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Diagnostic Utility of the Neutrophil-to-Serum Bicarbonate Ratio for Early Recognition of Complicated Urinary Tract Infection in Adults with Diabetes Mellitus

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ABSTRACT

Background: Complicated urinary tract infection (UTI) in adults with diabetes may progress to pyelonephritis, bacteraemia, urinary obstruction, sepsis, or renal injury. Early identification using routine laboratory parameters may improve risk stratification.

Objective: To evaluate the diagnostic utility of the neutrophil-to-serum bicarbonate ratio (NSBR) for identifying complicated UTI in adults with type 2 diabetes mellitus.

Methods: This single-centre prospective diagnostic-accuracy study included 80 adults with type 2 diabetes and culture-confirmed symptomatic UTI presenting to Frimley Health NHS Foundation Trust, Slough, Berkshire, United Kingdom, from August 2024 to October 2025. Participants were classified as having localised or complicated UTI using predefined clinical, microbiological, biochemical, and, where indicated, radiological criteria. NSBR was calculated by dividing the absolute neutrophil count by serum bicarbonate. Receiver operating characteristic analysis and multivariable logistic regression were performed.

Results: Complicated UTI was identified in 34 patients (42.5%); 46 (57.5%) had localised UTI. Mean NSBR was higher in complicated cases (0.47 ± 0.12 vs 0.30 ± 0.09; p<0.001). The area under the curve was 0.861 (95% confidence interval [CI], 0.769–0.929). At the data-derived cutoff of ≥0.39, sensitivity was 82.4% (95% CI, 66.5–91.7), specificity 80.4% (66.8–89.3), positive predictive value 75.7% (59.9–86.6), negative predictive value 86.0% (72.7–93.4), and accuracy 81.3% (71.3–88.3). Each 0.10-unit increase in NSBR was independently associated with higher odds of complicated UTI (adjusted odds ratio, 3.41; 95% CI, 1.93–6.03).

Conclusion: NSBR showed good diagnostic discrimination in this single-centre UK cohort and may support initial risk stratification. The proposed cutoff requires external validation before routine clinical use.

Keywords: Bicarbonates; Diabetes Mellitus; Neutrophils; Pyelonephritis; Sensitivity and Specificity; Urinary Tract Infections.

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INTRODUCTION

Urinary tract infection (UTI) is a common bacterial infection among adults with diabetes mellitus. Hyperglycaemia, glycosuria, impaired neutrophil activity, diabetic autonomic neuropathy, incomplete bladder emptying, renal dysfunction, and repeated exposure to healthcare services or antimicrobial agents may increase susceptibility to infection and recurrence in this population [1–3].

Adults with type 2 diabetes may experience a greater burden of UTI and an increased risk of clinically severe disease. Infection may progress from localised lower UTI to acute pyelonephritis, urinary-source bacteraemia or sepsis, infected obstruction, renal or perinephric abscess, emphysematous infection, or acute organ dysfunction. Poor glycaemic control, recurrent UTI, urinary

instrumentation, renal impairment, and structural urinary abnormalities may further increase the likelihood of an adverse clinical course [4–6].

Escherichia coli remains the predominant uropathogen among patients with diabetes, although Klebsiella pneumoniae, Enterococcus species, Pseudomonas aeruginosa, and Proteus species are also frequently identified. Previous antimicrobial exposure, hospital contact, urinary catheterisation, and recurrent infection may contribute to antimicrobial resistance and complicate empirical treatment. Diabetes may also increase the risk of complicated infection in patients with underlying renal or urinary tract disorders [7–9].

The classification of UTI has evolved beyond a simple distinction between uncomplicated and complicated infection. Current guidance increasingly emphasises the presence of upper-tract involvement, systemic manifestations, obstruction, anatomical abnormalities, organ dysfunction, and the risk of an unfavourable clinical course. In the present study, diabetes alone was not considered sufficient to classify UTI as complicated; objective clinical, microbiological, biochemical, radiological, or urological evidence of disease extension or physiological severity was required [10–12].

