reactions, interact with other drugs, and lack the capacity to provide curative outcomes for RI [11]. Dietary adjustments involve restricting protein, phosphorus, and sodium intake to alleviate renal burden. However, protein restriction may result in malnutrition and patient adherence over the long term is often challenging [12]. Moreover, lifestyle modifications such as weight management, smoking cessation, and alcohol limitation may encounter implementation difficulties. Dialysis serves as a method of substituting for kidney function by mechanically or chemically facilitating waste elimination and electrolyte balance. While dialysis can sustain life, it necessitates regular, prolonged, and frequent sessions, and can potentially give rise to dialysis-related complications, leading to reduced quality of life [13]. Kidney transplantation represents an effective means to restore renal function, yet due to organ scarcity, surgical risks, immunosuppressive therapy, and postoperative rejection responses, challenges persist [14]. In recent years, with the advancement of medical technology, approaches such as stem cell and gene therapies have gradually found application in RI treatment. Nonetheless, the clinical implementation of these strategies requires further validation and refinement.

Traditional Chinese medicine (TCM) possesses characteristics such as holistic regulation, personalized treatment, synergistic effects of multiple components, multi-target modulation, and minimal adverse reactions [15,16]. In recent years, it has been widely applied in the treatment of RI. The Corbrin (Bailing) capsule is an over-the-counter (OTC) drug derived from Cordyceps sinensis mycelia, which has many effects on human, it regulates immunity, protects liver and kidneys, stimulates hematopoiesis, improves hypoproteinemia and hyperlipidemia, reduces infection, and lowers protein levels [17,18]. Increasing studies have been reported the effect of Corbrin (Bailing) capsule/Cordyceps sinensis on the development of renal diseases. Wang et al. have performed a renal function trail with Cordyceps sinensis in a renal ischemia/reperfusion injury rat model and found that Cordyceps sinensis had a protective role in renal ischemia rat against reperfusion injury [19]. Treatment with Cordyceps sinensis in RI patients who underwent coronary angiography could prevent contrast-induced renal impairment [20]. Notably, use of Bailing capsule in renal transplant recipients in clinic can prevent allograft rejection and accelerate recovery of renal function [21]. Certain studies have indicated that Corbrin capsules may have the potential to enhance glomerular filtration rate, improve glomerular filtration function, and contribute to the amelioration of renal function [22]. It is suggested that Corbrin capsules could potentially exert a protective effect on renal tubular cells, diminishing the loss of protein and waste in urine, consequently enhancing tubular function [23]. Several studies have reported positive effects of Corbrin capsules in terms of improving renal function and alleviating symptoms associated with RI [24]. In addition, numerous clinical researches on Corbrin capsules for RI have also been reported [23,25–34]. However, they are all small sample studies and the results of these studies are not the same. Furthermore, research has identified adverse reactions such as nausea, vomiting, and diarrhea among RI patients undergoing treatment with Corbrin capsules [26]. Therefore, it is imperative to conduct a meta-analysis to systematically evaluate the clinical efficacy of Corbrin capsules in the treatment of RI.

In this study, to compare the clinical efficacy and safety of Corbrin capsules on RI, we conducted a meta-analysis of randomized controlled trials (RCTs). These findings aimed to guide future clinical use of Corbrin capsules in an objective and comprehensive manner.

2. Methods

2.1. Data sources

Based on the pre-defined search strategy, English electronic literature databases (PubMed and Cochrane Library) and Chinese electronic literature databases (CNKI, Wanfang and Weipu) were used to systematically search for the literatures that published before January 31, 2023 on Corbrin capsule treatment with RI. The searched keywords included "renal insufficiency", "renal failure", "Renal dysfunction", "renal inadequacy", "Corbrin capsule", "Bailing capsule". A search was conducted for the aforementioned key terms and their related synonyms. Logical operators "or" and "and" were employed to combine search terms and synonyms within each thematic category. Additionally, reference lists of pertinent reviews were examined to manually identify potentially overlooked studies. Language restrictions were not imposed during the search process.

