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Comparison of Fully Automated Urine Sediment Analyzers H800-FUS100 and Labumat-Urised with Manual Microscopy

Hatice Yüksel,[1]* Elif Kiliç,[2] Aysun Ekinci,[2] and Osman Evliyaoğlu[1]

[1]*Department of Medical Biochemistry, Faculty of Medicine, Dicle University, Diyarbakir, Turkey*

[2]*Department of Medical Biochemistry, Obstetrics and Pediatrics State Hospital, Diyarbakir, Turkey*

Background: Recent technical developments have focused on the full automation of urinalyses, however the manual microscopic analysis of urine sediment is considered the reference method. The aim of this study was to compare the performances of the LabUMat-UriSed and the H800-FUS100 with manual microscopy, and with each other. *Methods:* The urine sediments of 332 urine samples were examined by these two devices (LabUMat-UriSed, H800-FUS100) and manual microscopy. *Results:* The reproducibility of the analyzers, UriSed and Fus100 (4.1–28.5% and 4.7–21.2%, respectively), was better than that with manual microscopy (8.5–33.3%). The UriSed was more sensitive for leukocytes (82%), while the Fus-100 was more sensitive for erythrocyte cell counting (73%). There were moderate correlations between manual microscopy and the two devices, UriSed and Fus100, for erythrocyte ($r = 0.496$ and 0.498, respectively) and leukocyte ($r = 0.597$ and 0.599, respectively) cell counting however the correlation between the two devices was much better for erythrocyte ($r = 0.643$) and for leukocyte ($r = 0.767$) cell counting. *Conclusion:* It can be concluded that these two devices showed similar performances. They were time-saving and standardized techniques, especially for reducing preanalytical errors such as the study time, centrifugation, and specimen volume for sedimentary analysis; however, the automated systems are still inadequate for classifying the cells that are present in pathological urine specimens. J. Clin. Lab. Anal. 27:312–316, 2013.

Key words: Automated urine analysis; Fus100; manual urine sediment analysis; urised

Abbreviations

SG = Specific gravity
HPF = high-power field

INTRODUCTION

Urinalysis is one of the most common examinations performed in microbiological and chemical laboratories, and it is frequently performed on inpatients and outpatients, especially to screen for kidney and urinary tract diseases, as well as for cholestatic, metabolic, and hemolytic diseases (1–3). In most laboratories, the urinalysis is still based on a urine strip analysis and microscopy in spite of the many disadvantages. Many factors have been identified that cause false-positive and false-negative results in the strip analyses, therefore urine strip analysis and microscopy are limited with regard to their precision and accuracy (4). In addition, traditional microscopy is time-consuming and involves the study of a large number of routine urine samples, which means that a long time can exist between voiding and the analysis of the sample, and this decreases the reliability of the results (5). The automation and standardization of the urinalyses could reduce these problems. New generation analyzers, based on different technologies, have been developed to automate microscopy. The main approaches for the auto-quantification and classification of urine particles are Fluorescence Flow Cytometry, which is based on staining particles, and the Digital Microscopic Image based

*Correspondence to: Assistant professor, Dr. Hatice Yüksel, Department of Medical Biochemistry, Dicle Üniversitesi Tıp Fakültesi, Tıbbi Biyokimya Anabilim Dalı, Seyrantepe mevkii 21280-Diyarbakır, Turkey. E-mail: hkyuksel@gmail.com

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technologies. Manufacturers have combined their microscopic analyzers with automated strip analyzers to form workstations, and the H800-Fus100 and the LabUMat-UriSed are the new fully automated devices, which were recently introduced for urine sediment analysis.

The UriSed (77 Elektronika Kft., Hungary) centrifuges urine with specially designed cuvettes, the sediment is then visualized with light microscopy, and a predefined number of high-power field (HPF) digital images are analyzed with recognition software.

The FUS100 (Dirui Industrial Co. Ltd., China) is the other digital image based automatic particle recognition system. The FUS100 uses uncentrifuged urine for digital imaging to capture and analyze 820 photos from each sample for an artificial intelligence identification technology in order to auto-classify the isolated images of the urine sediment constituents, and report them quantitatively.

The aim of this study was to compare the diagnostic performances of the fully automated urine analyzers, the LabUMat-UriSed and the H800-FUS100, with manual microscopy, and to compare these devices with each other.