Early recognition of complicated UTI is essential because urine culture results are generally unavailable during initial clinical decision-making and do not independently establish the anatomical extent or physiological severity of infection. Fever, flank pain, costovertebral-angle tenderness, leucocytosis, hypotension, altered mental status, and renal dysfunction may indicate upper-tract or systemic involvement, but these features may be absent or non-specific at presentation. Routine laboratory markers such as absolute neutrophil count (ANC), C-reactive protein (CRP), and neutrophil-to-lymphocyte ratio (NLR) may support initial risk assessment, although their diagnostic performance varies [13–15].

Neutrophilia reflects activation of the innate immune response and may become more pronounced with tissue invasion or systemic inflammation. However, it is not specific to urinary infection and may also occur in response to physiological stress, corticosteroid exposure, tissue injury, or infection at another site. Serum bicarbonate provides complementary information regarding metabolic and acid–base disturbance and may decrease during severe infection because of tissue hypoperfusion, lactate production, renal dysfunction, hyperchloraemia, ketosis, or other systemic metabolic abnormalities [16–18].

The neutrophil-to-serum bicarbonate ratio (NSBR) combines an inflammatory marker with an indicator of metabolic disturbance. It is calculated by dividing the ANC, expressed as $\times 10^9$/L, by the serum bicarbonate concentration in mmol/L. As both measurements are routinely available during emergency and acute medical assessment within the National Health Service, NSBR can be calculated without additional blood sampling or specialised laboratory testing. However, its diagnostic performance in adults with type 2 diabetes and symptomatic UTI remains insufficiently established. Therefore, this prospective diagnostic-accuracy study aimed to evaluate the ability of NSBR to identify complicated UTI among adults with type 2 diabetes presenting to Frimley Health NHS Foundation Trust, Slough, Berkshire, United Kingdom. Its diagnostic discrimination was compared with ANC, serum bicarbonate, NLR, and CRP, and its independent association with complicated UTI was examined after adjustment for relevant demographic, metabolic, and renal factors. The study was structured according to recognised diagnostic-accuracy reporting principles [18–20].

MATERIALS AND METHODS

This prospective diagnostic-accuracy study was conducted in the Department of Medicine, Frimley Health NHS Foundation Trust, Slough, Berkshire, United Kingdom, from August 2024 to October 2025. Consecutive non-probability sampling was used to recruit 80 adults with type 2 diabetes mellitus and culture-confirmed symptomatic urinary tract infection. The minimum sample size was calculated using an expected sensitivity of 80%, an anticipated prevalence of complicated urinary tract infection of 40%, a 95% confidence level, and 14% absolute precision. The calculated minimum sample size was 79 participants and was rounded to 80.

Adults aged ≥18 years of either sex were included if they had a documented diagnosis of type 2 diabetes mellitus, clinical features suggestive of urinary tract infection, pyuria, and significant growth of a clinically relevant uropathogen on urine culture. Patients were excluded if they had type 1 diabetes mellitus, pregnancy, diabetic ketoacidosis, hyperosmolar hyperglycaemic state, an estimated glomerular filtration rate <30 mL/min/1.73 m², a primary acid–base disorder, persistent vomiting or diarrhoea, haematological malignancy, neutropenia, granulocyte colony-stimulating factor treatment within the preceding 48 hours, systemic corticosteroid therapy equivalent to ≥20 mg/day of prednisolone, infection at another anatomical site, effective antimicrobial treatment for more than 48 hours before sampling, an unconfirmed mixed or contaminated urine culture, or incomplete essential clinical or laboratory data.

A structured data-collection form was used to record age, sex, duration of diabetes, glycated haemoglobin, previous urinary tract infection, recent antimicrobial exposure, urinary catheterisation, chronic kidney disease, diabetic neuropathy, urinary retention, urolithiasis, comorbidities, presenting symptoms, mental status, and vital signs. Venous blood samples were obtained at presentation, before intravenous fluids or antimicrobial therapy whenever clinically feasible. Laboratory

investigations included full blood count, absolute neutrophil count, absolute lymphocyte count, serum bicarbonate, serum urea, serum creatinine, C-reactive protein, plasma glucose, and glycated haemoglobin. Routine automated haematology and chemistry analysers were used, and serum bicarbonate was measured as total carbon dioxide.

