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Research Article

Evaluation of Advantages of Multiple Parameters of an Automated Urine Analyzer in Clinical Practice

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Abstract

Background and objectives: Analysis of urine accounts for a large portion of tests performed in a clinical laboratory. It costs the laboratory time as well as labor. Manual urine dipsticks tests lack precision and accuracy. The aim of the study is to evaluate various parameters of an automated urine analyzer.

Methods: The study was conducted in Department of Pathology of Rajiv Gandhi Super Specialty Hospital, Tahirpur, and Delhi. The samples received between April to September 2017 were included in the study. All the samples were run in the Sysmex UX 2000, a fully automated flow cytometry based urine analyzer.

Results: Total of 3199 specimens were included in the study. Male to female ratio of the study was 1.07:1. Cutoff values of WBC (19.8 cells/µl) and bacterial counts (198.8 cells/µl) showed high sensitivity, specificity and negative predictive value (NPV). Nitrites as well as leucocyte esterase showed high specificity and NPV. Glucose was elevated in15.1% of cases while yeast was present in 4.7%.

Conclusion: Automated urine analyzers aids in precise and accurate urine results while reducing turnaround time and workload of a laboratory. The results also guide the clinical towards a probable diagnosis and empirical treatment could be initiated at the earnest.

INTRODUCTION

Urinalysis is one of the most common routine investigations performed in laboratory medicine which aims to determine various components in the urine and aid in diagnosis and management of the patient. Urine examination is done to detect the status of renal and genitourinary system.

Urinalysis is composed to three parts; namely physical examination, chemical examination and microscopic examination. The physical examination of urine includes determination of quantity of urine sample, its color, and clarity. Chemical analysis of urine is conducted with aid of reagent strips. The strips can detect pH, glucose, proteins, bilirubin, urobilinogen, blood, ketones, nitrite, leucocyte esterase and specific gravity. These strips are contains chemical impregnated absorbent pads which on contact with the urine change color. The change in color is compared with the colors of reference chart and the results are given as trace 1+, 2+, 3+ or 4+. Microscopic examination of urine consists of examination of urine sediments after centrifugation to detect RBC's (Red Blood Cells), WBC's (White Blood Cells), epithelial cells, casts, crystals, yeast, parasites, mucus, spermatozoa and artifacts [1].

Manual examination of urine is high labor as well as time intensive test which also lacks standardization [2,3]. Manual urinalysis is most commonly utilizes chemical strips. For determination of cells, casts, crystals and bacteria, microscopic analysis of the urine sediment is done. Manual urinalysis using dipstick and sediment analysis is a good screening test [4-6]. Confirmation of UTI is done by culture, which is considered the gold standard for diagnosis of UTI. For diagnosis, bacterial count of ≥ 10^3 Colony Forming Units (CFU)/mL is recommended [7]. Urinalysis with culture, takes from 18 -48 hours, adds workload on the laboratory and delays the initiation of appropriate treatment [8].

Automated urine analyzers based on principles of flow cytometry and cytochemistry has revolutionized the reporting in laboratory medicine. Not only had it aided in quick and efficient reporting of routine urine samples, the results are precise and accurate also [9]. Flow cytometry based automated urine analyzers are in use nowadays which reduces the urine screening time to mere minutes. Automated urine flow cytometry based analyzers can detect particles in urine like WBC, RBC, crystals and bacteria while at the same time use chemical strips to detectconcentration of various compounds present in urine [10,11].

MATERIALS AND METHODS

The study was conducted in Pathology department of Rajiv Gandhi Super Specialty Hospital, Tahirpur, Delhi. All the mid-stream urine samples collected in a sterile container received

between April and September 2017 were enrolled in the study. Samples not collected by mid-stream method or collected in a non-sterile container were excluded from the study.

Each sample underwent biochemical and flow cytometric examination using the Sysmex UX 2000 (Sysmex Corporation, Japan), a fully automated urine analyzer (Figure 1). The UX 2000 aspirates 2.2 ml of urine; 0.95ml for cytochemistry (CHM) and 1.2 ml for flow cytometry (FCM). UX2000 uses transmission refractrometry to detect specific gravity, light scattering for determining turbidity and reflectivity for color detection. CHM analyses test strips using dual wavelength reflectance method for detection of glucose, proteins, bilirubin, urobilinogen, pH, and blood, ketones, nitrite and leucocyte esterase. The test strips are coated with the urine sample and is read after 60 seconds [10].

