Original article

Performance Evaluation of Automated Urine Analyzers: Laura XL

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KEYWORDS

LauraXL, Urine sediment, Automated urine analyzer, Microscopic Urinalysis.

ABSTRACT

Background

Urinalysis is the third most used diagnostic screening test in clinical practice. Manual urine analysis is labor-intensive and requires experienced staff for accurate results and interpretation. New-generation automated urianalysers have been introduced with microscopic analysis. The aim of this study was to evaluate the results of LauraXL, automated Urine Analyzer and validate it with UF 4000 Sysmex and manual method. **Method:** A cross-sectional study was conducted on 107 urine samples. Laura XL works on image-based microscopy, whereas UF 4000 works on the principle of flow cytometry. Epithelial cells (EC), red blood cells (RBC), white blood cells (WBC), crystals, cast, and yeast from both machines were compared with manual microscopy. **Results:** The degree of concordance was analyzed. UF4000 showed greater agreement than Laura for WBC, EC, and Crystals, kappa as 0.420, 0.238, and 0.437 respectively ($p < 0.0001$.) Yeast showed substantial agreement with kappa 0.650(UF 4000) and 0.643 (LauraXL). The agreement of Laura with Manual was greater than UF4000 for RBC (kappa 0.360 and $p<0.0001$). UF4000 revealed a sensitivity of >95% for WBC, EC, CAST, Crystal, and Yeast. Similar results were observed for Laura except for Crystal (sensitivity: 81%). **Conclusion:** Both automatic urine analyzers exhibited comparable performances and strongly correlated with manual microscopy. While manual urinalysis remains critical for diagnosis, automated systems offer enhanced efficiency, accuracy, and reliability, making them indispensable in modern clinical laboratories.

Introduction

Urinalysis ranks as the third most utilized in vitro diagnostic screening test in clinical practice, followed by serum chemistry and total blood count. It stands out as one of the most extensively employed non-invasive diagnostic tests for assessing urinary tract and renal disorders. The insights gained from urinalysis are critical for evaluating patients's renal and genitourinary health, as well as monitoring other systemic conditions.[1] The primary indications for urinalysis include the suspicion of urinary tract infection and urinary stone formation, as well as the assessment of renal functions in other systemic disorders like hypertension, diabetes, pregnancy toxaemia, drug-induced renal disease, and so on.[1]

The European Urinalysis Guidelines advocate for a conventional two-stage urinalysis approach. The initial stage involves a meticulous visual inspection combined with a dipstick analysis. If the semi-quantitative dipstick tests for erythrocytes, leukocyte esterase activity, nitrite, and protein come back negative during this phase, the urine samples will not be used for further testing. Microscopy further investigates samples indicating the presence of erythrocyturia, leukocyturia, bacteriuria, or proteinuria in the second stage. However, relying solely on dipstick screening carries the risk of missing infections and other urinary diseases due to its low sensitivity and negative predictive value. [2]

The automation of clinical pathology, once deemed unfeasible, has now become a reality in many large laboratories, thanks to the advent of automated analysers equipped with digital imaging technology. These innovations have revolutionised laboratory practices by introducing new procedures, reorganising workbenches, and establishing schedules that support continuous, round-the-clock operations. [3]

In recent years, a new generation of advanced automated urinalysis devices has emerged, each offering distinct advantages and limitations. Fully automated workstations, which incorporate automated microscopic and strip analyzers, represent a significant advancement in urinalysis technology. [4] In this study, we utilised LAURA XL, Fully Automated Urine Analyser with an image-based analytic system manufactured by Erba Tranasia and compared its results with another automated system UF 4000. The goal of this study was to evaluate the efficacy of these automated urine analyzers compared to manual microscopy to evaluate erythrocytes, leukocytes, epithelial cells, crystals, cast, and budding.

