

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus



Infections

Point-of-care Testing in Complicated Urinary Tract Infection: Evaluation of the Vivalytic One Urinary Tract Infection Analyser for Detecting Uropathogenic Bacteria and Antimicrobial Resistance in Urine Samples of Urological Patients in a Point-of-care Setting

Jessica Hartmann^{a,b,*}, Moritz Fritzenwanker^{a,c}, Can Imirzalioglu^{a,c}, Torsten Hain^{a,c}, Borros Michael Arneth^d, Florian Wagenlehner^{a,b}

^a German Center for Infection Research (DZIF), Partner Site Giessen-Marburg-Langen, Giessen, Germany; ^b Clinic for Urology, Pediatric Urology and Andrology, Justus Liebig University Giessen, Giessen, Germany; ^c Institute of Medical Microbiology, Justus Liebig University Giessen, Giessen, Germany; ^d Institute for Laboratory Medicine and Pathobiochemistry, Justus Liebig University Giessen, Giessen, Germany

Article info

Article history:

Accepted September 25, 2024

Associate Editor: Christian Gratzke

Keywords:

Vivalytic
Urinary tract infection
point-of-care testing

Abstract

Background and objective: Urinary tract infections (UTIs) are some of the most encountered infections in clinical practice, exhibiting increasing antimicrobial resistance. Bacterial species identification and antimicrobial resistance testing at point of care (POCT) could improve adequate initial antibiotic therapy and antimicrobial stewardship. In this work, the Vivalytic UTI test, which represents a qualitative PCR-based microarray test, able to detect specific uropathogenic bacteria and associated antimicrobial resistance genes was evaluated at POCT.

Methods: In September 2023, we used this point-of-care testing (POCT) to analyse 126 consecutive urine samples of patients with complicated UTI. Samples processed with the Vivalytic UTI POCT were preselected for the presence of bacteriuria by screening with urine flow cytometry (cut-off ≥ 70 bacteria per microlitre). We performed the POCT before and after sample transport, and compared the results to standard urine culture and antibiotic sensitivity tests according to the European Committee on Antimicrobial Susceptibility Testing.

Key findings and limitations: Nineteen different bacterial species were detected. Sixteen species reached a diagnostic accuracy of $\geq 90.27\%$ with negative predictive values of $\geq 93.67\%$. The POCT was able to detect bacterial species under the estimated concentration of 10^4 – 5×10^4 CFU/ml. The concordant (Vivalytic vs. culture) antimicrobial resistance gene detection rate reached a higher accuracy after transport ($\geq 84.15\%$) compared to POC-testing before transport ($\geq 81.71\%$), except for Vancomycin. *Aerococcus urinae*, *Enterococcus hirae*, *Hafnia alvei*, and *Staphylococcus lugdunensis* are not part of the POCT test panel; these were detected by urine culture only in 19% of cases.

* Corresponding author. Clinic for Urology, Pediatric Urology and Andrology, Justus-Liebig University Giessen, Giessen, Germany. Tel. +49 17622953401.
E-mail address: jessi_hartmann@yahoo.de (J. Hartmann).

<https://doi.org/10.1016/j.euf.2024.09.018>

2405-4569/© 2024 European Association of Urology. Published by Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Please cite this article as: J. Hartmann, M. Fritzenwanker, C. Imirzalioglu et al., Point-of-care Testing in Complicated Urinary Tract Infection: Evaluation of the Vivalytic One Urinary Tract Infection Analyser for Detecting Uropathogenic Bacteria and Antimicrobial Resistance in Urine Samples of Urological Patients in a Point-of-care Setting, Eur Urol Focus (2024), <https://doi.org/10.1016/j.euf.2024.09.018>

Conclusions and clinical implications: The Vivalytic UTI POCT displayed high sensitivity and specificity in identifying uropathogenic bacteria and antibiotic resistance markers to be further evaluated in clinical practice. However, it would be helpful to expand the resistance to include information about more commonly used antibiotics like aminopenicillins, cephalosporines and fluoroquinolones.

Patient summary: In this study, we tested 126 consecutive urine samples of urological patients with complicated urinary tract infections (UTIs) by using the Vivalytic UTI point-of-care testing before and after sample transport. We found out that the sample transport to some extent influences the pathogen and resistance detection rate of the Vivalytic UTI assay. Compared to standard-of-care diagnostics, pathogen identification was more accurate before sample transport, while the concordant antimicrobial resistance gene detection rate reached higher accuracy after transport.

© 2024 European Association of Urology. Published by Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

1. Introduction

Urinary tract infection (UTI) is a common disease in urological everyday health care [1] constituting one of the main reasons for hospitalization [2], exhibiting increasing antimicrobial resistance [3]. The clinical phenotypes of UTI are heterogeneous and range from rather benign, uncomplicated infections to complicated UTIs (cUTIs), pyelonephritis and severe urosepsis [4].