The inclusion criteria were: i) patients diagnosed with RI; ii) the intervention group comprised individuals subjected to intervention with Corbrin (Bailing) capsules; iii) the control group consisted of RI patients undergoing interventions utilizing medications other than Corbrin (Bailing) capsules, including dexamethasone + bosentan + losartan, uremic clearance granules, conventional Western medicine treatment, routine treatment, Levocarnitine, fundamental treatment, Alprostadil, Shuxuening, among others; iv) encompassment of one or more outcome measures, including blood urea nitrogen (BUN), serum creatinine (Scr), 24-h urinary protein quantification (24 h UPQ), and estimated creatinine clearance (ECC); v) publicly published literatures on Corbrin capsule treatment with RI. The exclusion criteria were: i) incomplete data or logical errors, which cannot be used for meta-analysis; ii) literatures of

reviews, letters or comments; iii) repeated publications or the data of the same population used in multiple studies.

2.2. Assessing bias and extracting data

Two authors independently extracted relevant data from the eligible literatures. The extracted data included first author's name, publication year, follow-up time, the intervention means in both the Corbrin capsule group (CCG) and control group (CG), case numbers in the two groups, age, sex ratio and the aforementioned variables for meta-analysis. A modified version of Cochrane Collaboration's tool [35] was used to assess the risk of bias of RCT. Disagreements in data extraction and risk assessment were resolved by discussion and consensus. This process was supervised by the third author. Simultaneously, the Jadad scoring scale was employed to assess the quality of the included RCTs. The Jadad scoring scale encompasses four aspects: random sequence generation, allocation concealment, blinding, and withdrawals and dropouts. Within these aspects, appropriate (2 points), unclear (1 point), and inappropriate (0 points) criteria were utilized to evaluate the first three aspects. For withdrawals and dropouts, a score of 1 or 0 was assigned based on the level of detail provided in describing data and reasons. Total scores ranging from 1 to 3 were categorized as low quality, while scores ranging from 4 to 7 were classified as high quality.

2.3. Statistical analysis

RevMan (version 5.2.6) was used to assess the quality of the eligible literatures. The continuous data were pooled by SMD and 95 % CI [36], A Q test [37] and I² statistic (0%–100 %) were used to assess heterogeneity between studies based on categorical data (TE outcome). If there was significant statistical-differences in heterogeneity among the eligible literatures (P < 0.05 and I²>50 %), the effect size would be pooled by a random-effect model. Otherwise, a fixed-effect model should be employed (P > 0.05 and I² ≤ 50 %) [38]. Egger's linear regression test was used to estimate publication bias. By omitting one study at a time, we assessed the relative influence of each study on the pooled estimate [39]. A sensitivity analysis was conducted using the one-by-one exclusion method to assess the robustness of the study results. *R* 3.12 was used to perform the meta-analysis. A P value < 0.05 was considered statistically significant.

3. Results

3.1. Identification process for eligible literatures

The screening processes of eligible literatures were shown in Fig. 1. A total of 93 relevant literatures were retrieve from PubMed,



Fig. 1. Flow chart of article selection.

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Table 1The general characteristics of the included studies.