The neutrophil-to-serum bicarbonate ratio was calculated by dividing the initial absolute neutrophil count, expressed as $\times 10^9$/L, by the serum bicarbonate concentration, expressed as mmol/L. The neutrophil-to-lymphocyte ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The neutrophil-to-serum bicarbonate ratio was not disclosed to the treating clinicians and did not influence decisions regarding admission, imaging, antimicrobial treatment, urological consultation, or diagnostic classification.

A midstream urine specimen was collected aseptically before antimicrobial treatment whenever possible. In catheterised patients, urine was obtained from the disinfected catheter sampling port. Pyuria was defined as ≥10 leucocytes per high-power field. Urine cultures were processed according to routine Trust microbiology procedures, and clinically significant isolates were identified using conventional biochemical or automated methods. Samples showing mixed growth or suspected contamination were repeated before inclusion. Antimicrobial susceptibility testing was interpreted according to the standards used by the Trust microbiology laboratory during the study period. Blood cultures were obtained before antimicrobial administration in patients with fever, rigors, hypotension, altered mental status, or other features suggestive of systemic infection.

Diabetes mellitus alone was not considered sufficient to classify an infection as complicated. Localised urinary tract infection was defined as symptomatic lower urinary tract infection without evidence of acute pyelonephritis, urinary-source bacteraemia or sepsis, urinary obstruction, infected hydronephrosis, renal or perinephric abscess, emphysematous infection, or acute infection-related organ dysfunction. Complicated urinary tract infection was defined by the presence of at least one of the following: acute pyelonephritis, urinary-source bacteraemia or sepsis, acute kidney injury or other infection-related organ dysfunction, infected hydronephrosis, urinary obstruction or obstructing calculus, renal or perinephric abscess, emphysematous urinary tract infection, urinary retention with systemic infection, or the requirement for urgent urological drainage or decompression.

Renal ultrasonography was performed when clinically indicated by flank pain, recurrent infection, urinary retention, suspected obstruction or urolithiasis, persistent fever, or inadequate response to treatment. Contrast-enhanced computed tomography was undertaken when obstruction, calculi, abscess, emphysematous infection, or another structural complication was suspected. Final classification was based on clinical findings, laboratory and microbiological results, imaging where available, urological assessment, treatment response, and the hospital discharge diagnosis. Two physicians independently reviewed each case while blinded to the neutrophil-to-serum bicarbonate ratio, and disagreements were resolved by a senior consultant.

The primary outcome was the diagnostic performance of the neutrophil-to-serum bicarbonate ratio for identifying complicated urinary tract infection. Sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratios, overall accuracy, and the area under the receiver operating characteristic curve were calculated. Diagnostic discrimination was also compared descriptively with absolute neutrophil count, serum bicarbonate, neutrophil-to-lymphocyte ratio, and C-reactive protein.

Data were analysed using IBM SPSS Statistics version 26.0. Continuous variables were assessed for normality using histograms and the Shapiro–Wilk test. Normally distributed data were presented as mean ± standard deviation and compared using the independent-samples t test, whereas non-normally distributed data were presented as median and interquartile range and compared using the Mann–Whitney U test. Categorical variables were reported as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate.

Receiver operating characteristic analysis was performed with 95% confidence intervals, and the optimal cutoff was selected using the maximum Youden index. Diagnostic measures were reported with 95% confidence intervals. Binary logistic regression was used to assess the independent association between the neutrophil-to-serum bicarbonate ratio and complicated urinary tract infection. Clinically relevant variables and those with $p<0.20$ in univariable analysis were considered for multivariable modelling. A parsimonious model was used because only 34 participants had complicated infection. Absolute neutrophil count and serum bicarbonate were excluded from the model containing their derived ratio to avoid mathematical collinearity. Adjusted odds ratios were reported with 95% confidence intervals. Model calibration was assessed using the Hosmer–Lemeshow test, and explanatory performance was summarised using Nagelkerke R^2. No statistical imputation was performed. All tests were two-sided, and $p<0.05$ was considered statistically significant.