Accurate diagnosis and evidence-based treatment of UTIs will lead to better clinical care for many patients and limit unnecessary antibiotic use [5].

UTIs are caused by both Gram-negative and Gram-positive bacteria, as well as by certain fungi [6]. For complicated UTIs (cUTIs), the order of prevalence for causative agents, following *Escherichia coli* as most common is *Enterococcus* spp., *Klebsiella pneumoniae*, *Candida* spp., *Staphylococcus aureus*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* [7].

The prognosis of cUTIs is good if diagnosis and appropriate treatment are given promptly [8]. Suspected UTIs are usually diagnosed according to associated clinical symptoms, (eg. dysuria, urgency, frequency, flank pain, costovertebral angle tenderness, suprapubic pain, and fever) [9], as well as the standard-of-care diagnostic tests such as positive urine culture tests [10], where bacterial colony counts vary from 10^2 to 10^5 CFU/mL and results are available after app. 48 h [11].

Microbiologists need to interpret the microbiological relevance of growth on culture plates to determine whether further identification and antimicrobial susceptibility testing are necessary [12]. This approach is time consuming and requires a considerable workload [13].

Recommended standard-of-care-diagnostics for UTIs include urine analysis (UFC), urine dipstick test and standard urine culture for cUTIs [14].

Flow cytometry has been shown to be an accurate and rapid method to determine significant bacteriuria in urological patients and is superior to dipstick analysis. It does however lack pathogen identification and antimicrobial resistance testing.

Rapid diagnostics, such as the Urine dipstick test, that diagnose UTIs based on results for nitrite, leucocytes, and

erythrocytes [3] suffer from low test sensitivity and specificity [15], leading to many false-positive and false-negative results [16].

Given the increasing prevalence of UTIs and associated antimicrobial resistance, a high level of diagnostic accuracy for a new diagnostic test is essential [17]. An ideal test should be fast, easy to use, and highly accurate.

In this study, we tested the Vivalytic UTI point-of-care testing (POCT), and evaluated its diagnostic accuracy in clinical practice by comparing the results to standard urine culture and antibiotic sensitivity tests according to the European Committee on Antimicrobial Susceptibility Testing [18].

This POCT allows qualitative test results by detecting uropathogenic bacteria and associated antibiotic-resistance genes in native urine samples (Fig. 1). The test can be performed directly with the native urine at the point of care, without the need for further urine preparation and without the need to send the urine to a laboratory.

This study aims to answer the questions:

- (1) What is the diagnostic accuracy of the Vivalytic UTI POCT assay compared to standard-of-care diagnostics?
- (2) Does sample transport influence the pathogen and resistance detection rate of this POCT assay?

1.1. Is the Vivalytic UTI POCT the test of tomorrow?

1.1.1. Vivalytic UTI POCT

The Vivalytic system, currently under development, is designed as an all-in-one solution for molecular diagnostics and integrates as an automated polymerase chain reaction test, able to detect nucleic acids of selected uropathogenic species with a concentration of above 10^4 – 5×10^4 CFU/ml.

1.1.2. Test equipment

In this study, we used the *Vivalytic One Analyser* with the UTI cartridge, both manufactured by Bosch Healthcare Solutions GmbH. Additional equipment included a pipettor (100–1000 μ l) and sterile filter pipette tips (100–1000 μ l).

Gram-negative uropathogenic bacteria	Gram-positive uropathogenic bacteria	Antimicrobial resistance genes
<i>Acinetobacter baumannii</i> <i>Enterobacter cloacae</i> <i>Escherichia coli</i> <i>Citrobacter freundii</i> <i>Citrobacter koseri</i> <i>Morganella morganii</i> <i>Klebsiella aerogenes</i> <i>Klebsiella oxytoca</i> <i>Klebsiella pneumoniae</i> <i>Proteus spp.</i> <i>Providencia rettgeri</i> <i>Providencia stuartii</i> <i>Pseudomonas aeruginosa</i> <i>Serratia marcescens</i>	<i>Enterococcus faecalis</i> <i>Enterococcus faecium</i> <i>Staphylococcus aureus</i> <i>Staphylococcus epidermidis</i> <i>Staphylococcus saprophyticus</i> <i>Streptococcus agalactiae</i>	Trimethoprim resistance dfrA1 dfrA5 dfrA12 dfrA17 Methicillin resistance mecA Vancomycin resistance vanA vanB
	Fungal	
	<i>Candida albicans</i>	

Fig. 1 – The Vivalytic UTI POCT is able to detect 21 specific uropathogenic bacteria and seven associated antimicrobial resistance genes. POCT = point-of-care testing; UTI = urinary tract infection.