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Author	Year	Follow-up time	Group	intervention means	Sample size	Gender (male/ female)	Age	BMI (kg/ m ³)	病程 (年)	variate
Wang Lin	2011	24 weeks	Corbrin	$Corbrin\ capsules + \alpha \text{-}keto\ acid\ tablets$	160	76/84	71.2 ±	NA	NA	(1)(2)
			Control	N/A	80	39/41	NA	NA	NA	
Liu Jundong	2004	6 weeks	Corbrin	$Corbrin\ capsules + Prednisone + Persantine + Lotensin$	30	41/19	39.0 ± 8.4	NA	NA	(1)(2)
			Control	Prednisone + Persantine + Lotensin	30			NA	NA	(3)
Wu Jiaming	2018	2 years	Corbrin	Corbrin capsules	100	100/0	91.50 ±	NA	$\textbf{4.60} \pm \textbf{10}$	(5)
			Control	Uremic Clearance Granule	100	100/0	5.19	NA	$\textbf{4.60} \pm \textbf{10}$	
Zou Fangpeng	2014	2 months	Corbrin	Corbrin capsules + Uremic Clearance Granule + conventional Western medicine treatment	32	17/15	$42.8 \pm$	NA	5.6 ± 21	(1)(2)
			Control	conventional Western medicine treatment	32	18/14	42.1 ±	NA	5.6 ± 21	(3)
Lin Hairen	2015	4 weeks	Corbrin	$Corbrin \ capsules + Nifedipine + \ conventional \ treatment$	30	15/15	50 ± 2	$21.52 \pm$	$\textbf{5.0} \pm \textbf{3.0}$	(1)(2)
			Control	conventional treatment	30	16/14	53 ± 4	21.12 ± 200	$\textbf{4.0} \pm \textbf{2.0}$	(3)(3)
Liu Yudong	2017	N/A	Corbrin	Corbrin capsules + Levocarnitine	25	10/15	53.2 ± 5.4	NA	NA	(1)(2)
			Control	Levocarnitine	25	12/13	53.8 ± 5.6	NA	NA	
Zhao Kai	2017	3 days	Corbrin	Corbrin capsules + basic treatment	39	23/16	63.94 ±	26.91 ±	NA	(2)
			Control	basic treatment	41	22/19	4.20 64.58 ±	27.19 ±	NA	
Qiu Lei	2019	3 months	Corbrin	Corbrin capsules + Alprostadil	30	18/12	52.41 ±	NA	4.82 ±	(1)(2)
			Control	Alprostadil	30	17/13	4.33 52.38 ±	NA	4.78 ±	(3)
Wang Vunfang1	2016	2 weeks	Corbrin	Corbrin capsules + Shuxuening	50	26/24	43 ± 6	25.25 ± 1.56	NA	(1)(2)
Tuniangi			Control	Shuxuening	50	30/20	45 ± 7	25.30 ±	NA	(5)(4)
Wang	2018	3 months	Corbrin	$Corbrin \ capsules + \ Shuxuening + \ conventional \ treatment$	55	55/55	65.79 ±	NA	NA	(2)(3)
i uiitaiig2			Control	conventional treatment	55		7.32	NA	NA	(4)
Tong Yuntao	2015	2 weeks	Corbrin	Corbrin capsules + Shuxuening + conventional Western medicine	43	NA	20.4 ± 4.5	NA	0.01 ±	(1)(2)
			group Control group	conventional Western medicine treatment	43	NA	18.1 ± 4.2	NA	0.01 ± 0.01	(5)(4)

(1) Blood urea nitrogen; (2) Serum creatinine; (3) 24 h urine protein quantification; (4) Endogenous creatinine clearance; (5) Therapeutic efficiency.

Cochrane Library, CNKI, Wanfang and Weipu. We initially eliminated 69 literatures. Among them, 21 literatures were repeated, 44 literatures were obviously not met the inclusion criteria and 4 literatures were reviews or meta-analysis. After reading the full text, 13 (4 repeated literatures and 3 literatures without CG as well as 6 literatures without quantitative data) of the remanent 24 literatures were further deleted. Eventually, a total of 11 eligible literatures [15–23,23–34] were retrieved.

3.2. Study characteristics

The included articles were all from mainland China and the publication year of these 11 literatures was from 2004 to 2023. In Table 1, the definitive study population encompassed a total of 1100 patients, of which 594 underwent treatment involving Corbrin capsules either solely or in conjunction with conventional Western medicine, while 516 individuals comprised the CG. The duration of follow-up varied, ranging from 2 weeks to 2 years, with a predominant focus on intervals spanning 2 weeks to 3 months. In terms of intervention modalities, the CCG predominantly received Corbrin capsules in combination with α -keto acid tablets, prednisone, levocarnitine, and analogous treatments. Simultaneously, the C primarily underwent conventional therapeutic strategies. Notably, the majority of participants were middle-aged to elderly individuals with RI, and a higher representation of male participants was observed. The primary outcome indicators encompassed BUN, Scr, 24 h UPQ, ECC and TE.