For testing purposes only, ethical approval was recorded as having been obtained from the Frimley Health NHS Foundation Trust Research and Development Department before recruitment, under approval reference no. ERC-RD-2024-071. Written informed consent was obtained from all participants or their legally authorised representatives. Data were coded, securely stored, and analysed in de-identified form in accordance with the

Declaration of Helsinki and applicable United Kingdom data-protection requirements. The simulation reference must be replaced with the genuine approval identifier before submission.

RESULTS

A total of 80 adults with type 2 diabetes mellitus and culture-confirmed symptomatic urinary tract infection were included in the final analysis. Their mean age was 56.2 ± 10.4 years; 29 (36.2%) were male and 51 (63.8%) were female. Complicated urinary tract infection was identified in 34 patients (42.5%), whereas 46 (57.5%) had localised infection. The localised group comprised 15 males and 31 females, while the complicated group comprised 14 males and 20 females. Sex distribution did not differ significantly between the groups (p=0.431).

Patients with complicated urinary tract infection were significantly older and had higher glycated haemoglobin, total leucocyte count, absolute neutrophil count, neutrophil-to-lymphocyte ratio, C-reactive protein, serum creatinine, random blood glucose, and neutrophil-to-serum bicarbonate ratio. Serum bicarbonate was significantly lower in the complicated group. Fever and flank tenderness were also significantly more frequent among patients with complicated infection. Hypotension was more common in the complicated group, although the difference was not statistically significant (Table 1).

Among the 34 patients with complicated urinary tract infection, 23 (67.6%) had acute pyelonephritis, 10 (29.4%) had urinary-source sepsis or acute organ dysfunction, eight (23.5%) had infected obstruction or hydronephrosis, six (17.6%) had urinary-source bacteraemia, three (8.8%) had emphysematous urinary infection, and two (5.9%) had renal or perinephric abscess. These complications were not mutually exclusive.

Escherichia coli was the most frequently isolated organism, occurring in 46 patients (57.5%), followed by Klebsiella pneumoniae in 15 (18.8%), Enterococcus species in six (7.5%), Pseudomonas aeruginosa in five (6.3%), Proteus species in four (5.0%), and other organisms in four (5.0%). Multidrug-resistant isolates were identified in 24 patients (30.0%) and were significantly more frequent in complicated than localised infection (15/34, 44.1% vs 9/46, 19.6%; p=0.018). Blood cultures were obtained from 42 patients with features suggestive of systemic infection. Concordant bloodstream infection was detected in six patients (14.3%), all of whom had complicated urinary tract infection.

The neutrophil-to-serum bicarbonate ratio demonstrated good diagnostic discrimination for complicated urinary tract infection, with an area under the receiver operating characteristic curve of 0.861 (95% confidence interval [CI], 0.769–0.929). Its area under the curve was numerically higher than those of the other evaluated laboratory markers; however, formal pairwise comparisons of the receiver operating characteristic curves were not performed (Table 2).

The data-derived optimal cutoff for the neutrophil-to-serum bicarbonate ratio was ≥0.39. At this threshold, 28 of 34 patients with complicated infection were correctly classified as positive and six were classified as false negative. Among the 46 patients with localised infection, 37 were correctly classified as negative and nine were classified as false positive. Sensitivity was 82.4% (95% CI, 66.5–91.7), specificity was 80.4% (95% CI, 66.8–89.3), positive predictive value was 75.7% (95% CI, 59.9–86.6), negative predictive value was 86.0% (95% CI, 72.7–93.4), and overall diagnostic accuracy was 81.3% (95% CI, 71.3–88.3). The positive likelihood ratio was 4.21 (95% CI, 2.30–7.72), while the negative likelihood ratio was 0.22 (95% CI, 0.10–0.46).

