Original Article

Diagnostic value of different urine tests for urinary tract infection: a systematic review and meta-analysis

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Background: There are differences in specificity and sensitivity of different routine urine tests for urinary tract infection, so meta-analysis was used to compare the diagnostic value of various urine analysis and detection methods in urinary tract infection, including bacterial culture, urine sediment microscopy, automated urinalysis, and routine urine dry chemical methods.

Methods: The PubMed, Embase, Cochrane Library, SpringerLink, CNKI, and Wanfang databases were searched from inception to December 2021. Two system assessors independently screened the literature according to the inclusion and exclusion criteria. RevMan version 5.3 (the Cochrane Collaboration) and Meta-DiSc were used to calculate the combined sensitivity (Sen), specificity (Spe), positive likelihood ratio (LR+), negative likelihood ratio (LR–), and diagnostic ratio (DOR) of the diagnostic tests and draw summary receiver operating characteristic (SROC) curves.

Results: A total of 14 documents were included according to the inclusion and exclusion criteria. There was a significant statistical difference between the urine sediment microscopy group and the urine normalization group in urine leucocyte detection (OR =2.15, 95% CI: 1.29–3.56, P=0.003, I^2=19%, Z=2.95), urine erythrocyte test (OR =1.87, 95% CI: 1.13–3.09, P=0.01, I^2=0%, Z=2.45), quantitative determination of urinary protein composition (OR =2.32, 95% CI: 1.27–4.23, P=0.006, I^2=30%, Z=2.73), and determination of urinary enzymes (OR =1.67, 95% CI: 1.03–2.72, P=0.04, I^2=0%, Z=2.07).

Discussion: When examining red and white blood cells in urinary tract infection diagnosis, urine dry chemistry is superior to automated urinalysis in terms of area under the curve (AUC), Sen, Spe, etc. When examining urine bacteria, urine dry chemistry can be recommended for urine bacteria screening, with bacterial culture required for confirmation.

Keywords: Multiple urine tests; urinary tract infection; systematic review; meta-analysis; retrospective study

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Introduction

Urinary tract infection is a common nosocomial infection. Many factors contribute to the development of urinary tract infection, such as lengthy indwelling catheter time or untimely treatment of the infection. Diagnosis of urinary tract infection cannot rely on clinical symptoms alone and should be combined with biochemical test results to effectively determine the infection site and allow for targeted treatment in order to promote patient recovery (1). If urinary tract infection is not treated effectively, the infection will become chronic, which can

have a serious impact on a patient's health and quality of life (2). Routine urine dry chemical testing is favored by the majority of doctors and is often used in clinical practice due to its rapid and efficient results (3-5).

If urinary tract infection occurs more than 3 times in 1 year, it can be characterized as a recurrent urinary tract infection. Recurrent urinary tract infection is a persistent disease of the urinary system that seriously affects quality of life. Currently, clinical treatment of recurrent urinary tract infection is difficult, and there is an urgent need to improve the level of diagnosis and treatment (6). Recurrent urinary tract infection requires timely and standardized treatment to actively improve the cure rate (7). The pathogens of urinary tract infection are bacterial, but the main pathogenic bacteria have yet to be defined. Antimicrobial drugs are the front-line treatment for urinary tract infection. However, as many patients are prescribed broad-spectrum antibiotics, differing degrees of drug resistance have developed in the population, leading to a significant reduction in drug effectiveness. Therefore, it is necessary to actively analyze the distribution of pathogenic bacteria in patients with recurrent urinary tract infection and explore the sensitivity of pathogenic bacteria to commonly used antimicrobial drugs so as to develop more reliable treatments (8).

Existing tests for urinary tract infections: (I) Urinary routine is a very important basic examination in clinical practice, especially in the diagnosis of urinary tract infection, which has the advantages of simple operation, fast price and low price, and can be accepted by the majority of patients, and this diagnosis method has high diagnostic accuracy. Urine routine has a high frequency of application in clinical practice, which can effectively diagnose a variety of diseases. (II) Urography: Lead to urinary tract infection pathogens types varied, if it is n/med tuberculosis bacterium infection, then completes the urinary tract imaging examination is very important, and want to make the diagnosis on the basis of more powerful, so should also be ultrasound examination, the urinary system can discover whether urinary tract obstruction or whether any stones, better able to analyze the type of urinary tract infection. (III) CT: This examination can find the lesion of urinary tract infection very well. This examination method can better understand the whole process of the lesion in detail, which is of high value for the diagnosis of urinary tract infection.