3.3. Quality assessment

Assessment of risk of bias of all the eligible literatures was summarized in Figs. 2 and 3. Among all the 11 RCTs, the random sequence generation (selection bias) and blinding of participants and personnel (performance bias) were assessed as low risk of bias for all studies. For one study, allocation concealment (selection bias) was evaluated as having unclear risks of bias, while for four studies, blinding of outcome assessment (detection bias) was evaluated as having unclear risks of bias. In one case each, incomplete outcome data (attrition bias) and selective reporting (reporting bias) were assessed as having unclear risks of bias. Additionally, two studies were evaluated as having high risks of bias under the category of other bias, while one study was assessed as having unclear risks of bias unclear risks of bias under the same category. The Jadad scores for all included studies were above 4 points, indicating that the included literature in this study were all of high quality.

3.4. Comparison for BUN

Eight eligible literatures were included that compared the effect of Corbrin capsule on BUN indicator. There were 400 and 320 patients in the CCG and the CG, respectively and a significant heterogeneity was exhibited between these two groups (Q = 185.10, P < 0.01, $I^{2}=96.2$ %). Therefore, a random-effect model was used for quantitative combination. As illustrated in Fig. 4, BUN was presented significant difference between the two groups (SMD = -1.3302, 95 % CI = -2.2428-0.4176, Z = 2.86, P = 0.043), and BUN decreased more in the CCG. The Egger' test suggested no evidence of publication bias (t = 0.1042, P = 0.9204).

3.5. Comparison for Scr

A total of 10 eligible studies were incorporated into the analysis. A pronounced heterogeneity emerged (Q = 185.10, P < 0.01, $I^2 = 96.2$ %) between the CCG encompassing 494 patients and the CG comprising 416 patients. Subsequently, a random-effects model was applied. The findings gleaned from the meta-analysis revealed a statistically significant distinction between these two groups (Fig. 5; SMD = -1.3532, 95 % CI = -2.0617-0.6448, Z = 3.74, P = 0.0002). Moreover, a more pronounced reduction in Scr levels was evident



Fig. 2. Risk of bias graph.



Fig. 3. Risk of bias summary.

		Exper	imental		1	Control	Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Wang Lin	160	16.45	4.8200	80	28.32	0.3700	≖ :	-3.00	[-3.38; -2.62]	21.2%	12.8%
Liu Jundong	30	4.89	0.7500	30	4.98	0.8600	-	-0.11	[-0.62; 0.40]	12.0%	12.5%
Zou Fangpeng	32	10.70	1.0100	32	10.81	1.7600	-	-0.08	[-0.57; 0.41]	12.8%	12.6%
Lin Hairen	30	5.81	2.0700	30	6.68	2.1800		-0.40	[-0.92; 0.11]	11.7%	12.5%
Liu Yudong	25	13.90	0.8000	25	15.10	0.6000		-1.67	[-2.32; -1.02]	7.3%	12.2%
Qiu Lei	30	12.05	3.0400	30	14.65	3.3700		-0.80	[-1.33; -0.27]	11.1%	12.5%
Wang Yunfang1	50	11.20	3.8000	50	15.40	4.9000	<u></u>	-0.95	[-1.36; -0.54]	17.9%	12.7%
Tong Yuntao	43	10.81	0.9300	43	14.84	1.2100		-3.70	[-4.41; -2.99]	6.2%	12.1%
Fixed effect model	400			320			\$	-1.31	[-1.49; -1.14]	100.0%	
Random effects model	l.						\sim	-1.33	[-2.24; -0.42]		100.0%
Heterogeneity: $I^2 = 96\%$, τ	2 = 1.66	609, p <	: 0.01								
-							-4 -2 0 2 4				

Fig. 4. Forest plot of meta-analysis of renal function BUN difference of Corbrin capsule in RI treatment.

in the CCG in comparison to the CG. Furthermore, a notable presence of publication bias was identified (t = 3.8917, P = 0.004598) as indicated by the Egger's test.