Materials and methods

A prospective observational study was conducted over 3 months on 107 urine samples. The Institutional Ethics Committee clearance was obtained. (Ref No: I.E.S.C/92/2023)

Inclusion criteria

- Urine samples of randomly selected cases admitted indoors and visiting OPD (Outdoor Patient Department) for routine diagnostic urinalysis at the Central Clinical Laboratory of the Department of Pathology, Dr. D. Y. Patil Medical College and Research Centre, Pune, Maharashtra over two months were included in the study.

Exclusion Criteria

- The study excludes samples that are less than 15 mL in volume, contaminated, or spilling out of the container. The study excluded samples containing preservatives and urine collected over 24 hours.
- Urine specimens were collected in preservative-free containers, and transferred to three different test tubes, two for automated urine analyzers which were not centrifuged, and one test tube which was centrifuged for manual microscopy. Within two hours of their arrival at the laboratory, all samples underwent analysis. Specifications of the LauraXL manufactured by Erba Transasia and UF 4000 are shown in Table 1.

Table 1- Specifications of the LauraXL manufactured by Erba Transasia and UF 4000.

General Characteristics	**LAURA XL**	**UF 4000**
Specimen application	Pipetted	Pipetted
Specimen per hour	125	80
Specimen consumption	2.5 ml	0.9 ml
Required specimen volume	2.5 ml	0.9 ml
Data memory	>5,00,000 (Chemistry + sediment)	1,00,00
Physical dimension	1150 x 690 x 580	950x 700 x 450
Physical and chemical parts		
Turbidity method and specific gravity method	Turbidity method	Turbidity method
Wavelength used	488nm	488 nm
Microscopic component		
Specimen application	Cuvettes	Cuvettes
Centrifuge	No	No
Principle of analysis	Automatic microscopy and image analysis	Fluorescence flow cytometry
Stain	No	Yes
Image	Monochrome	Monochrome
Output of image	Image available	Image available

LAURA XL: 5ml urine was taken in a tube, scanned, and loaded in the rack. The rack was then inserted into the machine. The semi-quantitative evaluation of diagnostic strips for urine analysis and digital camera photos were captured and sent to the computer via the eyepiece of the microscope. The programmer categorized these photos before being shown to the operator on the screen.

UF 4000: 5ml urine was taken in a tube, scanned, and loaded in the rack. The rack was then inserted into the machine. The machine asses via the flow cell, specialized light source lights urine, and digital camera photos were captured and sent to the computer via the eyepiece of the microscope. The programmer categorized these photos before being shown to the operator on the screen.

Manual microscopic examinations

Manual microscopic sediment examination was performed following the European Urinalysis Guidelines. 5 mL of each urine specimen was centrifuged at 1500 rpm for 5 min. After centrifugation, the supernatant was removed and the sediment contents were resuspended. A drop was taken on the slide, coverslip was put and examined by light microscope at magnifications of 100x (low power field; LPF) for casts and 400x (high-power field; HPF) for erythrocytes, leukocytes, epithelial cells, and bacteria. The particles were counted per field, and the results were classified into 3 categories for evaluation. erythrocytes, leukocytes and epithelial cells were classified semi-quantitatively (0–1,2-3,3-4,4-5, 6–8,8-10, 10–12, 12-15, 15-20, 20-25, 25-30, 30-40, 40-50, 50-60, 60-70, 70-80, 80-90, and 90-100 cells/HPF). Casts, crystals, and budding yeast

were classified as not found and found. Manual microscopy was used as the reference standard method for urine sediment evaluation in all reports. All samples were independently examined by 3 experienced pathologists using the same microscope slide. The results were accepted when two or three evaluators reported the same category of cells or particles. If all 3 assessors reached notably different results for any particular slide, the analysis was repeated with a new urine sample to resolve the discrepancy.