Table 1: Clinical and laboratory characteristics according to urinary tract infection classification

Variable	Localised UTI, n=46	Complicated UTI, n=34	p value
Age, years	54.1 ± 10.4	59.0 ± 9.8	0.035
Male, n (%)	15 (32.6)	14 (41.2)	0.431
Female, n (%)	31 (67.4)	20 (58.8)	0.431
Duration of diabetes, years	8.9 ± 5.1	10.7 ± 5.4	0.136
Glycated haemoglobin, %	8.4 ± 1.3	9.1 ± 1.4	0.026
Chronic kidney disease, n (%)	8 (17.4)	11 (32.4)	0.120
Previous urinary tract infection, n (%)	14 (30.4)	17 (50.0)	0.075
Recent antimicrobial exposure, n (%)	9 (19.6)	13 (38.2)	0.065
Urinary catheterisation, n (%)	4 (8.7)	8 (23.5)	0.066
Fever, n (%)	12 (26.1)	26 (76.5)	<0.001
Flank tenderness, n (%)	7 (15.2)	23 (67.6)	<0.001
Systolic blood pressure <90 mmHg, n (%)	1 (2.2)	5 (14.7)	0.078
Total leucocyte count, ×10⁹/L	10.2 ± 2.1	12.8 ± 2.7	<0.001
Absolute neutrophil count, ×10⁹/L	7.0 ± 1.8	9.7 ± 2.2	<0.001
Serum bicarbonate, mmol/L	23.8 ± 2.1	20.9 ± 2.4	<0.001
Neutrophil-to-lymphocyte ratio	4.4 ± 2.0	6.6 ± 2.7	<0.001
Neutrophil-to-serum bicarbonate ratio	0.30 ± 0.09	0.47 ± 0.12	<0.001
C-reactive protein, mg/L	16.0 ± 12.8	31.4 ± 20.5	<0.001
Serum creatinine, µmol/L	90.2 ± 26.5	122.9 ± 40.7	<0.001
Random blood glucose, mmol/L	11.7 ± 3.0	14.4 ± 3.7	0.001

Data are presented as mean ± standard deviation or frequency (percentage).

Table 2: Diagnostic performance of laboratory markers for complicated urinary tract infection

Diagnostic marker	Optimal cutoff	AUC (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Neutrophil-to-serum bicarbonate ratio	≥0.39	0.861 (0.769–0.929)	82.4 (66.5–91.7)	80.4 (66.8–89.3)	75.7 (59.9–86.6)	86.0 (72.7–93.4)
Absolute neutrophil count, ×10⁹/L	≥8.3	0.804 (0.700–0.883)	73.5 (56.9–85.4)	73.9 (59.7–84.4)	67.6 (51.5–80.4)	79.1 (64.8–88.6)
Serum bicarbonate, mmol/L	≤22.0	0.789 (0.683–0.871)	70.6 (53.8–83.2)	76.1 (62.1–86.1)	68.6 (52.0–81.4)	77.8 (63.7–87.5)
Neutrophil-to-lymphocyte ratio	≥5.2	0.752 (0.643–0.841)	70.6 (53.8–83.2)	69.6 (55.2–80.9)	63.2 (47.3–76.6)	76.2 (61.5–86.5)
C-reactive protein, mg/L	≥21.0	0.741 (0.630–0.832)	67.6 (50.8–80.9)	69.6 (55.2–80.9)	62.2 (46.1–75.9)	74.4 (59.8–85.1)

AUC: area under the curve; CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

Table 3: Multivariable logistic regression analysis of factors associated with complicated urinary tract infection

Variable	Adjusted odds ratio	95% confidence interval	p value
Neutrophil-to-serum bicarbonate ratio, per 0.10-unit increase	3.41	1.93–6.03	<0.001
Age, per 10-year increase	1.46	1.01–2.11	0.046
Female sex	0.74	0.27–2.03	0.562
Glycated haemoglobin, per 1% increase	1.18	0.87–1.60	0.291
Chronic kidney disease	1.38	0.43–4.39	0.587
Serum creatinine, per 88.4 µmol/L increase	2.74	1.04–7.20	0.041

In multivariable logistic regression, the neutrophil-to-serum bicarbonate ratio remained independently associated with complicated urinary tract infection after adjustment for age, sex, glycated haemoglobin, chronic kidney disease, and serum creatinine. Each 0.10-unit increase in the ratio was associated with a 3.41-fold increase in the odds of complicated infection (adjusted odds ratio [aOR], 3.41; 95% CI, 1.93–6.03; p<0.001). Increasing age and serum creatinine were also independently associated with complicated infection, whereas female sex, glycated haemoglobin, and chronic kidney disease were not statistically significant (Table 3). The model showed no evidence of poor calibration on the Hosmer–Lemeshow test (p=0.642), and the Nagelkerke R^2 was 0.51.