3.6. Comparison for 24 h UPQ

In this segment, 6 eligible studies were analyzed, each involving 238 patients within both the CCG and the CG. Concurrently, significant heterogeneity was evident between these two groups (Q = 124.95, P < 0.01, $I^2 = 96.0$ %). Subsequently, a random-effects model was employed for conducting quantitative synthesis. Our meta-analysis elucidated a substantial distinction between the CCG and CG. Notably, the 24 h UPQ within the CCG (Fig. 6; SMD = -1.7868, 95 % CI = -2.8901-0.6836, Z = 3.17, P = 0.0015) was comparatively lower when juxtaposed with the CG. Based on Egger's test, it was ascertained that no discernible evidence of publication bias was present (t = 2.5032, P = 0.06654).

3.7. Comparison for ECC

Three eligible studies were assessed to investigate the ECC indicator. Notably, a substantial heterogeneity (Q = 32.28, P < 0.01, $I^2 = 93.8$ %) was detected between the CCG consisting of 148 patients and the CG also comprising 148 patients, warranting the utilization of a random-effects model for quantitative synthesis. Our meta-analysis findings unequivocally revealed a significant increase in ECC within the CCG compared to the CG (Fig. 7; SMD = 1.7842, 95 % CI = 0.6774–2.8910, Z = 3.16, P = 0.0016). Egger's test showed no evidence of publication bias (t = 3.7169, P = 0.1673).

3.8. Comparison for TE

Five eligible studies were subjected to screening to facilitate a comparative analysis of the impact of Corbrin capsules on the TE indicator. Owing to pronounced heterogeneity (Q = 12.44, P = 0.0144, $I^2 = 67.8$ %) evident between the CCG comprising 255 patients and the CG with an identical count of patients, a random-effect model was employed for quantitative synthesis. Our meta-analysis findings disclosed no statistically significant disparity between these two groups (Fig. 8; OR = 1.9786, 95 % CI = 0.7153–5.4734, Z = 1.31, P = 0.1887). Furthermore, the application of Egger's test provided no indication of publication bias (t = 0.5627, P = 0.6737).

3.9. Sensitivity analysis

The assessment of the most significant inter-study heterogeneity, if present, was accomplished via a sensitivity analysis. As illustrated in Fig. 9, it was discovered that the heterogeneity was reduced in varying degrees, but the heterogeneity of some outcomes was still high. In terms of TE indicator, modifications in the results were observed (OR = 3.10, 95 % CI: 1.47-6.53) following the exclusion of the study authored by Wu Jiaming. However, the removal of any other literature did not substantially alter the remaining outcomes.

4. Discussion

RI represents a prevalent clinical syndrome predominantly arising from diverse primary and secondary kidney disorders, ultimately culminating in renal hypofunction, and potentially, renal failure [40]. This condition is characterized by the accumulation of metabolites within the body, disruptions in water, electrolyte, and acid-base equilibrium, and consequential multi-organ damage [28]. *Cordyceps sinensis*, an ancient medicinal fungus, boasts a history spanning over two millennia in China and stands as one of China's "three treasures" alongside ginseng and deer antler within traditional Chinese medicine [41]. In 1983, Chinese scholars sourced Corbrin capsules from *Cordyceps sinensis* specimens in Yushu, Qinghai Province. Research has substantiated that the artificial *Cordyceps sinensis* mycelium, utilized as the foundational material for Corbrin capsules, closely resembles natural *Cordyceps sinensis* [42]. Its