1.1.3. Vivalytic system

The Vivalytic system consists of two main components, the Vivalytic analyser and the UTI cartridge. The Vivalytic analyser, as shown in Fig. 2, is an all-in-one stand-alone device consisting of a touch-sensitive display as a graphical user interface, a cartridge slot for inserting the cartridge, and a scanning module for sample and cartridge identification via quick response codes or bar codes. The UTI cartridge consists of a network of microfluidic channels and chambers for sample preparation, chambers for reagent prestorage, and a reservoir for sample input. After sample measurement and evaluation, the cartridge is removed from the system and discarded.

1.1.4. Four steps from urine sampling to test results

First, the cartridge code needs to be scanned, followed by the scanning or manual entering of the sample code. Next,

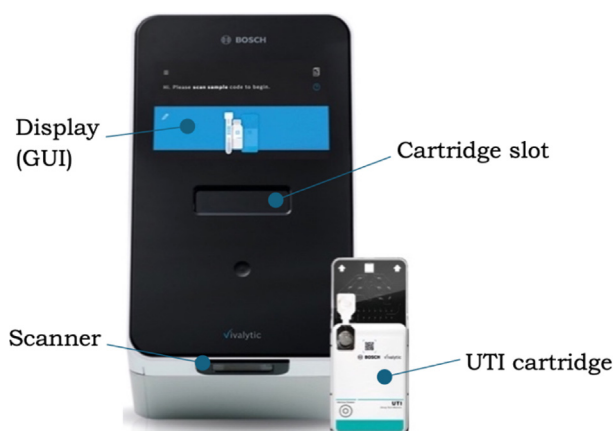


Fig. 2 – The Vivalytic analyser with the cartridge for urinary tract infections. Reprinted with permission of Bosch Healthcare Solutions GmbH. GUI = graphical user interface; UTI = urinary tract infection.

300 µl of native urine needs to be filled into the cartridge and finally inserted into the Vivalytic analyser (cartridge slot) to start the test.

The cartridge contains all the reagents required for processing the sample. The processing includes cell lysis, nucleic acid extraction, DNA amplification, hybridisation reaction, and detection. After an automatic processing of the urine sample, the test result is shown on the screen of the Vivalytic analyser in about 2.5 h (146 min).

2. Patients and method

2.1. Ethical approval

Ethical approval of the study AZ 158/20 was obtained.

2.2. Study design

In September 2023, during a period of 4 weeks, we used the Vivalytic UTI test system to analyse 126 consecutive urine samples of urological patients who presented with cUTIs at the Department of Urology, Pediatric Urology, and Andrology of the Justus-Liebig University of Giessen in Germany (Fig. 3). The clinical trial did not imply any change in the normal diagnostic and therapeutic procedures.

In Fig. 3, we illustrate the study design and the average time from urine sampling to the test results.

The POCT was performed at the urological laboratory before urine sample transport (test results after a mean time of 3.8 h after urine collection) and at the microbiology department, after sample transport (test results after a mean time of 11.06 h after urine collection).

2.3. Hospital laboratory tests

After urine collection at the urological department, every urine sample was sent in parallel (= routinely) in two different urine fractions to the (1) clinical laboratory for a urine

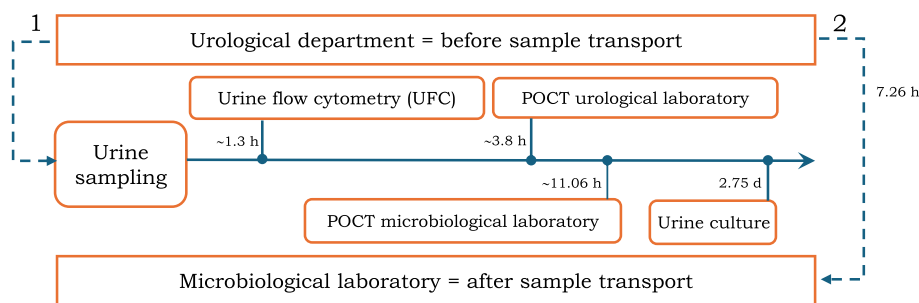


Fig. 3 – Illustration of the study design and the average of time from urine sampling to the test results. POCT = point-of-care testing.

dipstick analysis (UC-3500; Sysmex, Kobe, Japan) and flow cytometry (UF-1000i; Sysmex), and (2) microbiology department for urine culture and antibiotic sensitivity testing.