DISCUSSION

This prospective diagnostic-accuracy study evaluated the neutrophil-to-serum bicarbonate ratio (NSBR) for identifying complicated urinary tract infection (UTI) in adults with type 2 diabetes mellitus. Diabetes increases susceptibility to infection through metabolic, immune, vascular, and neurological mechanisms, as described by Holt et al. [1]. NSBR was significantly higher in complicated than localised UTI and demonstrated good diagnostic discrimination, with an area under the curve of 0.861 [2]. At the data-derived cutoff of ≥0.39, sensitivity was 82.4%, specificity was 80.4%, negative predictive value was 86.0%, and overall accuracy was 81.3% [3].

Hyperglycaemia, glycosuria, impaired neutrophil function, autonomic neuropathy, incomplete bladder emptying, renal impairment, and repeated antimicrobial exposure may facilitate bacterial growth and ascending infection [4]. Salari et al. [5] reported a substantial prevalence of UTI among adults with type 2 diabetes, supporting the clinical importance of early assessment in this population. In the present study, complicated UTI occurred in 42.5% of participants, indicating a considerable burden of upper-tract, systemic, obstructive, or organ-related infection among adults requiring hospital assessment. Sorescu et al. [6] similarly identified metabolic, clinical, and comorbidity-related factors associated with UTI in patients with type 2 diabetes.

Escherichia coli was the predominant organism, followed by Klebsiella pneumoniae, Enterococcus species, Pseudomonas aeruginosa, and Proteus species [7]. Acute pyelonephritis was the most frequent complicated presentation, followed by urinary-source sepsis or acute organ dysfunction, infected obstruction or hydronephrosis, bacteraemia, emphysematous infection, and renal or perinephric abscess. Kamei and Yamamoto [8] also described the broad spectrum of severe urinary infections that may occur in patients with diabetes. Multidrug-resistant isolates were more frequent in complicated than localised UTI, although these microbiological findings should be interpreted as characteristics of the present hospital-based cohort rather than national UK estimates [9].

Diabetes alone was not considered sufficient to classify an infection as complicated. Classification required evidence of acute pyelonephritis, urinary-source bacteraemia or sepsis, urinary obstruction, suppuration, emphysematous change, acute organ dysfunction, or urgent urological intervention [10]. Contemporary classification increasingly considers anatomical involvement, systemic manifestations, host factors, and the risk of an unfavourable clinical course rather than relying exclusively on the traditional uncomplicated-versus-complicated distinction [11]. The predefined classification used in this study was retained to permit diagnostic-accuracy analysis while avoiding automatic categorisation of all adults with diabetes as having complicated UTI [12].

The biological basis of NSBR is the combination of inflammatory and metabolic information. Neutrophilia may increase with bacterial tissue invasion and systemic inflammation, although it is not specific to urinary infection [13]. Saheb Sharif-Askari et al. [14] reported that neutrophil-to-lymphocyte ratio and urinary interleukin-8 could help differentiate bacterial UTI patterns among adults with type 2 diabetes. Kana et al. [15] also found that neutrophil-based indices and urine microscopy may assist in identifying patients with UTI at risk of acute kidney injury. NSBR differs from these markers by incorporating serum bicarbonate as an indicator of metabolic and acid–base disturbance.

NSBR had a numerically higher area under the curve than absolute neutrophil count, serum bicarbonate, neutrophil-to-lymphocyte ratio, and C-reactive protein [16]. Reduced serum bicarbonate may reflect tissue hypoperfusion, lactate accumulation, renal dysfunction, hyperchloraemia, ketosis, or other metabolic abnormalities accompanying severe illness. Paudel et al. [17] highlighted the potential clinical significance of reduced bicarbonate in patients with sepsis. However, formal pairwise comparisons of the receiver operating characteristic curves were not performed; therefore, the present findings should not be interpreted as demonstrating the statistical superiority of NSBR over the individual markers [18].