Evaluation protocols and analysis of results

- **Precision test:** In order to evaluate the analytical performances of the workstations, between- and within-run variations and carry-over measurements of the workstations were evaluated against control material. Liquichek, urinalysis control levels 1 and 2 (Biorad Laboratories, CA, USA) was used to provide analytical quality control, including for erythrocytes, leukocytes, and epithelial cells. We used 20 repetitions for both within-run (20 times within a day) and between-run (once per day on 20 separate days) precision. The precision of each automated urine analyzer was assessed by mean SD and percentage coefficient of variation (CV%). CV values less than 30% are considered to be acceptable.
- **Urine sediment comparisons:** For the sediment component of the study, we evaluated erythrocytes, leukocytes, epithelial cells, crystals, cast, and budding yeast comparing between the automated and the manual method for each analyzer, and among the automated analyzers. Cohen's kappa coefficient was used to estimate agreements between the manual method and the automated urine analyzer results. Values for the kappa coefficient of 0–0.20, 0.21–0.40, 0.41–0.60, 0.61–0.80, and 0.81–1.00 were characterized as poor, fair, moderate, good, and very good agreement, respectively. We categorized the data for crystals, casts, and budding yeast as not found or found. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for these data. Concordance rates of urine sediment with the same grade and within +/- 1 grade difference between the machines were calculated.

Result

- **Precision test: -** The within-run and between-run coefficients of variations, standard deviation, and mean of the erythrocytes, leukocytes, and epithelial cells for the two automated urine analyzers, LAURA XL and UF 4000 are shown in Table 2a and 2b.

Table 2A - Results of Precision Test

LAURA XL.	Mean	Standard deviation	Coefficient of variation
Erythrocytes	179.5	21.63	12.05
Leucocytes	1520.30	46.23	3.04
Epithelial cells	73.50	10.23	13.92

UF 4000	Mean (cell/ul)	Standard deviation	Coefficient of variation (%)
Erythrocytes	156.3	20.63	11.00

Leucocytes	1603.40	43.67	2.99
Epithelial cells	65.33	14.20	10.12

- **Sediment comparison:** The pairwise agreements within the same grade and one-grade difference between the manual and automated methods for erythrocytes, leukocytes, epithelial cells, crystals, cast, and budding yeast were shown in Table 3.

Table 3- Degree of agreement represented as weighted Cohen's kappa result between the manual method and two analyzers.

	LAURA XL Vs Manual		**UF 4000 Vs**	**Manual**
Sediments	Kappa	P value	Kappa	P value
Erythrocyte	0.360 (0.213-0.507)[b]	< 0.0001	0.046 (0.79- 0.171)	0.429[a]
Leukocyte	0.224 (0.820-0.984)[b]	< 0.0001	0.420 (0.068- 0.467) [c]	< 0.0001
Epithelial cell	0.058 (0.045-0.161)	0.145 [a]	0.238 (0.146- 0.622)[b]	< 0.0001
Crystal	0.011 (0.065-0.087)	0.787 [a]	0.437 (0.199- 0.674) [c]	<0.0001
Cast	0.036 (0.006-0.078)	0.343	0.043 (0.006- 0.092)	0.127 [a]
Budding yest	0.643 (0.249-0.856)[d]	< 0.0001	0.650 (0.426- 0.873)[d]	< 0.0001

([a] p value > 0.05, Kappa is not significant. There is no agreement between methods, [b] fair agreement, [c] Moderate agreement, [d] Substantial agreement and [e] substantial agreement.)

- According to the data, erythrocytes showed higher agreement in LAURA XL and Manual's than UF 4000 and Manual's. For leukocytes, epithelial cells, and crystals agreement between UF 4000 and Manual was higher than agreement between Laura's and Manual. Yeast showed substantial agreement between LAURA XL and Manual and UF 4000 and Manual.

- The sensitivity, specificity, and positive and negative predictive values were obtained using established criteria and given in Table 4. The sensitivity of both automated machines is better than the specificity.