2.4. Urine collection

Urine samples were provided by patients themselves following self-sampling of midstream clean-catch urine specimens or collected by medical staff in patients with a urinary catheter. Urine samples included 111 (88.1%) midstream urine and 15 (11.9%) catheter specimens. After collection, samples were kept refrigerated and stored at 4°C until the clinical laboratory results were available.

2.5. Preselection of the urine samples

Samples were preselected for the presence of bacteriuria by screening with urine flow cytometry (cut-off for inclusion UFC ≥ 70 bacteria/ μl). This cut off was determined previously for our institution as described here [19].

In this work, the panel range for UFC was as followed: In 8 samples (6.3%) $\leq 10^2$ bacteria/ μl , in 51 samples (40.5%) between 10^2 and 10^3 bacteria/ μl , in 35 samples (27.8%) between 10^3 and 10^4 bacteria/ μl and in 32 of the tested samples (25.4%) $> 10^4$ bacteria/ μl .

2.6. Patients' characteristics

A total of 126 consecutive urological patients were included in this study (51 female (40.48%) and 75 male (59.52%) patients, mean age of 62.9 yr). The patients' medical history has shown asymptomatic bacteriuria 70 (55.6%) tested before urological intervention, lower cUTI 48 (38%), pyelonephritis 7 (65%), and urosepsis 1 (1%).

24 (19%) of the patients had previous antibiotic treatment before urine sampling.

2.7. Standard urine culture and AST

The urine sample transport from the urological clinic to the microbiology department took a mean time of 7.26 h. The urine culture test provides quantitative and qualitative test results in about 2.75 d. According to the urine analysis measured at the microbiological laboratory, after urine transport, the selected urine samples tested positive in 91.27% for leucocytes, 29.37% for nitrite, and 15.08% for bacterial

growth inhibitors. The panel range (bacterial load) of urine culture was between $\leq 10^3$ and 10^7 CFU/ml.

3. Results

3.1. Species detection

In this study, nineteen different species were detected. Sixteen bacterial species reached a diagnostic accuracy of $\geq 90.27\%$ with negative predictive values of $\geq 93.67\%$.

Compared to standard urine culture tests, the Vivalytic UTI POCT test is qualitative but not quantitative.

The Vivalytic POCT test can detect bacterial species under the estimated concentration of 10^4 – 5×10^4 CFU/ml (Figure 4). However, for 28 pathogens (Table 1.1, at POCT before and after transport) false negative results for pathogen detection was the case in species with a concentration $\leq 10^4$.

The most frequently found uropathogenic bacteria for cUTIs were *Escherichia coli*, *Enterococcus faecalis*, *Proteus spp.*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* (Table 1).

As described in Table 1, the species detection rate differs slightly between the test done before and after sample transport. Related to the most found species, *E. coli* and *P. aeruginosa* species detection rates decreased after transport, while *E. faecalis*, *Proteus spp.*, and *K. pneumoniae* species detection rates increased after transport at the POCT. Compared with the standard urine culture test, we observed a higher degree of concordant pathogen identification before transport ($p = 0.0336$).

Klebsiella aerogenes and *Providencia stuartii* were not detected, either by POCT or by urine culture. *Staphylococcus saprophyticus* and *Citrobacter koseri* were detected by POCT before transport only.

3.2. Positive test results

A test was considered positive when one or more uropathogenic bacteria and/or antimicrobial resistance genes were found. Positive test results were obtained in 80.95% ($n = 102$) of the urine samples before transport and in 78.56% ($n = 99$) of the samples at the POCT after specimen transport. The standard urine culture detected 69.84% ($n = 88$) of the selected urine samples as positive.

As described in Table 2, the method and the transport of the urine samples had an influence on the number of bacterial species and antimicrobial resistance genes detected per urine sample.