There are many pathogenic types of recurrent urinary tract infection, including both Gram-negative and relatively low Gram-positive bacteria. Gram-negative bacteria consist of *Escherichia coli*, *Pseudomonas aeruginosa*, with each strain accounting for about 20% to 60% of the total Gram-negative bacteria. Urinary tract infection is an inflammatory condition caused by pathogens invading the urinary tract mucosa and nearby tissues (9). Generally, urinary tract infections are divided into upper urinary tract infections (pyelonephritis) and lower urinary tract infections (cystitis, urethritis), most of which occur in women. When diagnosing urinary tract infection, most practitioners will use a urine dipstick test. However, clinical evidence suggests that this method is not sufficient to complete the diagnosis. Therefore, this paper will explore the different tests used in the diagnosis of urinary tract infection (10).

Lesion changes in the endocrine, circulatory, urinary, and digestive systems are often reflected in the changes of urine biochemical indicators. Current urine analysis methods include visual measurement, physics, chemistry, microscopy, and automatic analysis using urine analyzer instruments. The detection of bacteria, leukocytes, and red blood cells in urinary tract infection can be assessed by sediment microscopy, automated urinalysis, bacterial culture, and routine urine dry chemical methods. The selection of an appropriate urine detection method can provide better evidence for the diagnosis of the disease. Different studies believe that the clinical diagnostic value of different urinary tract tests is different, but some studies have found that the sensitivity and specificity of different urinary tract tests are not different, and there are certain controversies. In this study, meta-analysis was used to compare the effectiveness of multiple urine analysis detection methods. We present the following article in accordance with the PRISMA-DTA reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-65/rc).

Methods

Search strategy

The PubMed, Embase, Cochrane Library, SpringerLink, Web of Science databases were searched from inception to December 2021. The search keywords were "Bacterial culture", "Urine sediment microscopy", "Urinalysis", "Urine routine dry chemistry", "Urography", "CT of urinary system" and "Infection", and free words respectively. In order to avoid bias caused by language limitations, this study searched English. In order to avoid missing relevant studies, relevant references listed in the article and conference abstracts found in the search were traced (*Figure 1*).