Table 4- Sensitivity, specificity, and predictive values of sediment analysis for the automatic urine analyzers compared with manual microscopy

Table 4	Sensitivity (%)	Specificity (%)	PPV* (%)	NPV** (%)
****LAURAXL				
Erythrocyte	95.7	74.1	86.5	90.9
Leukocyte	94.6	41.1	71.7	85.7
Epithelial cell	100	77	88.7	100
Crystal	81	90	27	73

Cast	95	40	61	67
Budding yeast	98	59	93	83
***UF 4000				
Erythrocyte	90.5	56.3	73.1	81.1
Leukocyte	100	71.4	97.1	100
Epithelial cell	100	14.3	94.3	100
Crystal	95	41	89	63
Cast	100	50	45	100
Budding yest	97	64	95	25

- *PPV- Positive predictive value, **NPV- Negative predictive value, *** UF 4000, ****LAURAXL -

The correlations between two automatic analyzers and a manual microscopy are shown in Table 5.

Table 5- Result of correlation of two automated analyzers with manual microscopy.

Table5	**LAURA XL**	**UF 4000**	**Sediment**
M	0.725	0.546	Erythrocyte
A	0.614	0.610	Leukocyte
N	0.368	0.451	Epithelial cell
U	0.90	0.320	Crystal
A	0.029	0.068	Cast
L	0.689	0.466	Budding yest

For leucocytes, epithelial cells, and yeast, there is a significant high correlation (P<.0001) between UF 4000, LAURA XL and Manual. It was found that crystal does not correlate in both LAURA XL and UF 4000 when compared to manual microscopy. The cast does not correspond with Manual or UF400 or LAURA XL.

Discussion -

Indian laboratories recently started adapting automated urine analyzers for routine microscopic examination. To our knowledge, this is the first study in India to compare UF 4000 and LAURA XL with the manual microscopic method.
For the LAURA XL, a urine specimen is pipetted into a special cuvette that employs the principle of digital microscopy with the latest artificial Intelligence technology, to auto-recognize the widest range of urine sediments. The machine takes 15 full-viewed clear and sharp sediment images for each sample and the Intelligent Element Zoom feature allows easy evaluation and labeling of other element types for erythrocytes, leukocytes, squamous epithelial cells, casts, crystals, and yeasts.[8] LAURA XL shows a similar principle as that of Cobas 6500 except for preparation of the sample; LAURA XL machine uses the sample directly whereas Cobas 6500 one centrifuges the sample. [5]

In this study, we have focussed mainly on the microscopic examination of erythrocytes, leukocytes, epithelial cells, crystals, cast, and budding yeast and had not considered biochemical analysis. [5]

Erythrocytes, Leukocytes, Epithelia Cells-

T Piraya et al[5] compared few automated urine analyzers with manual microscopic urinalysis. The study stated that agreement between the manual method and the three instruments was very good to good for erythrocytes, leukocytes and epithelial cells.

We found that the agreement between LAURA XL and Manual was greater than the agreement between UF 4000 and Manual for erythrocytes, on other hand agreement between UF 4000 and Manual was greater than that between Erba LAURA XL and Manual for leukocytes, and epithelial cells. Our study showed that the sensitivity of the automated measurements was better than their specificity. In more than 95% of the urine samples UF 4000 identified leukocytes and epithelial cells correctly, and for erythrocytes, 90% of urine samples were reported. In our study, Erba LAURA XL and Sysmex UF 4000 were performed with the same sensitivity. Erba LAURA XL generates above 70% negative results for erythrocytes and epithelial cells in the urine samples where the sediments were absent, and UF 4000 showed specificity of 71.4% and 56.3% of samples of urine sample for erythrocytes and leukocytes respectively. [5]