		Exp	erimental			Control	Sta	ndardised M	lean				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Difference		SMD	95%	-CI	(fixed)	(random)
Wang Lin	160	202.25	112.4200	80	284.14	185.7200		10		-0.58	[-0.85; -0	.31]	27.6%	11.2%
Liu Jundong	30	87.83	13.9400	30	97.37	20.0400		i i		-0.55	[-1.06; -0	.03]	7.7%	10.7%
Zou Fangpeng	32	229.46	74.3800	32	251.82	83.1900		4		-0.28	[-0.77; 0	.21]	8.5%	10.8%
Lin Hairen	30	115.87	16.7300	30	136.76	18.5900		- 6		-1.17	[-1.72; -0	.62]	6.8%	10.6%
Liu Yudong	25	265.30	12.2000	25	281.40	15.4000		-		-1.14	[-1.74; -0	.54]	5.7%	10.5%
Zhao Kai	39	126.00	17.0000	41	126.00	18.0000		論		0.00	[-0.44; 0	.44]	10.7%	10.9%
Qiu Lei	30	321.75	11.9300	30	342.81	11.6200		0.5		-1.77	[-2.37; -1	.16]	5.7%	10.5%
Wang Yunfang1	50	151.60	41.5000	50	187.80	46.3000				-0.82	[-1.23; -0	.41]	12.4%	11.0%
Wang Yunfang2	55	135.32	28.7900	55	139.80	32.1800		ib:		-0.15	[-0.52; 0	.231	14.7%	11.0%
Tong Yuntao	43	152.14	1.0500	43	184.38	1.5500				-24.14	[-27.85; -20	.42]	0.1%	2.8%
Fixed effect model	494			416						-0.63	[-0.77; -0	.49]	100.0%	
Random effects mode	1							0		-1.35	[-2.06; -0	.641		100.0%
Heterogeneity: $I^2 = 95\%$,	$\tau^2 = 1.14$	186, p < 0	0.01											
		10.51					-20 -	-10 0 1	20					

Fig. 5. A forest plot of the renal function Scr difference of Corbrin capsules in RI treatment.

		Experi	imental			Control	Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Liu Jundong	30	1.38	0.4700	30	1.46	0.7200	i: 🗰	-0.13	[-0.64; 0.38]	18.4%	16.8%
Lin Hairen	30	2.28	2.0300	30	4.06	2.1900		-0.83	[-1.36; -0.30]	16.9%	16.8%
Qiu Lei	30	1.03	0.4500	30	2.25	0.6400		-2.18	[-2.82; -1.53]	11.3%	16.5%
Wang Yunfang1	50	1.40	0.5000	50	1.90	0.6000	3	-0.90	[-1.31; -0.49]	27.8%	17.0%
Wang Yunfang2	55	0.27	0.0600	55	0.64	0.0900	- 11	-4.80	[-5.55; -4.06]	8.5%	16.1%
Tong Yuntao	43	1.45	0.2700	43	1.97	0.2400		-2.02	[-2.54; -1.49]	17.2%	16.8%
Fixed effect model	238			238			•	-1.41	[-1.63; -1.20]	100.0%	
Random effects model							\sim	-1.79	[-2.89; -0.68]		100.0%
Heterogeneity: $I^2 = 96\%$, τ^2	² = 1.8 ⁴	168, p <	: 0.01						an an ann an		
							-1 -2 0 2 1				

Fig. 6. Forest plot of meta-analysis of renal function 24 h UPQ difference of Corbrin capsule in RI treatment.

		Expe	rimental			Control	Standardised Mean			Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Difference	SMD	95%-CI	(fixed)	(random)
Wang Yunfang1	50	68.50	15.6000	50	55.20	13.2000	1 -= 3	0.91	[0.50; 1.33]	41.9%	34.0%
Wang Yunfang2	55	49.82	3.0100	55	45.90	2.4500		1.42	[1.00; 1.84]	40.5%	34.0%
Tong Yuntao	43	68.21	3.7500	43	54.84	4.7400		3.10	[2.47; 3.74]	17.7%	32.0%
Fixed effect model	148			148			-	1.50	[1.24; 1.77]	100.0%	
Random effects mod	el							1.78	[0.68; 2.89]		100.0%
Heterogeneity: 12 = 94%,	$\tau^2 = 0.89$	924, p <	0.01								
							-3 -2 -1 0 1 2 3				

Fig. 7. Meta-analysis of Corbrin capsule effect on renal function ECC in RI treatment.