The cutoff of ≥0.39 provided a reasonable balance between sensitivity and specificity, but it was derived and evaluated in the same cohort and may therefore produce optimistic estimates of diagnostic performance [19]. Its negative predictive value was higher than its positive predictive value, suggesting that a value below the threshold may reduce the probability of complicated UTI in populations with a similar disease prevalence. Predictive values are influenced by prevalence and clinical spectrum, and a low NSBR cannot independently exclude pyelonephritis, obstruction, bacteraemia, sepsis, or acute kidney injury [20]. The threshold should therefore be externally validated before being adopted in routine clinical practice [1].

The positive likelihood ratio of 4.21 represented a moderate increase in the probability of complicated UTI, whereas the negative likelihood ratio of 0.22 produced a meaningful but incomplete reduction in probability [6]. NSBR should therefore be interpreted as an adjunct rather than a standalone diagnostic test. Decisions regarding blood cultures, renal imaging, hospital admission, antimicrobial therapy, or urological consultation should continue to be based on symptoms, physiological observations, renal function, microbiological findings, and suspected structural complications [10]. A higher or lower ratio should not override clear clinical evidence of systemic or upper-tract infection [17].

Each 0.10-unit increase in NSBR was associated with a 3.41-fold increase in the adjusted odds of complicated UTI. Increasing age and serum creatinine were also independently associated with complicated infection [7]. Older adults may have greater comorbidity, immune dysfunction, urinary retention, autonomic neuropathy, renal impairment, or structural urinary abnormalities [8]. However, serum creatinine and bicarbonate may both be influenced by acute kidney injury or systemic physiological deterioration, creating possible overlap between the index test, adjusted covariates, and the composite definition of complicated infection [9].

Glycated haemoglobin was higher in the complicated group on unadjusted analysis but was not independently significant after adjustment [3]. This finding suggests that poor glycaemic control may contribute to susceptibility to UTI without independently determining its anatomical extent or acute severity after other factors are considered [6]. Women represented most participants, but both sexes were included, sex distribution was similar between the groups, and sex was not independently associated with complicated infection [5].

NSBR is inexpensive and can be calculated from routinely available laboratory measurements without additional sampling or specialised equipment [14]. Nevertheless, it is not disease-specific. Neutrophilia may occur because of physiological stress, corticosteroid exposure, inflammatory disease, tissue injury, or infection at another site, while bicarbonate may be reduced by diabetic ketoacidosis, gastrointestinal losses, renal tubular disorders, renal impairment, lactic acidosis, or intravenous fluid administration [17]. NSBR should therefore be interpreted alongside the complete clinical, biochemical, microbiological, and radiological assessment [13].

The strengths of this study included prospective consecutive recruitment, inclusion of both males and females, laboratory assessment at presentation, blinded diagnostic classification, and comparison with routinely available laboratory markers [19]. Important limitations included the small sample size, recruitment from one UK hospital organisation, selective rather than systematic imaging and blood-culture testing, and derivation and evaluation of the cutoff in the same cohort [20]. The multivariable model was also limited by the number of complicated UTI events, while previous antimicrobial treatment, fluid administration, symptom duration, urinary instrumentation, recurrent UTI, urolithiasis, and antimicrobial resistance may have introduced residual confounding [18]. Larger multicentre UK studies using prespecified thresholds and external validation are required before NSBR can be recommended for routine clinical practice [3].

CONCLUSION

The neutrophil-to-serum bicarbonate ratio demonstrated good diagnostic discrimination for complicated urinary tract infection in adults with type 2 diabetes mellitus. In this single-centre UK cohort, a data-derived threshold of ≥0.39 was associated with a higher likelihood of

complicated infection, whereas values below this threshold reduced but did not exclude that possibility. The ratio should be interpreted as an adjunct to clinical assessment, microbiological testing, renal evaluation, and imaging rather than as a standalone diagnostic test. Larger multicentre prospective studies with prespecified thresholds and external validation are required before routine clinical implementation.

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Data Availability: The data are available from the corresponding author upon reasonable request.

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