MATERIALS AND METHODS

Urine Specimens

A total of 332 freshly collected urine specimens, from inpatients and outpatients, submitted for diagnostic urinalysis to our laboratory at the Diyarbakir Obstetrics and Pediatrics State Hospital, were used in this study. The samples were collected without any preservatives and transferred to three different test tubes consisting of 10 mL for manual microscopy, 5 mL for the H800-Fus100, and 5.5 mL for the LabUMat-UriSed. The samples were analyzed within 1 hr of their arrival at the laboratory. The HPF results from the Fus100 and the UriSed devices were recorded for the study. Between- and within-run variations for sediment analysis were determined by repeated measurements (10 times).

Dipstick Urine Analysis

The specific gravity (SG), pH, protein, glucose, ketone, urobilinogen, bilirubin, nitrite, blood, and leukocyte levels were measured by a dipstick analysis.

LabStrip U11Plus (77 Elektronika Kft., Hungary) strips were interpreted on the LabUMat. This device dips the strip in urine, and then puts it in a parallel configuration to avoid cross-color contamination. After the incubation time, it reports 11 biochemical parameters with ascorbic acid, semiquantitatively in the urine.

The H800 Analyzer (Dirui Industrial Co. Ltd., China) uses H10–800 strips (Dirui Industrial Co. Ltd., China). It aspirates and drops urine onto each reaction pad separately in order to avoid cross-color contamination. After the incubation time, it reports 10 biochemical parameters, semiquantitatively in the urine. In addition to the semiquantitative results, the quantitative and accurate SG results measured in the refractometer's units are possible in this system.

Automated Urine Microscopy Analysis

The UriSed operates by performing the microscopic examination of a urine sample in a special disposable cuvette. The UriSed device pipettes a 200 μL urine specimen and creates a preparation of 0.145 mm^2 so that the depth of the native urine in the cuvette becomes 1.1 mm. After centrifuging for 10 s at 260 g (2000 rpm), high-resolution complete views of the field images are recorded automatically by a microscope, by scanning 10 field images. These images are evaluated by a special neural network-based image-processing algorithm. Each image is recognized in "real time" just after recording while the evaluation procedure is running on the image, and the evaluation takes 3–4 s per image. The recognition software is implemented in the UriSed user software, fully developed, and improved by 77 Elektronika. The device also counts the particles by comparing the images obtained from the areas examined with standard images. In addition, it shows the field image to the user and allows corrections and new definitions (6). The UriSed uses Quantimetrix control material, and the control name is DipandSpin. It is a combination product for the dipstick and the microscopic quality control.

The Fus100 (DIRUI Industrial Co., Ltd., China) uses Flat Flow Digital Imaging technology and a trained neural network. The AII (Artificial Intelligence Identification) software is used to classify and quantify the cells and formed particles in the native, uncentrifuged urine. The Fus100 aspirates 0.95 mL of urine, and the particles in the urine sample are directed by axial hydrodynamic focusing with an orthostatic particle orientation to form a single layer through the objective lens of a CCD (charged coupling device) video camera. A digital camera captures 820 frames per sample, which are illuminated by a high-speed flashing light source (40 times per second). The artificial intelligence identification software isolates all visible components and particle images from the whole image, and classifies each particle image according to the shape, contrast, texture, and frequency domain features. The calibration was performed with the Fus Standard Solution (DIRUI Industrial Co., Ltd., China) at the beginning of the study, and as-needed based on a 1-month calibration stability. Before the testing of the urine samples each day the Fus Focus, Fus Positive Control, and Fus Negative Control samples (DIRUI Industrial Co., Ltd., China) were run according to the manufacturer's instructions.

TABLE 1. Semi-quantitative range classification of urine particles

Parameters	Ranges				
Leukocyte, HPF	0–5	6–10	11–20	21–30	>30
Erythrocyte, HPF	0–5	6–10	11–20	21–30	>30
Bacteria, HPF	Negative	Low	Moderate	High	
Cyristals, HPF	Negative	Positive			

HPF; high power field.

TABLE 2. Diagnostic accuracy of sediment analysis, comparing with manual microscopy

	Sensitivity	Specificity	PPV	NPV
Erythrocyte–UriSed	50	94	60	92
Leukocyte–UriSed	82	84	56	95
Erythrocyte–Fus-100	73	86	47	95
Leukocyte–Fus-100	68	89	60	92

Data are given as percentage. NPV; Negative predictive value, PPV; positive predictive value.
Cut-off point for erythrocyte and Leukocyte in microscopy is >5 cells/HPF.