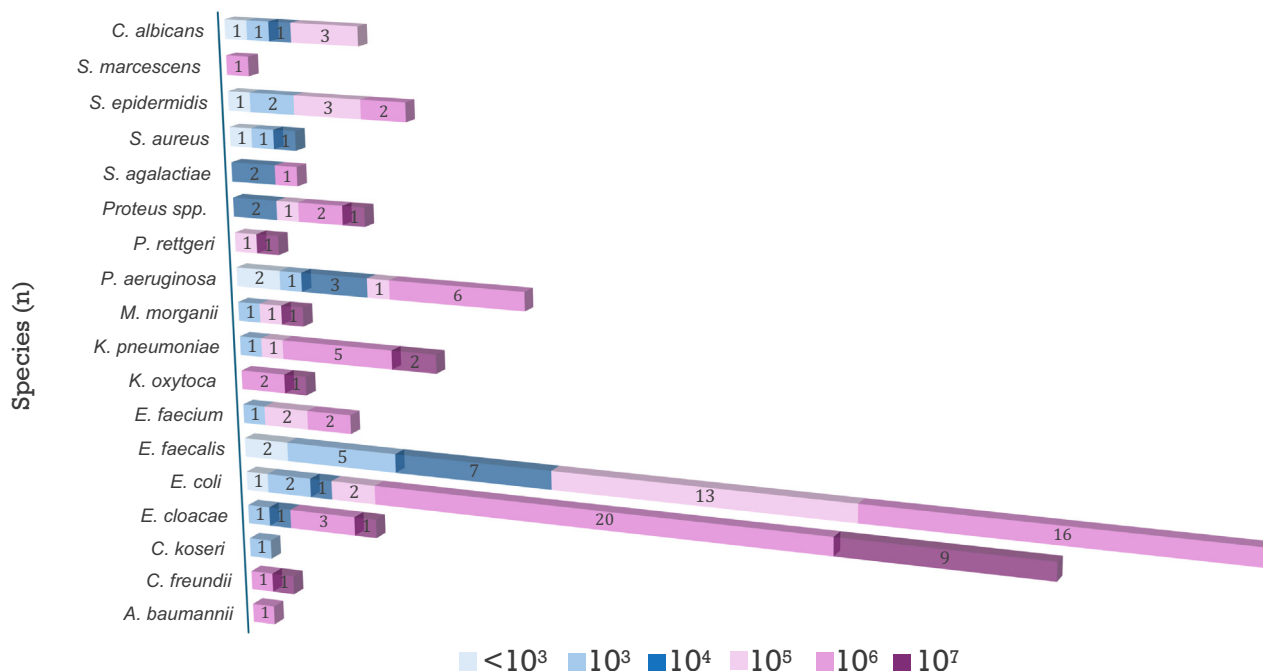


Fig. 4 – Valytic true positive species detection with specified bacterial load (standard culture). How is the distribution of the bacterial load at standard culture, how often did the culture showed bacterial load $\leq 10^4$ and how many times $>10^5$?

Table 1 – n-uropathogenic bacteria & antibiotic resistance genes detected by POCT before and after sample; SE-Sensitivity, SP-Specificity, ACC-Accuracy in %. How is the diagnostic accuracy for the most common found species and antibiotic resistance gene detection before vs. after transport?

Comparison of POCT to standard urine culture and antibiotic sensitivity test before transport					Comparison of POCT to standard urine culture and antibiotic sensitivity test after transport				
POCT-detected uropathogens before transport	n	SE (%)	SP (%)	ACC	POCT-detected uropathogens after transport	n	SE (%)	SP (%)	ACC
<i>Acinetobacter baumannii</i>	2	100.00	99.15	99.15	<i>Acinetobacter baumannii</i>	2	100.00	99.11	99.12
<i>Citrobacter freundii</i>	3	100.00	99.14	99.15	<i>Citrobacter freundii</i>	3	100.00	99.10	99.12
<i>Citrobacter koseri</i>	1	0.00	99.15	98.13	<i>Citrobacter koseri</i>	0	0.00	100.00	99.12
<i>Enterobacter cloacae</i>	10	100.00	97.30	97.46	<i>Enterobacter cloacae</i>	7	83.33	98.13	97.35
<i>Escherichia coli</i>	39	94.29	92.77	93.22	<i>Escherichia coli</i>	36	90.62	91.36	91.15
<i>Enterococcus faecalis</i>	39	87.18	93.67	91.35	<i>Enterococcus faecalis</i>	41	88.10	94.37	92.04
<i>Enterococcus faecium</i>	7	80.00	97.35	96.61	<i>Enterococcus faecium</i>	7	100.00	98.15	98.23
<i>Klebsiella aerogenes</i>	0	–	100.00	–	<i>Klebsiella aerogenes</i>	0	–	100.00	–
<i>Klebsiella oxytoca</i>	3	66.67	99.13	98.31	<i>Klebsiella oxytoca</i>	1	50.00	100.00	99.12
<i>Klebsiella pneumoniae</i>	11	90.00	98.15	97.46	<i>Klebsiella pneumoniae</i>	18	88.89	90.38	90.27
<i>Morganella morgani</i>	3	33.33	98.26	96.61	<i>Morganella morgani</i>	3	66.67	99.09	98.23
<i>Pseudomonas aeruginosa</i>	12	90.91	98.13	97.46	<i>Pseudomonas aeruginosa</i>	9	72.73	99.02	96.46
<i>Providencia rettgeri</i>	4	100.00	98.28	98.31	<i>Providencia rettgeri</i>	2	100.00	99.11	99.12
<i>Providencia stuartii</i>	0	–	100.00	–	<i>Providencia stuartii</i>	0	–	100.00	–
<i>Proteus spp.</i>	12	100.00	96.36	96.61	<i>Proteus spp.</i>	13	100.00	94.83	95.12
<i>Streptococcus agalactiae</i>	6	100.00	97.39	97.47	<i>Streptococcus agalactiae</i>	1	50.00	100.00	99.12
<i>Staphylococcus aureus</i>	4	0.00	96.55	94.92	<i>Staphylococcus aureus</i>	3	0.00	97.30	95.58
<i>Staphylococcus epidermidis</i>	26	62.50	80.91	79.66	<i>Staphylococcus epidermidis</i>	23	62.50	83.81	82.30
<i>Serratia marcescens</i>	17	0.00	85.59	–	<i>Serratia marcescens</i>	11	100.00	91.89	92.04
<i>Staphylococcus saprophyticus</i>	1	–	99.15	–	<i>Staphylococcus saprophyticus</i>	0	–	100.00	–
<i>Candida albicans</i>	5	50.00	98.17	96.46	<i>Candida albicans</i>	4	80.00	99.12	98.31
Antibiotic susceptibility testing					Antibiotic susceptibility testing				
Trimethoprim	19	62.50	93.1	84.15	Trimethoprim	18	68.18	95.00	87.80
Methicillin	15	50.00	83.33	81.71	Methicillin	16	100.00	83.54	84.15
Vancomycin	1	–	98.78	–	Vancomycin	1	–	98.78	–

