Research Article

Routine urinalysis-predictor of urinary tract infection

A C Pinto[1*], S Devaraju[2], V K Basavaraju[3], B M Thomas[4]

[1,2,3,4]Father Muller Medical College Hospital, Father Muller Road, Kankanady, Mangalore-575002, Karnataka, INDIA.
Email: pinto.mandy@gmail.com, drsumanthd@yahoo.com, vatsala18@gmail.com, bmt8324@gmail.com

Abstract
Introduction: Urinary tract infection (UTI) is one of the most common problems warranting medical attention. The purpose of this study was to determine the usefulness of routine urine analysis in predicting UTI, to facilitate presumptive treatment. Data of 500 culture positive urine samples were collected. The colony counts were correlated with physical, chemical and microscopic parameters of the urine sample. Of particular interest were tests for nitrites (NIT) and leukocyte esterase (LEU). Sensitivity, specificity and predictive values were calculated with regard to NIT, LEU and a combination of both (NIT+LEU). Chi square test was used to calculate p-value and thereby association of culture positivity with various above mentioned parameters. Most parameters showed significant correlation with colony count (p value <0.05). Sensitivity of NIT, LEU and (NIT+LEU) to detect infection was 22.33%, 66.1% and 50% respectively. Specificity of NIT, LEU and (NIT+LEU) was 90.9%, 54.3% and 92.7% respectively. In our study (NIT+LEU) had higher specificity and positive predictive value and are therefore useful in predicting the presence of UTI.
Keywords: Urinary tract infection, colony count, esterases, nitrites.

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INTRODUCTION

Urinary tract infections (UTI's) have become the most common hospital acquired infection accounting for as many as 35% of nosocomial infections;[1] *Escherichia coli(E.coli)* being the most commonly isolated organism.[1] Laboratory examination of urine specimen accounts for a large part of the workload in many hospital based laboratories. The gold standard used for diagnosis of UTI is culture. However, the biggest disadvantage is the time factor. Time for culture positivity on growth plates depends on the causative organism- varying between days to weeks. Clinical deterioration is the natural consequence of delay in treatment initiation. Urinalysis which is rapid and cost effective plays an important role in giving an early diagnostic clue to start empirical treatment. It includes physical, chemical and microscopic tests. Dipstick tests are also available for testing specific gravity, pH, nitrites, leucocyte esterase, protein, glucose, RBC's, ketone bodies, bile salts and bile pigments. Various studies have shown significance of routinely used urinalysis parameters in predicting UTI.[1-12] The advantages being rapidity, ease of performance and cost effectiveness. In this study we analyzed its usefulness in presumptive diagnosis of UTI.

MATERIAL AND METHODS

Urine analysis results of 500culture positive urine specimens were collected over three consecutive months. In our laboratory, mid-stream clean catch urine specimens, collected under aseptic precautions in sterile containers is used for analysis and Culture is done on Mac Conkey's agar and blood agar at 37° C for at least 24-36 hrs. The colony count was correlated with physical, chemical and microscopic parameters. The Gold standard for presence of UTI was culture positivity of the specimen with a colony count of $>10^5$ colony forming unit (CFU)/ml of urine. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of LEU, NIT and their combination in predicting UTI was calculated. Association between urinalysis parameters and culture positivity was determined by Chi-Square Test. The statistical analysis was performed using SPSS for windows.

OBSERVATIONS AND RESULTS

Among 500 patients, 197 were males and 303 were females. Majority of patients were adults, rest being in paediatric and adolescent age group.
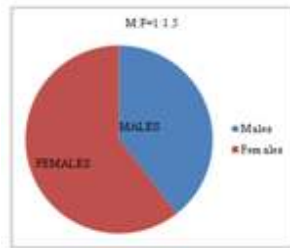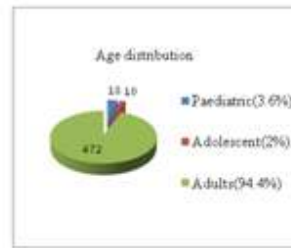

Figure 1: Pie chart of gender distribution

Figure 2: Pie chart of age distribution

The most common organism isolated from the samples was *Escherichia coli(E. coli)*. 70.6% of the organisms were nitrate reducing and the remaining 29.4% were non nitrate reducing organisms.
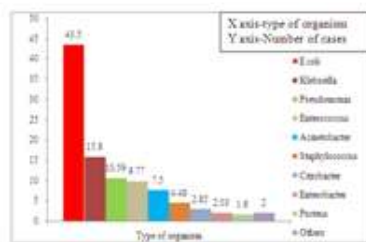