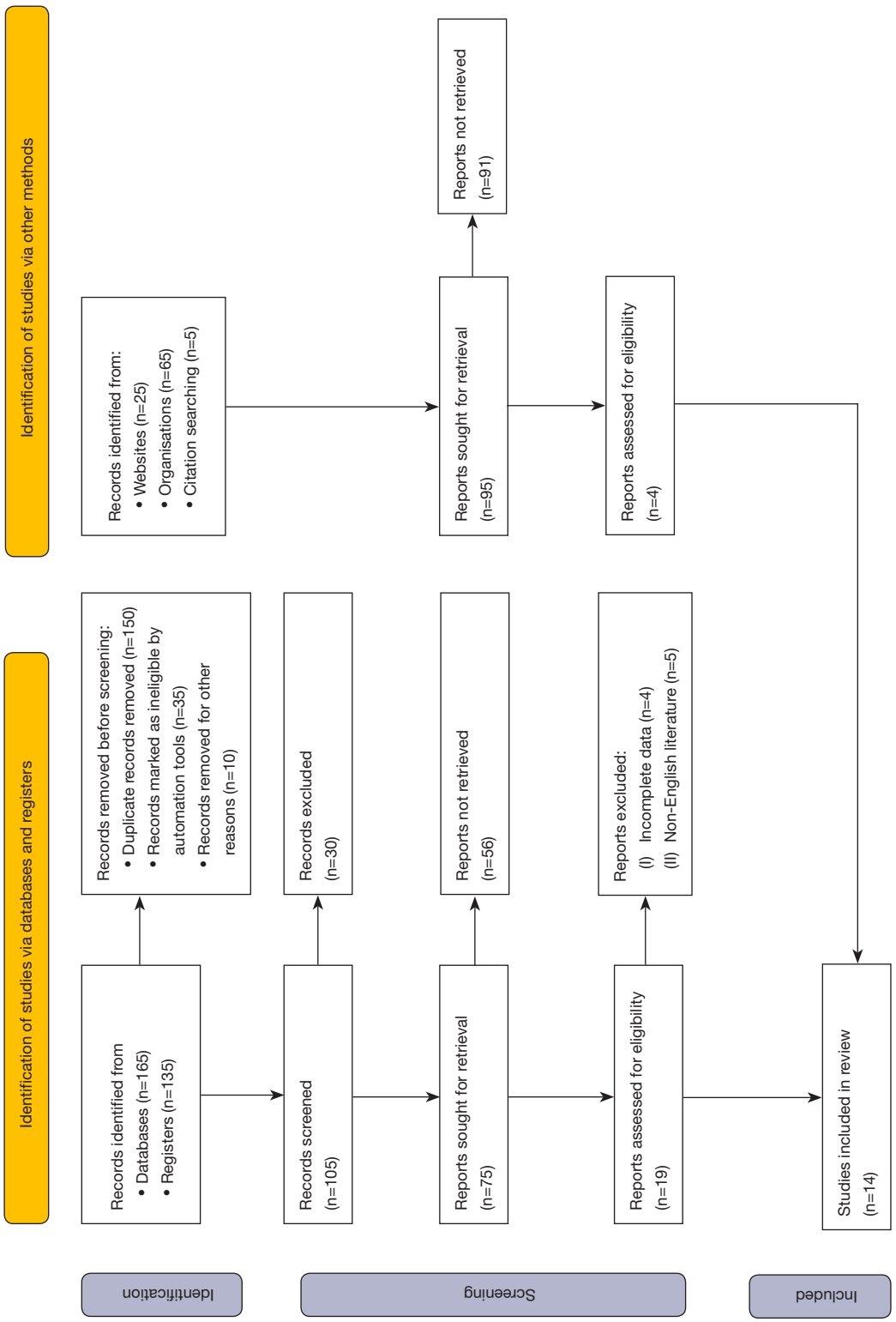

Figure 1 Flow chart of the literature screening.

Inclusion criteria

The inclusion criteria were as follows: (I) The study type was a diagnostic test. (II) The study subjects were bacterial culture, urine sediment microscopy, automated urinalysis, and urine routine dry chemistry used to detect bacteria, leukocytes, and red blood cells. (III) Full text was available and true positive (TP), false positive (FP), false negative (FN), and true negative (TN) values could be directly obtained or calculated from the diagnostic test data. (IV) Inclusion criteria for inclusion studies should be clarified using PICOS criteria.

Exclusion criteria

The exclusion criteria were as follows: (I) The research subjects and study type did not meet the inclusion criteria after reading the title and abstract. (II) The diagnostic test data could not be directly obtained or extracted from the document. (III) The document had incomplete data. (IV) Evaluation indicators were not related to this study.

Evaluation criteria for literature quality

Two reviewers used the Jadad rating scale to independently evaluate 14 studies, mainly to evaluate the randomized controlled experimental design of the included literature. The quality assessment of diagnostic accuracy studies (QUADAS) scale, was used to evaluate the quality of the literature. The QUADAS scale has 14 assessment indicators, and each indicator is evaluated as "yes", "no", or "uncertain". These indicators assess bias (indicators 3, 4, 5, 6, 7, 10, 11, 12, and 14), variation (indicators 1 and 2), and quality (indicators 8, 9, and 13). As the evaluation standard for diagnostic tests, items 3, 8, and 9 of the 14 criteria can be used as optional evaluation indexes. The 14 evaluation indexes are listed together in our study.

The QUADAS assessment of the 14 documents included in this meta-analysis showed that the test results, except the difficult interpretation of the disease spectrum and the reports of the 3 withdrawal cases, were not outstanding (*Figure 2*).

Analysis of data

Data extracted from the diagnostic tests included TP (gold standard and diagnostic test are positive), FP (diagnostic test is positive and gold standard is negative), FN (diagnostic test is negative and gold standard is positive), and TN (gold standard and diagnostic test are negative).

Bias analysis

Heterogeneity between studies was assessed using I^2 statistics, with 25%, 50%, and 75% representing low, medium, and high heterogeneity, respectively. If I^2 was <50% and P was >0.1, a fixed-effect model was used for meta-analysis. If I^2 was >50% and P was <0.1 and chi-squared analysis showed study heterogeneity, a random-effects model was used for meta-analysis, and the source of the heterogeneity was analyzed using a subgroup analysis. A sensitivity analysis was conducted, and each included study was removed one by one to see whether the pooled effect values were stable and reliable. As shown in the figure, the main part of the literature included in this study is within the scope of the triangle region, and there is no obvious literature publication bias (*Figure 3*).