ACC = accuracy in %; POCT = point-of-care testing; SE = sensitivity; SP = specificity.

3.3. Antibiotic susceptibility testing

Compared to standard antibiotic sensitivity tests, the antimicrobial resistance gene detection was between 81.71% and 87.80% accurate, and reached a higher accu-

racy for Trimethoprim (87.80%) and Methicillin (84.15%) after sample transport, compared to POC-testing before transport for Trimethoprim (84.15%) and Methicillin (81.71%), except for Vancomycin resistance.

Table 1.1 – Vivalytic false negative pathogen detection, compared to standard urine culture bacterial load. How many times did the Vivalytic system “miss” bacterial species, and when it did, how few or how many of these species were present in these samples?

Vivalytic test at POCT	Vivalytic test at the urological laboratory						Vivalytic test after transport into the microbiology laboratory					
	Amount of these samples with that species in urine, with the specified bacterial load						Amount of these samples with that species in urine, with the specified bacterial load					
Vivalytic false negative for species:	<10 ³	10 ³	10 ⁴	10 ⁵	10 ⁶	10 ⁷	<10 ³	10 ³	10 ⁴	10 ⁵	10 ⁶	10 ⁷
<i>E. coli</i>				1	1	1				2		2
<i>E. faecium</i>				1		1						
<i>E. faecalis</i>	1	1	2	2			1	1	1			
<i>P. aeruginosa</i>	1						1				1	
<i>S. epidermidis</i>		1	1	1				1	1	1		
<i>S. aureus</i>		1						1	1			
<i>M. organii</i>		1						1	1			
<i>A. baumannii</i>						1						
<i>S. marcescens</i>												
<i>E. cloacae</i>								1				
<i>S. agalactiae</i>									1			
<i>C. koseri</i>		1						1				
<i>K. pneumoniae</i>		1			1		1	1				
<i>C. striatum</i>					1						1	
<i>C. albicans</i>		1			1			1		1		
Total	2	7	3	5	4	3	3	8	5	4	2	2

In three urine samples (2.38%), POCT was positive for antibiotic resistance detection but negative for Uropathogen detection.

In Table 3, we illustrate the resistance gene detection with associated species in the standard urine culture. Trimethoprim and Methicillin were positive in both POCT and urine culture (true positive) versus negative in POCT but positive in urine culture (false negative).

For the resistance gene detection, in the case of Trimethoprim false positives were 4 and true negatives

were 33. For Methicillin false positives were 5, true negatives 6. For Vancomycin false positive was 1, true negative was 53.

3.4. Negative test results

A test is considered negative if no species and/or antimicrobial resistance genes are detected. Negative test results were obtained at the POCT in 15.87% of urine samples before transport and in 12.69% after the sample transport.

Table 2 – Positive urine samples detected by the POCT before and after sample transport and compared with standard urine culture test results

Method	One species	Two species	Three species	Four species	Five or more species
POCT before transport	39 (30.95)	33 (26.19)	13 (10.32)	11 (8.73)	3 (2.38)
POCT after transport	43 (34.13)	30 (23.81)	15 (11.90)	6 (4.76)	2 (1.58)
Standard urine culture	35 (27.78)	37 (29.37)	12 (9.52)	3 (2.38)	1 (0.79)

POCT = point-of-care testing.