Manual Sediment Microscopy

All of the urine samples were examined by microscopy. The same technician performed all of the microscopic urinalyses with the same microscope in order to minimize interobserver variability. The 10 mL urine specimens were centrifuged at 1500 rpm (400 × *g*) for 5 min and the sediments were prepared for microscopic examination (5). Microscopy was performed within 30 min after the sedimentation of the urine samples. One drop of the sediment was pipetted onto a microscope slide and covered with a cover slip (18 × 18 mm). The microscopic examination was performed by using a light microscope (Olympus, CX21FS1) at the magnifications of 100× for the casts and 400× for the other parameters. The particles were counted per field, and the results were classified semiquantitatively within ranges (e.g. 0–(5–10)), or as negative or positive (Table 1) (7). In all of the calculations, manual microscopy was used as the reference method.

Statistical Analyses

The normality of the parameters was tested by the Kolmogorov–Smirnov test. The Spearman's correlation procedures, including the correlation coefficients (*r*) and the statistical significance, were also calculated in order to correlate the three different methods for the nonparametric data. A value of $P < 0.05$ was considered statistically significant.

RESULTS

All of the urine samples were examined within an hour by the three methods.

The diagnostic accuracy, relative to the manual microscopy for both the UriSed and the Fus100, is shown in Table 2. The UriSed was more sensitive for leukocyte cell counting, while the Fus100 was more sensitive for erythrocyte cell counting.

The within-run and between-run coefficients of variations of the erythrocyte and leukocyte cells for the three methods were shown in Table 3. The manual method showed higher coefficients of variations than the automated systems, especially at lower particle counts.

There were moderate correlations between manual microscopy and two urine sediment analyzers UriSed and Fus100 especially for erythrocyte ($r = 0.496$ and 0.498, respectively) and leukocyte (0.597 and 0.599, respectively) cell counting, and these correlations were statistically significant (Table 4).

The relationships between the two devices for the chemistry and sedimentary analyses were also examined (Table 5). There were good correlations for the chemistry

TABLE 3. The coefficients of variation of the microscopic analysis (UriSed, Fus100 and manual microscopy)

		Within precision				Between precision			
		Level 1		Level 2		Level 1		Level 2	
Method	Cells	Mean ± SD	CV(%)	Mean ± SD	CV(%)	Mean ± SD	CV(%)	Mean ± SD	CV(%)
UriSed	Erythrocyte	6,4 ± 0,5	7,8	61,1 ± 2,5	4,1	3,9 ± 1,1	28,2	22,6 ± 2,1	9,2
	Leukocyte	7,6 ± 1,0	13,1	19,9 ± 2,9	14,5	2.8 ± 0,8	28.5	6,7 ± 1,0	14,9
Fus100	Erythrocyte	3.1 ± 0.6	19.3	25.9 ± 1.3	5.1	0.0 ± [a]	[a]	97.0 ± 4.6	4.7
	Leukocyte	3.3 ± 0.7	21.2	14.8 ± 1.5	10.1	0.0 ± [a]	[a]	5.9 ± 1.1	18.6
Manual	Erythrocyte	2.7 ± 0.9	33.3	15.4 ± 2.1	13.6	2.3 ± 0.7	30.4	14.2 ± 2.9	20.4
	Leukocyte	4.2 ± 1.1	26.1	27.0 ± 2.3	8.5	2.0 ± 0.7	35.0	22.4 ± 2.8	12.5

CV, Coefficients of variations, SD, Standard deviation.
[a]SD and CV did not get calculated because the mean value of erythrocyte and leukocyte results was 0.

TABLE 4. The correlation coefficients of microscopic analysis results between the manual microscopy and automated analyzers

Parameters		UriSed *r*	Fus100 *r*
Manual Microscopy	Erythrocyte	0.496[a]	0.498[a]
	Leukocyte	0.597[a]	0.599[a]
	Bacteria	0.204[a]	0.470[a]
	Epithelial Cells	0.391[a]	0.443[a]
	Crystals	0.503[a]	0.338[a]

r; Spearman correlation of coefficient.
[a] $P < 0.01$.

TABLE 5. Correlation coefficients of parameters between urine analyzers

Strip tests		Microscopy	
Parameters	URISED – FUS100 CC (*r*)	Parameters	URISED – FUS100 CC (*r*)
SG	0.782[a]	Erythrocyte	0.643[a]
pH	0.805[a]	Leukocyte	0.767[a]
Protein	0.501[a]	Bacteria	0.297[a]
Glucose	0.665[a]	Epithelial Cells	0.814[a]
Ketone	0.599[a]	Crystals	0.414[a]
Urobilinogen	0.383[a]		
Bilirubine	0.246[a]		
Nitrite	0.350[a]		
Blood	0.865[a]		
Leukocyte	0.764[a]		

CC, correlation coefficient.
[a] $P < 0.01$ (Spearman correlation of coefficient).

parameters of SG, pH, blood, and leukocytes, and moderate correlations for the protein, glucose, and ketones. The microscopic parameters, such as the leukocyte and epithelial cell counts, showed good correlations, however the erythrocyte counts showed a moderate correlation.