Statistical analysis

Meta-DiSc were used to calculate the sensitivity (Sen), specificity (Spe), positive likelihood ratio (LR+), negative likelihood ratio (LR–), and diagnostic ratio (DOR) of the combined literature and the corresponding 95% CI. The Cochrane Collaboration Center provided Rewiew Manger 5.2 software [Cochrane Information Management System (IMS)] for statistical analysis, and the risk ratio of dichotic variables was adopted. RR and 95% CI were used as compare the diagnostic value of different tests analysis statistics in meta-analysis.

Results

Included studies

A total of 300 relevant documents were collected through the database search, and 195 documents were excluded by reading the title, abstract, full text, and quality evaluation independently. A total of 14 studies (11-24) were finally included (*Table 1*). In addition, there was no significant publication bias in the literature included in this study.

Urine leucocyte detection

A heterogeneity test of 4 randomized controlled trials (RCTs) found that the heterogeneity of the selected studies

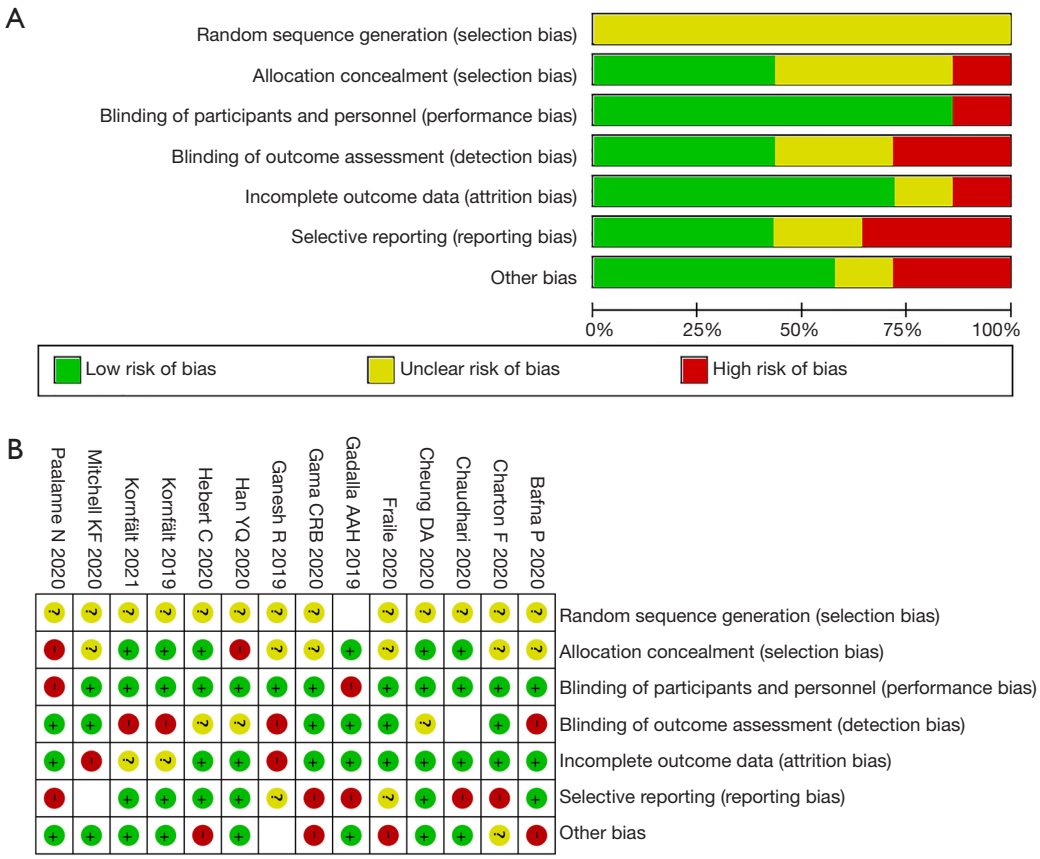

Figure 2 Literature quality evaluation chart. (A) Risk of bias graph; (B) risk of bias summary.

was small and a fixed-effect model could be used for meta-analysis. The results of the meta-analysis showed that there was a significant statistical difference between the urine sediment microscopy group and the urine normalization group in urine leucocyte detection (OR =2.15, 95% CI: 1.29–3.56, P=0.003, I^2=19%, Z=2.95; *Figure 4*).