Table 3 – Vivalytic true positive and false negative for antibiotic resistance genes detection. How many times did the Vivalytic system identified correctly/ wrong the detection of antibiotic resistance genes compared to standard urine culture results?^a

Resistance	True positive	n	False negative	n
Trimethoprim	<i>E. coli</i>	13	<i>E. coli</i>	2
	<i>K. pneumoniae</i>	4	<i>Proteus</i> spp.	1
	<i>Proteus</i> spp.	3	<i>M. organii</i>	1
	<i>S. epidermidis</i>	1	<i>E. cloacae</i>	1
	<i>E. cloacae</i>	2		
Methicillin	Total	23	Total	5
	<i>S. epidermidis</i>	1	<i>S. haemolyticus</i>	1
	<i>S. hominis</i>	1		
	<i>S. haemolyticus</i>	3		
	Total	5	Total	1

POCT = point-of-care testing.

^a *S. hominis* and *S. haemolyticus* are not part of the POCT test panel.

In the standard urine culture tests, 28.57% of the urine samples were tested as negative.

3.5. Invalid or failed test results

An invalid or failed test made retesting necessary. This was the case in 9.5% before transport and 11.1% after transport. The test was still invalid, even after retesting in 3.17% before transport and in 1.59% after transport. Possible reasons for an invalid test run might be poor sample quality due to partial or complete absence of human cellular material in the sample.

4. Discussion

The use of POCTs for the diagnosis of UTIs and as treatment-guiding rapid test, can have an important impact in routine clinical practice, but for inpatients, as well as outpatients. Bacterial species identification and antimicrobial resistance testing at point of care (POCT) could improve adequate initial antibiotic therapy and antimicrobial stewardship.

In our clinic, the standard-of-care-diagnostics for UTIs include urine analysis (UFC), urine dipstick test, and urine culture tests for cUTIs [14].

The urine culture test provided quantitative and qualitative test results in an average of 2.75 d. For a urine culture test to be done, the urine samples are transported from the clinic to the microbiological laboratory. Furthermore, the evaluation of the urine culture and AST needs a laboratory and specialised technicians. For optimal urine specimen transport, the urine samples should be transported from the urological department to the microbiological department in <4 h after urine sampling [9].

A transport time of >4 h can influence the species identification within the urine samples due to contamination and inappropriate storage. In 47 (37.3%) urine samples, the transport time was <4 h, whereas in 79 (62.69%) samples, the transport time was ≥ 4 h. In this study, the average time of urine transport was 7.26 h, while urine stored at 4°C. Several studies have demonstrated the adverse effect of delays in transportation or processing of urine specimens on their quality [20,21].

Compared to the standard urine culture tests, dipstick test suffers from low specificity and a urine urinalysis is helpful primarily as a means of excluding bacteriuria [12].

The Vivalytic UTI POCT, is a new diagnostic device and has been developed to provide fast and accurate test results, by detecting specific uropathogenic bacteria and antibiotic resistance markers in native urine samples. Compared to standard-of-care diagnostics, this POCT can be performed directly with native urine guiding the physician to choose the best adequate antibiotic treatment. As described above, standard-of-care diagnostics like urine culture and AST provided results in a mean time of 2.75 d, necessitating the start of an empirical antibiotic treatment before available test results. This might result in inadequate treatment and the development of antibiotic resistance. By reducing the timeframe from 2.75 d to 3.8 h, the use of such a POCT in routine clinical practice, would allow clinicians to promptly treat patients without the need of empiric antibiotic therapy.

4.1. Limitations

According to our results, limitations regarding the pathogen detection rate are that negative test results do not exclude the presence of specific UTI-causing pathogens. This can be the case in urine samples in which pathogens are present at levels below the detection limit of 10^4 – 5×10^4 CFU/ml. *Aerococcus urinae*, *Enterococcus hirae*, *Hafnia alvei*, and *Staphylococcus lugdunensis*, which are known as uropathogens, are not part of the POCT test panel and were solely detected by urine culture in 19% of the cases. Compared to standard urine culture tests, the Vivalytic UTI POCT is a qualitative but not quantitative test. In relation to antibiotic resistance gene detection, in 56.35% of the tested urine samples, antimicrobial resistances that are not covered by the Vivalytic UTI test panel were detected in urine culture.

5. Conclusion

In this study, we tested 126 consecutive urine samples of urological patients with cUTIs by using the Vivalytic UTI POCT.

Given the combination of the high prevalence of UTIs and increasing antimicrobial resistance, there has been growing interest in developing new and efficient technology, which can rapidly and accurately diagnose UTIs and inform the clinician on which antibiotic to prescribe for maximum therapeutic benefit.