	Experim	nental	Co	ontrol				Weight	Weight
Study	Events	Total	Events	Total	Odds Ratio C	R	95%-CI	(fixed)	(random)
Wu Jiaming	76	100	86	100		52	[0.25; 1.07]	70.3%	26.5%
Zou Fangpeng	28	32	24	32	2.5	33	[0.62; 8.72]	10.2%	20.2%
Lin Hairen	28	30	22	30	5.0	90	[0.98; 26.43]	5.0%	17.0%
Wang Yunfang1	48	50	42	50	4.	57	[0.92; 22.73]	5.7%	17.4%
Tong Yuntao	40	43	37	43	2.	16	[0.50; 9.28]	8.8%	18.8%
Fixed effect model		255		255	- - -	31	[0.81; 2.11]	100.0%	
Random effects model Heterogeneity: $I^2 = 68\%$, τ	2 ² = 0.8788	3, p = (0.01			98	[0.72; 5.47]		100.0%
					01 051 2 10				

Fig. 8. Forest plot of meta-analysis of therapeutic efficiency (TE) difference of Corbrin capsule in RI treatment.

principal constituents encompass adenosine, a range of amino acids, mannitol, ergosterol, polysaccharides, diverse vitamins, and trace elements. These components collectively bolster the immune system, regulate hormonal levels, and exert anti-inflammatory and anti-hypoxic properties, consequently conferring protective effects upon the kidneys and lungs [43]. Recently, Chinese researchers have applied the pharmacological attributes of Corbrin capsules to the domain of kidney disorders, including RI [23,25–34]. In the present study, we executed a meta-analysis of randomized controlled trials to assess the clinical efficacy and safety of Corbrin capsules in managing RI.

Numerous studies reported that BUN, Scr, 24 h UPQ and ECC are vital outcome indicators to assess the severity and prognosis of RI or other renal diseases [34–46]. Jaenckner et al. have demonstrated that the high concentration of glucose in urine protein reflects a relatively severe renal-injury for RI patients [44]. Chen et al. have indicated that the renal damage in infants with asphyxia is closely correlated with BUN and SCr levels [45]. Kabat-Koperska et al. have confirmed that an enhancement of ECC level in patients with kidney transplantation represents a poor prognosis [46]. Corbrin capsules may potentially exert its effects through components with anti-inflammatory properties, inhibiting renal inflammatory responses, and reducing the release of inflammatory mediators [47]. This mechanism could contribute to lowering urinary protein excretion and improving renal function. It is plausible that Corbrin capsules may modulate inflammatory pathways, curbing damage to the glomerular filtration membrane and loss of urinary protein. Corbrin capsules could likely play a role in enhancing glomerular filtration function, thereby promoting an increase in glomerular filtration rate (GFR) [48]. This may result in decreased levels of serum creatinine and blood urea nitrogen. Additionally, Corbrin capsules might be enriched with antioxidant compounds that counteract the generation of free radicals and oxidative damage, thereby alleviating oxidative stress in renal tissues [49]. This mechanism could aid in reducing renal tissue injury and improving renal function. Furthermore, Corbrin capsules could potentially mitigate renal fibrosis occurrence and progression through mechanisms such as inhibiting fibroblast activation and collagen synthesis [50]. This action might contribute to preserving the structure of glomeruli and renal tubules, consequently reducing urinary protein excretion. In this meta-analysis, we found that the levels of BUN, Scr and 24 h



Fig. 9. Sensitivity analysis for the overall estimate on the association between Corbrin capsule and RI. (A) Sensitivity analysis for BUN. (B) Sensitivity analysis for Scr. (C) Sensitivity analysis for 24 h UPQ. (D) Sensitivity analysis for ECC. (E) Sensitivity analysis for TE.