Urine erythrocyte test

A heterogeneity test of 4 RCT studies found that the heterogeneity of the selected studies was small and a fixed-effect model could be used for meta-analysis. The results of the meta-analysis showed that there was a significant statistical difference between urine the sediment microscopy group and the urine normalization group in urine erythrocyte testing (OR =1.87, 95% CI: 1.13–3.09, P=0.01, I^2=0%, Z=2.45; *Figure 5*).

Quantitative determination of urinary protein composition

A heterogeneity test of 4 RCT studies included found that the heterogeneity of the selected studies was small and a fixed-effect model could be used for meta-analysis. The results of the meta-analysis showed that there was a significant statistical difference between the urine sediment microscopy group and the urine normalization group in quantitative determination of urinary protein composition (OR =2.32, 95% CI: 1.27–4.23, P=0.006, I^2=30%, Z=2.73; *Figure 6*).

Determination of urinary enzymes

A heterogeneity test of 4 RCT studies found that the heterogeneity of the selected studies was small and a fixed-effect model could be used for meta-analysis. The

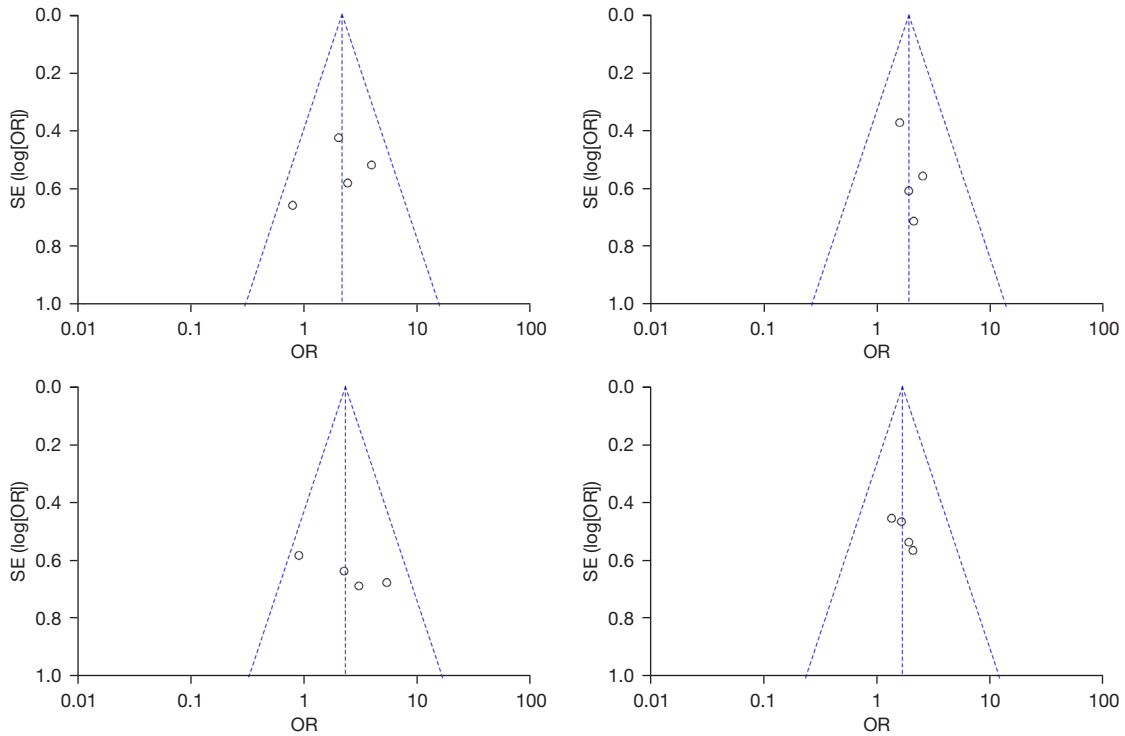

Figure 3 Funnel plot of literature publication bias.

results of the meta-analysis showed that there was a significant statistical difference between the urine sediment microscopy group and the urine normalization group in the determination of urinary enzymes (OR =1.67, 95% CI: 1.03–2.72, P=0.04, I^2=0%, Z=2.07; *Figure* 7).