Compared to standard-of-care diagnostics, this POCT displayed high sensitivity and specificity in identifying uropathogenic bacteria and antibiotic resistance markers even under the assumed concentration of 10^4 – 5×10^4 CFU/ml. According to our results, the transport of the urine samples influenced the pathogen detection rate and antibiotic susceptibility testing of the Vivalytic UTI Analyser. In clinical practice, the addition of UTI POCT to standard-of-care diagnostics, provided rapid and sufficiently accurate test results for the treating physician, however, it would be helpful to expand the resistance panel to include information about more commonly used antibiotics like aminopenicillins, cephalosporines and fluoroquinolones.

Author contributions: Jessica Hartmann had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Imirzalioglu, Wagenlehner.

Acquisition of data: Hartmann, Fritzenwanker, Arneth.

Analysis and interpretation of data: Hartmann.

Drafting of the manuscript: Hartmann.

Critical revision of the manuscript for important intellectual content: Fritzenwanker, Imirzalioglu, Hain, Wagenlehner.

Statistical analysis: Hartmann.

Obtaining funding: None.

Administrative, technical, or material support: Imirzalioglu, Hain, Wagenlehner.

Supervision: Wagenlehner.

Financial disclosures: Jessica Hartmann certifies that all conflicts of interest, including specific financial interests and relationships and affiliations

relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

References

- [1] Manseck AS et al. Geriatric patients and symptomatic urinary tract infections: analysis of bacterial range and resistance rates at a 3rd level of care hospital in Germany. *Urol Int* 2022;106(3):298–303.
- [2] Penaranda GE et al. Urinary tract infections in hospitalized patients. *Rev Fac Cien Med Univ Nac Cordoba* 2020;77(4):265–71.
- [3] Schot MJ et al. Analytical performance, agreement and user-friendliness of six point-of-care testing urine analysers for urinary tract infection in general practice. *BMJ Open* 2015;5(5):e006857.
- [4] Wagenlehner FME et al. Epidemiology, definition and treatment of complicated urinary tract infections. *Nat Rev Urol* 2020;17(10):586–600.
- [5] Al Lawati H, Blair BM, Larnard J. Urinary tract infections: core curriculum 2024. *Am J Kidney Dis* 2024;83(1):90–100.
- [6] Flores-Mireles AL et al. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol* 2015;13(5):269–84.
- [7] Marantidis J, Sussman RD. Unmet needs in complicated urinary tract infections: challenges, recommendations, and emerging treatment pathways. *Infect Drug Resist* 2023;16:1391–405.
- [8] Chen SS et al. Complicated urinary tract infection: analysis of 179 patients. *Zhonghua Yi Xue Za Zhi (Taipei)* 1998;61(11):651–6.
- [9] Kranz J et al. European Association of Urology Guidelines on urological infections: summary of the 2024 guidelines. *Eur Urol* 2024;86(1):27–41.
- [10] Foxman B. The epidemiology of urinary tract infection. *Nat Rev Urol* 2010;7(12):653–60.
- [11] Kouri TT et al. The EFLM European Urinalysis Guideline 2023. *Clin Chem Lab Med* 2024;62(9):1653–786.
- [12] Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. *Clin Infect Dis* 2004;38(8):1150–8.
- [13] Arienzo A et al. A new point-of-care test for the rapid detection of urinary tract infections. *Eur J Clin Microbiol Infect Dis* 2020;39(2):325–32.
- [14] Langlois MR, Kouri TT. EFLM European Urinalysis Guideline. *Clin Chem Lab Med* 2024;62(9):1649–50.
- [15] Berger RE. The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy. *J Urol* 2005;174(3):941–2.
- [16] Demilie T et al. Diagnostic accuracy of rapid urine dipstick test to predict urinary tract infection among pregnant women in Felege Hiwot Referral Hospital, Bahir Dar, North West Ethiopia. *BMC Res Notes* 2014;7:481.
- [17] Schmiemann G et al. The diagnosis of urinary tract infection: a systematic review. *Dtsch Arztebl Int* 2010;107(21):361–7.
- [18] Giske CG et al. Update from the European Committee on Antimicrobial Susceptibility Testing (EUCAST). *J Clin Microbiol* 2022;60(3):e0027621.
- [19] Fritzenwanker M et al. Comparison of urine flow cytometry on the UF-1000i system and urine culture of urine samples from urological patients. *Urol Int* 2022;106(8):858–68.
- [20] Hindman R, Tronic B, Bartlett R. Effect of delay on culture of urine. *J Clin Microbiol* 1976;4(1):102–3.
- [21] Jefferson H et al. Transportation delay and the microbiological quality of clinical specimens. *Am J Clin Pathol* 1975;64(5):689–93.