DISCUSSION

The manual microscopic analysis of urine sediment using the traditional urinalysis method may be affected by preanalytical processes such as the centrifugation, sediment preparation, and long analysis times, which may result in imprecision and inaccuracy (8). Recent technical developments have focused on the full automation and standardization of the urinalysis, and may be helpful for shortening the duration of the study and improving the accuracy and precision. Tzu-I et al. suggested that the automation of urine sedimentary examinations may reduce the interpersonal variation and manual review rates, and that it has comparable results to manual microscopy (9). Several studies compared the different models of fully automated urine analyzers with manual microscopy (6, 7, 10–14).

The Fus100 and UriSed are two analyzers currently used for the microscopic examination of urine. The microscopy results are in cells/HPF and cells/low-power field, as in manual microscopy in both analyzers, and it should be appropriate to compare them. To the best of our knowledge, this is the first study that compares the Fus100 and the UriSed. The LabUMat-UriSed was compared with the IQ200, which is the one of the digital microscopic image-based technologies. The Fus100 and the IQ200 run with a similar technology. Akin et al. reported that two automated techniques, the UriSed and IQ200, are highly reproducible and are able to analyze large numbers of urine samples quickly and simultaneously, however it is important to confirm the results by manual urine analysis, especially for the pathological cases at the limits of the techniques, and/or to compare them with the urine strip results (6). Also, Altekin et al. compared the IQ200 with the manual urine analysis, and concluded that the automated techniques are not completely free of error, and therefore combining the results with the strip analysis and other laboratory tests allows for the further reduction of clinically important errors (15).

In this study, the sensitivity of the Fus100 for erythrocytes was higher, while the sensitivity of the UriSed was higher for counting leukocytes. In addition, the sensitivity of the UriSed for leucocytes has been reported to be higher than for the erythrocytes in a previous study (6). The negative predictive value of the two devices was similar and better than the positive predictive value. These results showed that the two devices have low false-negative results, however they can give false-positive results. Therefore, the technician should review especially pathological urine results. In this study, we classified the manual microscopy results semiquantitatively. The sensitivity and specificity of the devices could be better if a standardized method, such as the Fuchs-Rosenthal Cell Chambers or the KOVA® system, was used for the manual microscopy.

The between- and within-precision of the three methods were lower for the specimens with fewer cells (Table 3), although for the specimens containing a large number of cells the reproducibility is much better, which is similar to the previous studies (6). The level 1 control for the Fus100 was a negative control that had no erythrocyte and leukocyte cells, and the SD was not calculated.

The concordance of the two devices with manual microscopy was similar for both the erythrocyte and leukocyte counting with moderate correlations. In the concordance for the bacterial and epithelial cells, the Fus100 was better, however the UriSed was much more concordant for the crystals (Table 4).

The concordance between the two devices was much better than the comparison with manual microscopy. The

strip tests such as the SG, pH, blood, leukocyte, and microscopic tests like the leukocyte and epithelial cell counts (Table 5) showed a good correlation, while the protein, glucose, ketones, and erythrocytes showed a moderate correlation. The nonconcordant parameters such as the urobilinogen, bilirubin, and nitrite could be as a result of the small number of positive specimens for these parameters. The number of the positive specimen results for the urobilinogen, bilirubin, and nitrites were 11, 3, and 8 for the LabUMat, and 0, 5, and 1 for the H-800, respectively.

The fully automated urine devices classify some cells as "unclassified" and allow the technician, who is a trained operator, to correct the designations of the cells. The technician examines all of these cells and makes the correct designations. However, no correction was made in this study to see the results of the devices without correction, therefore the accuracy of the tests could be much better if a trained technician evaluated the results.

The limitation of this study was the diversity of the specimens, because the majority of the specimens were from women and children, and they were outpatients. Therefore, the pathological urine specimen number was small.

It can be concluded that these two devices showed similar performances for automated urine analysis. In addition, they were time-saving and standardized techniques, especially for the preparation of the urine specimens for microscopic analysis. This is important for the prevention of preanalytical errors such as the study time, centrifugation, and specimen volume for sedimentary analysis. However, the automated systems are still inadequate for classifying the cells that are present in pathological urine specimens. There is a need for a new study that evaluates how much a trained technician can change the accuracy of urine analysis results.

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