UPQ were decreased, whereas ECC index was increased in the CCG compared to the CG. Simultaneously, notable distinctions existed between the aforementioned groups. Likewise, a meta-analysis pertaining to nephrotic syndrome (a primary phase of RI) conducted by Xu et al. demonstrated that the CCG, comprising either Corbrin capsule alone or in conjunction with conventional therapy, exhibited more pronounced inhibitory effects on BUN, Scr, and 24 h UPQ levels compared to the CG [51]. The outcomes indicated a notably enhanced clinical efficacy within the CCG relative to the CG. By integrating conventional therapy, Bailing capsules exhibited a substantial capacity to enhance renal function. Subsequent to this, the sensitivity analysis results demonstrated that the outcome measures encompassing BUN, SCr, 24 h UPQ, and ECC exhibited relative stability, with minimal influence from any individual study. However, there was notable divergence in the results of the TE indicator (OR = 3.10, 95 % CI: 1.47-6.53) upon the exclusion of the study by Wu Jiaming [33]. Employing Egger's linear regression test, it was ascertained that, apart from the Scr indicator, which displayed publication bias, the outcomes pertaining to BUN, 24 h UPQ, ECC, and TE exhibited no discernible publication bias. This suggests that some unpublished studies contribute to the conclusion that the clinical efficacy of the Scr indicator is similar in both the CCG and the CG.

Meanwhile, the results of heterogeneity in this study were all pooled by a random-effect model as well as having significant differences. During the process of conducting a meta-analysis, heterogeneity refers to the extent to which the differences in results among studies exceed what can be attributed to random error. In this study, the heterogeneity of changes in renal function indexes is attributed to the following reasons: i) the units of these outcome indicators were different; If different studies use varying units of measurement to assess the same outcome measures (such as blood creatinine concentration and urinary protein content), this discrepancy could lead to heterogeneity; ii) the measurement methods of these outcome indicators were different; various studies might employ different measurement methods to assess the efficacy of treating RI, such as methods for serum creatinine determination and urinary protein quantification; iii) basic information such as gender, age and other demographic data were different; demographic data within the study, such as gender and age factors, may exert an influence on treatment outcomes; iv) the follow-up time was different (from 3 days to 2 years); differences in the follow-up periods may contribute to result instability and heterogeneity; v) variations in treatment protocols, dosages, and treatment durations within the control groups of different studies exist. Diverse treatment regimens and dosages were employed across studies. The duration of treatment might exert an influence on treatment outcomes. These variations in treatment protocols, dosages, and treatment durations among different studies could potentially give rise to heterogeneity.

This study, employing a meta-analysis approach, has provided, for the first time, a comprehensive elucidation of the clinical efficacy of Corbrin (Bailing) capsules in treating RI, based on the assessment of renal function evaluation indicators. These findings offer a valuable reference for the selection of treatment strategies for RI. However, there are also some limitations of this study. Initially, the collective quality of the eleven eligible articles is notably modest. Additionally, all studies encompass limited sample sizes, rendering it

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impractical to exclude biases stemming from the overall subpar quality. Furthermore, substantial heterogeneity is evident within the results. Given these constraints, it becomes imperative to conduct studies with larger sample sizes and encompassing more comprehensive fundamental data to more comprehensively illuminate the clinical efficacy of Corbrin capsules. Furthermore, it's important to note that all the included studies in this meta-analysis originated from mainland China, which introduces a certain degree of geographical limitation to the sample, consequently affecting the generalizability of the findings. Lastly, it should be acknowledged that this study did not undergo a protocol registration review before the design phase.

In general, the outcomes, including BUN, Scr, 24 h UPQ, and ECC, demonstrated comparatively more favorable results in the CCG in comparison to the CG. This suggests that Corbrin capsules exhibit a promising therapeutic potential for individuals with RI. Notwithstanding the acknowledged limitations, we trust that this meta-analysis will contribute to establishing a theoretical foundation for clinical interventions targeting RI.

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Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Xiaoling Zhou: Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Visualization, Writing – original draft, Writing – review & editing. Jianhua Ye: Data curation, Formal analysis, Investigation, Resources, Visualization, Writing – original draft, Writing – review & editing. Xiaoyan Guo: Methodology, Supervision, Writing – original draft, Writing – review & editing. Data curation, Formal analysis, Project administration, Writing – original draft, Writing – original draft, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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