For flow cytometry, the aspirated sample is stained with fluorescent dye and analyzed in two channels; one for analysis of sediment and other for bacterial analysis. The sample passes through the flow channel where the laser beam of 635 nm strikes each particle individually and produces forward scattered light signal, laterally scattered light signal and lateral fluorescent light signal which is detected and converted into electrical signals. All signals are analyzed as scatter grams (Figure 2). This categorizes the particles in urine into RBC, WBC, epithelial cells, cast and bacteria using a classification algorithm [10,11]. In this study, we evaluated all the parameters, with special emphasis on Glu (Glucose), Pro (Proteins), WBC, BAC (Bacterial counts), YLC (Yeast like cells) and X'tal (Crystals).

All the samples were reexamined with the dipsticks for chemical analysis. Microscopic sediment analysis was performed on each urine sample. The sample was centrifuged at 1000 rpm for 10 min, supernatant was removed and prepared slides were examined at 400x (HPF). For each sample, at least 20 HPFs were examined. Also, each urine sample which increased WBC, BAC or YLC underwent microbiological culture and the plates were read for growth after incubating for 18 - 48 hours. Clinical details of the patients were sought from the referring clinicians. The statistical analysis was performed using Microsoft Excel (Microsoft Corporation, Washington, USA) as well as Statistical Package for the Social Sciences (IBM, Chicago, USA)

RESULTS

Total of 3199 patients were registered in the study with age ranging from 2 years to 88 years. Out of 3199 registered patients, 1658 (51.8%) patients were male and 1541 (48.2%) were females. The mean age for men was 45.2 ± 33.2 years and 43.4 ± 33.5 years for the women.

All the specimens with clinical history suspicious of urinary tract infection underwent microbiological culture. Mean WBC counts were 914.4 cells/µl for positive samples and 103.9 cells/µl for negative. Mean BAC counts were 9274.6 cells/µl for positive samples and 121.3 cells/µl for negative. The positive culture samples were correlated with the WBC, BAC, nitrates and leucocyte esterase. Both WBC and BAC show high sensitivity, specificity and negative predictive value. Nitrites show highest specificity of 97.4% and leucocyte esterase show high specificity and negative predictive value (Table 1).

Glucose was elevated to 4+ in 172 (5.4%) specimens and 3+ in 64 (2%); while 2715 (85.1%) came back negative. The results correlated with the clinical picture. Yeast like cells were noted in 6 specimens which also came positive for glucose (4+). Similarly, 6 specimens showed positivity for ketones. Bacterial counts were elevated in 52 specimens (Table 2, Figure 3).

Figure 1 Sysmex 2000i Fully Automated Urine Analyzer.

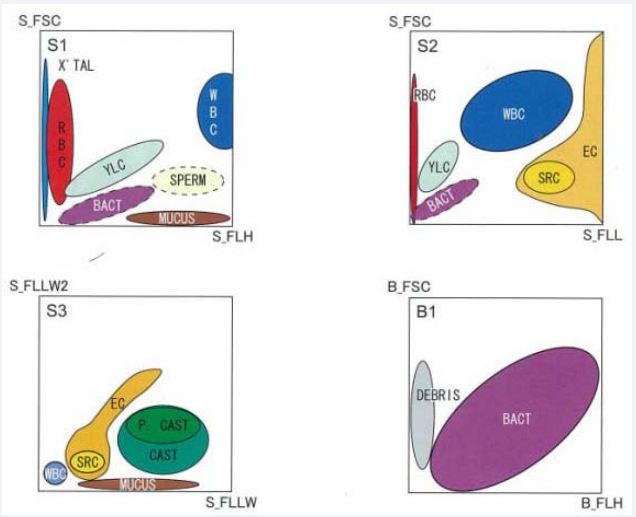

Figure 2 Scattergrams of UX2000.

Fungal infection was found in 149 (4.7%) specimens and it correlated with fungal culture. YLC was correlated with WBC, leucocyte esterase and bacterial counts. All of them showed high negative predictive value while leucocyte esterase showed highest sensitivity (75.5%) of them all (Table 3).

DISCUSSION

Urine analysis is a major part of a clinical laboratory's workload. It is a high volume, labor and time intensive test, which adds to cost of a laboratory [12]. Manual screening of a urine specimen takes up to six minutes per sample while an automated system generates the result in around one minute. Analysis in an automated system reduces the load on the laboratory and reduces the runaround time significantly. The Sysmex UX 2000 which works on the principle of flow cytometry differentiates between RBC, WBC, epithelial cells and bacteria with increased accuracy. It also generates flags for crystals, yeast like cells, small round cells, pathological casts, mucus and spermatozoa at

Table 1: Analysis of multiple parameters for detection of UTI.

	Sensitivity	Specificity	PPV	NPV
Nitrites	28.7	97.4	75.0	81.4
Leukocyte esterase	77.1	87.1	64.8	92.6
WBC	82.3	80.9	57.3	93.5
BAC	82.1	79.5	54.3	92.7

Table 2: Comparison of glucose with various parameters.