Figure 3: Distribution graph of organisms isolated in culture
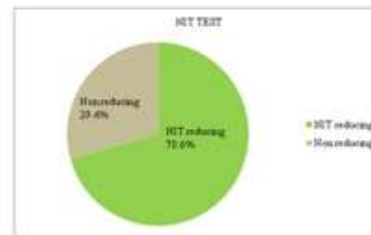

Figure 4: Pie chart-distribution of nitrate reducing and non-reducing organisms

The colony counts of the 500 culture positive urine specimens are as follows-

- 61 cases-$<10^3$CFU/ml of urine
- 146 cases-10^3-10^5CFU/ml of urine
- 293 cases-$>10^5$CFU/ml of urine

Therefore 293 patients had UTI according to the culture reports with a colony count of $>10^5$CFU/ml of urine. LEU and NIT reports could be traced only in 215/293 cases with UTI. The results of the urinalysis with respect to the above mentioned colony counts is enumerated in the table below

Table 1: Urinalysis positivity in culture positive cases

Tests Parameters	Number of positive cases		
	$<10^3$CFU/ml of urine (61 cases)	10^3-10^5CFU/ml of urine(146 cases)	$>10^5$CFU/ml of urine (293 cases)
NIT	1/46	14/118	48/215
LEU	24/46	64/118	160/215
NIT+LEU	0/46	12/118	45/215
Ketone bodies	1/61	14/146	16/293
Bile pigments	1/61	2/146	3/293
Bile salts	1/61	1/146	2/293
Leucocytes	24/61	53/146	178/293
Specific gravity	1/61	1/146	2/293
Protein	20/61	41/146	99/293
Transparency	34/61	91/146	232/293
Blood	8/61	30/146	48/293
Organisms	4/61	14/146	77/293
Glucose	12/61	36/146	42/293

The p-values of the urinalysis parameters in patients with UTI are as follows

Table 2: Correlation between culture positivity and urinalysis parameters

Test	p-value	Significance
NIT	0.000	Significant
LE	0.000	Significant
Ketone bodies	0.075	Not significant
Bile pigments	0.721	Not significant
Bile salts	0.589	Not significant
Leucocytes	0.000	Significant
Specific gravity	0.580	Not significant
Protein	0.299	Not significant
Transparency	0.000	Significant
Blood	0.352	Not significant
Organisms	0.000	Significant
Glucose	0.025	Significant

NIT, LEU, leucocytes, transparency of sample, presence of organisms and glucose all showed significant correlation with culture positive specimens with colony count >10^{5}CFU/ml of urine. The results and analysis of NIT and LEU tests along with a combination of the two are as follows:

Table 3: Statistical results of (NIT+LEU) test

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
NIT	22.33	90.9	76.2	47.2
LEU	66.1	54.3	65.4	54.9
NIT+LEU	50	92.7	93.4	47.2

LEU was more sensitive than NIT and NIT was more specific than LEU. An increase in specificity and PPV (92.7% and 93.4% respectively) was observed with combination of parameters (NIT+LEU).

DISCUSSION

Use of routine urine analysis as a rapid diagnostic test for UTI is a common clinical practice. Numerous studies in the past have shown the advantages of routine urinalysis by calculating their sensitivity, specificity and predictive values for detecting UTI.[1-11]

Analysis of Nit Test

The principle of the NIT test is based on the ability of micro-organisms to reduce nitrate to nitrite. This reaction is associated with the members of the family *Enterobacteriaceae*. The nitrite produced reacts with a diazonium salt to form an azo-dye showing positivity. However, non-nitrate reducing urinary tract pathogens like *S. saprophyticus*, *pseudomonas* species or *enterococci* are not detected, limiting its usefulness.

This test showed high specificity and PPV with values of 90.9% and 76.2% respectively. However, the NPV was low (47.2%).

Table 4: Comparison of NIT tests in various studies

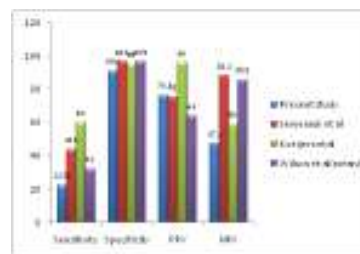| NIT test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Lenke *et al*[4]	72	100	-	-
Nostrand *et al*[5]	19.2	94.2	-	-
Semeniuk *et al*[2]	43.6	96.6	75	88.2
Koeijers *et al*[6]	60	95	96	59
Wilson *et al*[3]	19-45	95-98	50-78	82-89
Deville *et al*[7]	75-60	85-93	-	-
Present study	22.33	90.9	76.2	47.2