Discussion

Meta-analysis of diagnostic trials is the most accurate source of evidence for clinical decision makers. RCT research still has many deficiencies. Although more and more meta-analyses of diagnostic trials are being published, this has not led to a unified evaluation standard for meta-analysis methodology (25).

Urinary tract infection is a common disease of the urinary system (26), with a higher incidence in females. This difference is attributed to female anatomy, as the female urethral opening is adjacent to the vaginal opening, and the urethra is short and wide. Common urinary tract infection bacteria include *Klebsiella*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Relevant studies have shown that urinary tract infections are mostly caused by a single bacterium. If patients with acute infection do not receive appropriate treatment, chronic infection will occur, leading to decreased quality of life or even renal failure (27). Currently, urine dipstick tests are the most commonly used clinical test in the diagnosis of patients with urinary tract infection, as they are cheap and simple to operate. However, as this test relies on the clinical experience of the doctor and confirmation by microscopy, it is not the most convenient means of diagnosis (28).

Urine culture can be tested separately, but this operation is complicated and easily contaminated by miscellaneous bacteria. In addition, urine culture testing has a high FP rate and it needs to be used for a long time (29-31). Urine dipstick tests and quantitative urine culture often have different results. One study showed that combining the results of these 2 tests can improve the authenticity and accuracy of the diagnosis (32). In the test data, the positive rate (43.7%) was higher than the negative rate (40.6%), and the Spe and Sen of the observation group were significantly higher than those of the control group, with a statistically significant difference (P<0.05) (33). Pinkerton *et al.* (34) also found that combining the 2 test methods led to a significantly better Spe, Sen, positive predictive value, and negative predictive value than those of the urine dipstick

Table 1 Basic clinical features of the 14 included studies

Study	Age	Gender (male)	Diagnostic criteria	Diagnostic methods	Experimental group (N)	Control group (N)	NOS score	Research type
Gadalla AAH 2019	33.71±12.2	41.25%	Urinary depression mirror examination	Urinary analyzer (UF100)	93	72	8	RCT
Mitchell KF 2020	45.65±13.4	69.12%	Urinary depression mirror examination	Urinary analyzer (UF101)	83	60	7	RCT
Ganesh R 2019	33.12±14.5	45.72%	Urinary depression mirror examination	Urinary analyzer (UF102)	115	105	8	RCT
Kornfält 2021	37.15±14.5	44.12%	Urinary depression mirror examination	Routine urine chemistry	63	57	8	RCT
Fraile 2020	22.85±8.4	51.89%	Urinary depression mirror examination	Urinary analyzer (UF102)	55	70	8	RCT
Hebert C 2020	44.36±10.2	63.45%	Urinary depression mirror examination	Routine urine chemistry	51	62	7	RCT
Han YQ 2020	32.62±12.2	78.10%	Urinary depression mirror examination	Routine urine chemistry	77	72	9	RCT
Charton F 2020	32.61±13.0	48.75%	Urinary depression mirror examination	Routine urine chemistry	76	60	9	RCT
Gama CRB 2020	27.25±14.5	59.23%	Urinary depression mirror examination	Routine urine chemistry	38	53	7	RCT
Paalanne N 2020	36.22±15.2	56.22%	Urinary depression mirror examination	Urinary analyzer (UF102)	61	68	8	RCT
Cheung DA 2020	41.35±8.1	53.16%	Germiculture	Urinary analyzer (UF102)	105	97	8	RCT
Bafna P 2020	37.25±16.0	66.34%	Germiculture	Routine urine chemistry	93	74	8	RCT
Chaudhari 2020	38.51±8.6	48.34%	Germiculture	Urinary analyzer (UF102)	60	75	9	RCT
Kornfält 2019	35.51±8.6	58.25%	Germiculture	Routine urine chemistry	29	28	9	RCT

NOS, Newcastle-Ottawa score; RCT, randomized controlled trial.

test method alone, thus effectively improving the accuracy and authenticity of diagnosis (35). Because quantitative urine culture takes a long time, a urine dipstick test can be performed first and then confirmed by quantitative urine culture. The combination of these 2 test methods can effectively improve the detection rate and reduce the FP rate.

Our study has some limitations. (I) Due to the small sample size of the studies included here, the conclusions of the meta-analysis may not be generalizable to the larger population. (II) Some outcomes were not eligible for extraction, which affected the number of indicators included. (III) Not do subgroup analysis. Heterogeneity may result from differences and diversity in the inclusion criteria of patients in the studies, interventions, and measures across a range of studies, or from variations in the inherent authenticity of those studies. Statistical heterogeneity is used specifically to describe the degree of variation in effect sizes across a series of studies and to indicate variability between studies except for foreseeable chance.