Glucose	No. of patients	BAC (>150 cells/µl)	YLC	Ketones
4+	172	52	6	6
3+	64	10	3	3
2+	48	10	1	0
1+	51	13	2	3
Trace	148	47	3	4
Negative	2715	775	132	36

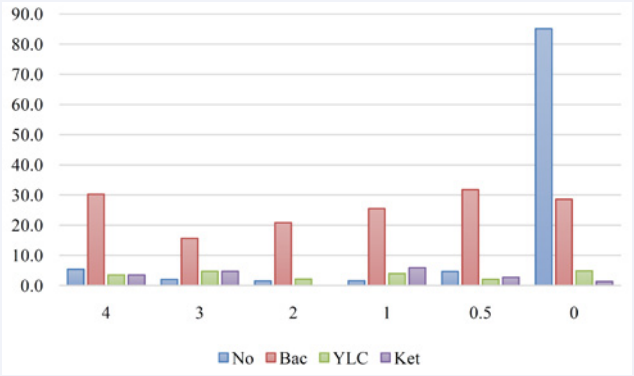

Figure 3 Comparison of glucose with various parameters.

Table 3: Comparison of multiple parameters in YLC positive cases.

	Sensitivity	Specificity	NPV	PPV
WBC	72.4	69.3	98.1	10.3
Leukocyte esterase	57.1	75.5	97.3	10.2
Bacterial counts	45.6	71.4	96.4	7.2

the same time; which helps isolate samples that require further analysis.

One of the primary reason for urine examination is to rule out urinary tract infections (UTI). Urinalysis is the first screening test performed to diagnose UTI while the confirmatory as well as gold standard test for UTI is urine culture. It usually takes 24-48 hours for a definitive result leading to delay in initiation of appropriate treatment [12]. We evaluated four parameters, namely WBC, BAC, nitrites and leucocyte esterase, to detect early UTI. The cutoff values for WBC of 19.8 cells/µl was established with high sensitivity, specificity and negative predictive value. It correlates with a study conducted in Brazil which showed similar results with cut off value of 20 cells/µl [13]. For bacterial counts cutoff value of 148 cells/µl gave sensitivity of 82.1% and specificity of 79.5%. Study performed by De Rosa et al took bacterial cutoff at 170 cells/µl with specificity of 76.5% and negative predictive value (NPV) of 99.5% [14]. Both leukocyte esterase and nitrites show high specificity and NPV, which correlated with various studies in the literature [4]. To summarize, all four parameters (WBC, BAC, nitrites and leucocyte esterase) could assist in establishing or ruling out the diagnosis of UTI in a short duration.

Examination of urine for glucose also hints at the status of renal health as well as overall blood sugar level. Glycosuria occurs when blood glucose exceeds renal threshold for glucose [15]. Glycosuria is commonly seen in diabetics. It is also associated with elevated numbers of bacteria as well as fungal elements, especially Candida species, in the urine [16]. In our study elevated glucose levels (4+ to trace) were detected in 483 (15.1%) specimens with 4+ in 172 (5.4%) cases. Among the patients with high glucose levels (4+), 30% shows elevated bacterial levels and 3.5% show elevated levels of YLC as well as ketones.

Yeast like cells were elevated in 149 (4.7%) urine specimens. All specimens with elevated YLC show presence of budding and hyphae forms of Candida species which was further correlated with fungal cultures. YLC was correlated with WBC, leucocyte esterase and bacterial counts; all of them show high negative predictive values. We also noted presence of secondary bacterial infections in the samples with elevated YLC and was also correlated with bacterial cultures. Presence of YLC could lead to increased suspicion of the presence of fungal infection and guide to clinician to initiate appropriate empirical therapy and prevent secondary bacterial infections.

Urinalysis by an automated urine analyzer has many advantages as well as disadvantages. The advantages being increased precision and reliability of the results, along with processing of large sample numbers in fraction of time as compared to manual analysis. The machine also provide insight for probable detection of multiple parameters, even in scant amounts, that could have been missed on manual analysis, like presence of yeast like cells, crystals, small round cells, etc. Also, the data is saved for a later day analysis and comparison. The only disadvantage we faced is the increased cost, which is higher than when done manually. It includes cost for the machine, controls as well as the reagents required for analysis.

CONCLUSION

Use of automated urine analyzers results in increased precision, accuracy and at the same time reduces laboratory cost, labor and turnaround time. Due to regular quality checks, results from an automated urine analyser are more standardized as compared to the manual urinalysis. Proper establishment of laboratory cutoff values aids in screening of negative samples and reduce unnecessary empirical treatments. Multiple parameters are evaluated at the same time; results of which guides towards a provisional diagnosis and initiation of appropriate treatment can be done at the earnest.

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