Figure 5: Graph comparing NIT test values of various studies

The causes for the false negatives in the test leading to low NPV are:

- Nitrate reducing property of the organism- 29.4% (Fig 2) of the organisms were non nitrate reducing which was a confounding factor
- Time of incubation of organism in the bladder- A minimum of 4 hours of incubation in the bladder is required for producing nitrites therefore, early morning samples are preferred due to longer incubation period in bladder. samples collected within 2 hours of previous void will increase false negativity of the test
- Patients diet deficient in nitrates could also contribute to false negatives

Analysis of LEU test

Leucocytes produce Leucocyte esterase. Hydrolysis of ester substances by these esterases form free indoxl, which reacts with diazonium salts to form an azo-dye. This is seen as a positive reaction in LEU Test. 160 out of 215 samples showed positivity for LEU indicating the presence of leucocytes (The pus cells of urine microscopy). This test showed high sensitivity of66.1% and high PPV of 65.4%. However, the NPV was low (54.9%).

Table 5: Comparison of LEU tests in various studies

LEU test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Nostrand *et al*[5]	75	72	-	-
Wael *et al*[8]	68.4	73.4	43.7	88.5
Semeniuk *et al*[2]	84.4	59.4	19.4	97.1

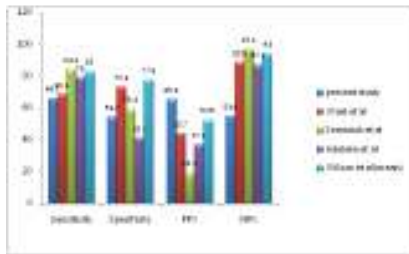|			
Koeijers et al[6]	82	53	-	-
Wilson et al[3]	68-98	59-96	19-86	91-97
Adeleke et al[9]	79	41.1	37.1	87.2
Deville et al[7]	48-86	17-93	-	-
Present study	66.1	54.3	65.4	54.9

Figure 6: Graph comparing LEU test values of various studies

The false negative LEU is due to prior Antibiotic therapy, elevated protein/glucose and presence of confounding factors like ascorbic acid.[3] We found significant number of our cases had elevated protein and glucose levels. It is also possible that our patients might have received antibiotic treatment, resulting in low NPV.

Analysis of (NIT+LEU) test

45 out of 215 samples showed positivity for (NIT+LEU).The combination of NIT and LEU showed high specificity and PPV with values of 92.7% and 93.4% respectively. However, the NPV was low (47.2%).

Table 6: Comparison of (NIT+LEU) tests in various studies

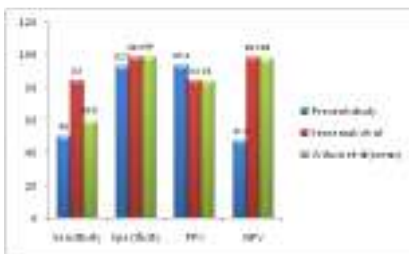| (NIT+LEU)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Semeniuk et al[2]	84	98.3	84	98.3
Wilson et al[3]	35-84	98-100	84	98
Present study	50	92.7	93.4	47.2

Figure 7: Graph comparing (NIT+LEU) test values of various studies

Therefore, when used in combination, (LEU+NIT) showed higher specificity and PPV for detecting UTI when compared to the tests used separately. However a low NPV was noted, reasons for which have been enumerated above for both the tests separately. Other reasons that could affect the tests are:

- Improper urine collection procedure
- Contamination of urine sample
- Improper transportation
- Manual/ automated reading

- Efficiency of technician/pathologist reading the test
- Interpretation errors
- Brand of dipstick

Therefore, overall the combination of the two tests namely; NIT and LEU are more useful than the tests used singly.

CONCLUSION

Urinalysis parameters will guide clinicians to a presumptive diagnosis in UTI to start empirical treatment without any delay. Summarizing, the most important routine urinalysis parameters which can be used to predict a UTI are

- (NIT+LEU)- high specificity and PPV
- NIT-high specificity
- LEU-high sensitivity

The present study shows high specificity and PPV with (NIT+LEU). Therefore if the test comes positive, the patient has UTI and treatment can be started. However, due the low NPV and sensitivity, if the test is negative, diagnosis of UTI cannot be ruled out and further investigations with culture confirmation are mandatory. Clinically excluding confounding factors may help in identifying false negative cases. In conclusion, of all the laboratory tests available, urinalysis is helpful primarily as a means for provisional diagnosis for presumptive treatment of UTI. Routine urinalysis is not a surrogate for culture which remains to be the gold standard.[1]

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