Crystals-

Khillare, et al[6] compared automated urine analyzers with a manual microscopic examination for urinalysis at tertiary care hospital, they studied Iris iQ® 200 which has a similar feature as that of Erba Mannheim Urine Analyser LAURA XL, here they concluded that agreement between Iris iQ® 200 and manual microscopy was good and similar results are seen in our study. In our study we also UF 4000 (Sysmex Corporation, Kobe, Japan) along the side of Erba Mannheim Urine Analyser LAURA XL with manual microscopy and found that the agreement between UF 4000 (Sysmex Corporation, Kobe, Japan) and Manual was greater than that between Erba Mannheim Urine Analyser LAURA XL and Manual. **Khillare, et al**[6] also found that some false-positive results due to the evaluation of dysmorphic erythrocyte as crystal by Iris iQ200. They also stated that the automated instrument detects fewer samples in comparison with the manual method, similar results were seen in our study for Erba Mannheim Urine Analyser LAURA XL with positive predictive value and negative predictive value as 27% and 73% respectively. Many other studies recommend careful manual microscopic re-inspection for the classification and confirmation of crystals. [6]

Cast –

A study conducted by **Khillare et al**[6] compared automated urine analyzers with a manual microscopic examination for urinalysis at a tertiary care hospital, they studied Iris iQ® 200 which has similar features as that Erba Mannheim Urine Analyser LAURA XL. The study showed that detection of the cast by the automated system was difficult. The automated urine analyzer showed substantial agreement with manual microscopy. In our study, we compared Erba Mannheim Urine

Analyser LAURA XL and UF 4000 (Sysmex Corporation, Kobe, Japan) with manual microscopy, for study considered all casts in a single group which showed moderate and substantial agreement with manual methods by two machines respectively. **Ince FD, et al**[1] in their study found out that there is poor agreement between automated machine and manual microscopy methods for cast.[1] **Shayanfar, et al**[7] stated that Iris iQ® 200 was good at detecting casts but unable to distinguish the type of cast. Our machine Erba Mannheim Urine Analyser LAURA XL could differentiate different casts as being an image-based artificial intelligence machine that recognized the elements. Both **Ince FD, et al**[1] and **Shayanfar, et al**[7] studies recommended manual microscopic examination in the presence of casts.

Yeast-

According to **Chien, et al**[8] yeast cells/crystals were not key elements for basic particle analysis and could be eliminated by adjusting the corresponding thresholds in Iris iQ200 reports. It also stated that Iris iQ® 200 had a high false positive rate for yeast cells. In a study done by FD İnce, there is a fair agreement for yeast cell analysis between Iris iQ200 and the manual microscopic method. [8]

Similar results were found in our study which showed substantial agreement for both UF 4000 (Sysmex Corporation, Kobe, Japan) and manual, Erba Mannheim Urine Analyser LAURA XL and manual.

Limitation-

The primary limitation of the study was random sample selection rather than focusing on renal-specific samples. Hence, we could not differentiate between squamous and non-squamous epithelial cells. Type of crystal and amorphous mass; and types of candida and mycelia for yeast were not analyzed. Hence this was considered as a pilot study. There is a future scope of study on patients with renal disease with a larger sample size. Our results for the UF 4000 and LAURA XL could not be compared with others in the literature, due to the lack of published studies on this instrument.

Conclusion –

- An automated analyzer can efficiently analyze a substantial quantity of samples within a limited timeframe, therefore reducing the turnaround time.
- The Erba Mannheim Urine Analyser LAURA XL showed more sensitivity toward the detection of erythrocytes as compared to UF 4000 whereas UF 4000 showed more sensitivity toward the remaining sediment elements i.e, leucocytes, epithelial cells, crystals, cast, and budding yeast. Nevertheless, to prevent any mistake or ambiguity, in pathological situations, some elements like dysmorphic cells, bacteria, squamous and non-squamous epithelial cells, pathological and physiological casts, and types of crystals had to be confirmed by manual microscopic examination. Consequently, the software programs employed in automated urine sediment analyzers need further enhancement to precisely recognize urinary-shaped components. Automatic urine analysis is becoming more important in India owing to the large volume of urine samples received, which makes the manual microscopic approach impractical. Systematic automation is crucial for saving time and establishing standardization.
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