Our meta-analysis included 14 documents. The small number of documents in the subgroups was mainly due to the diverse testing technologies and instrument models

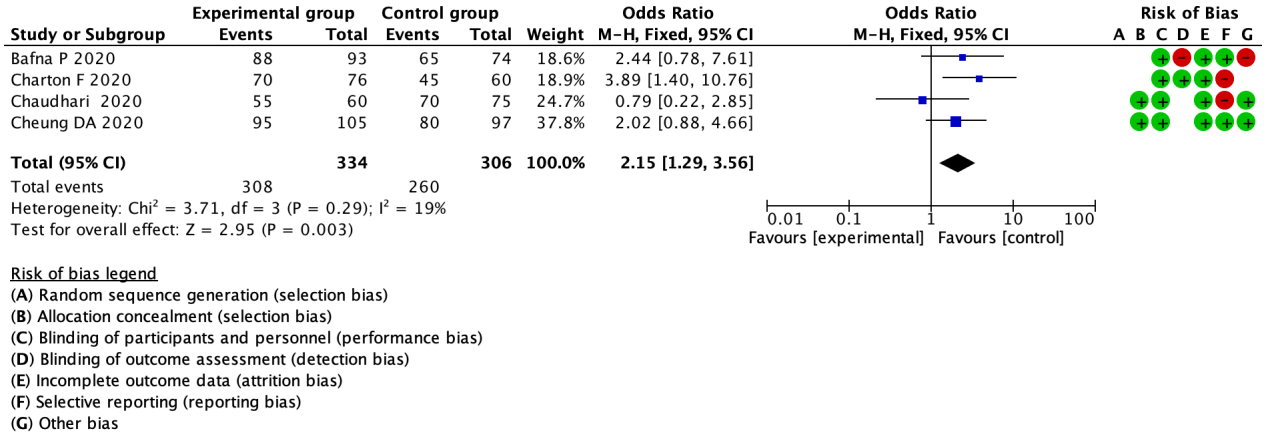

Figure 4 Meta-analysis of urine leucocyte detection between the 2 groups.

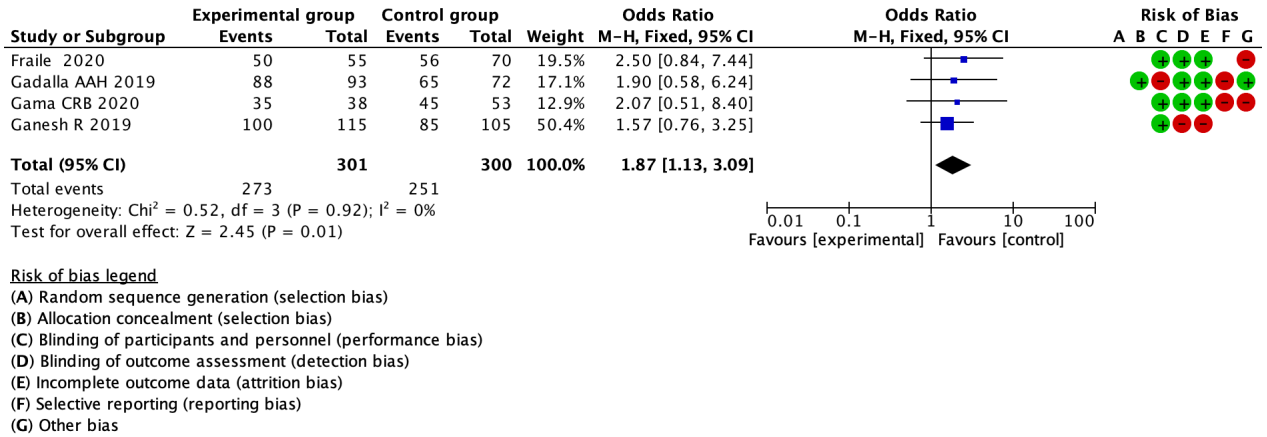

Figure 5 Meta-analysis of urine erythrocyte testing between the 2 groups.

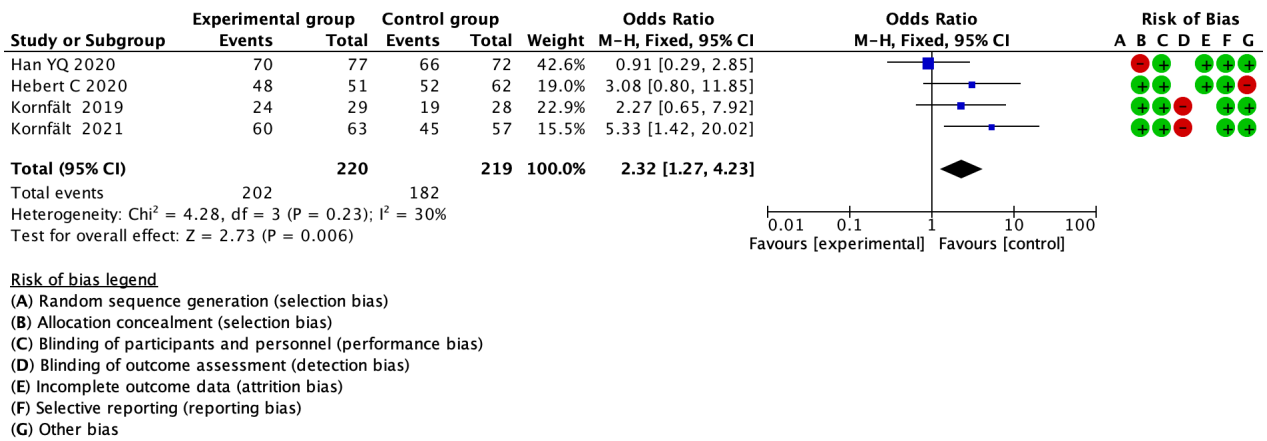

Figure 6 Meta-analysis of quantitative determination of urinary protein composition between the 2 groups.

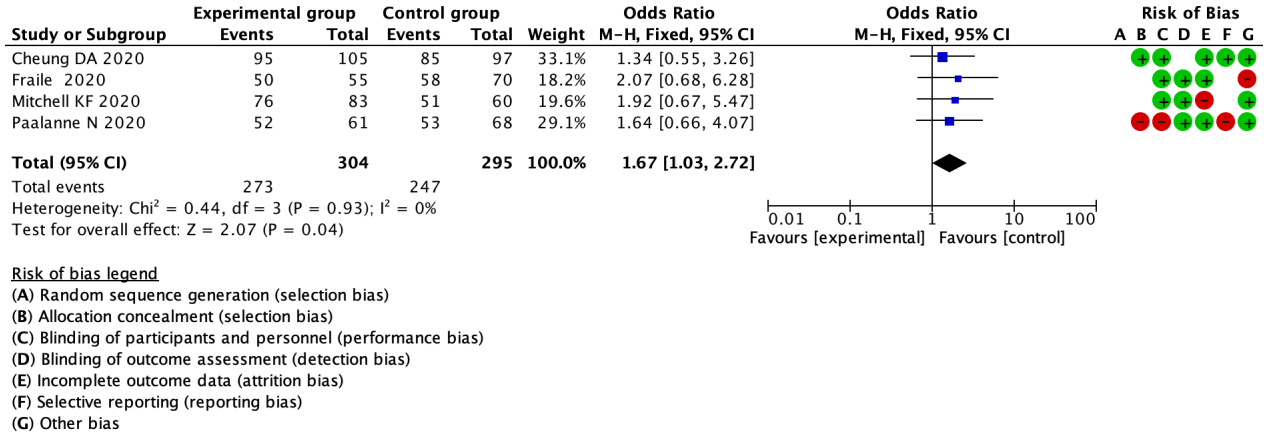

Figure 7 Meta-analysis of the determination of urinary enzymes between the 2 groups.

used in various hospitals and the rapid replacement of equipment, which had a certain impact on the homogeneity of screening and inclusion in the study. The results of this study showed that the automated urinalysis and urine dry chemistry methods have good accuracy. However, these methods need to be combined with urine sediment microscopy and urine culture to reach a conclusive diagnosis (36). Therefore, automated urinalysis, urine dry chemistry, and other detection methods can facilitate the early diagnosis, intervention, and treatment of urinary tract infections.

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Footnote

Reporting Checklist: The authors have completed the PRISMA-DTA reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-22-65/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-65/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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