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Discrepancy in chemical and microscopic urinalysis: Looking from a laboratory perspective

Kimyasal ve mikroskobik idrar tahlilinde tutarsızlık: Laboratuvar perspektifinden bakış

Bayram Şen **Medeni Arpa**

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ABSTRACT

Objective: The discrepancy between chemical and microscopic urine examination makes it demanding to interpret the results. We aimed to evaluate the laboratory personnels' effect on the consistency between chemical and microscopic urine examination results.

Material and Methods: The urinalysis results of a tertiary hospital's core and supervised laboratory between 2019 and 2020 were evaluated retrospectively. The consistency between chemical and microscopic urine examination and laboratory personnel's effect on this compliance was examined by correlation and measurement of agreement analysis.

Results: The core laboratory had higher consistency in erythrocyte count and blood, leukocyte count and leukocyte esterase. Accordingly, we determined that a yeast cell count of >30 significantly reduced the conformity between blood and erythrocyte counts in the supervised laboratory. The correlation between erythrocyte count and blood increased when controlling for yeast cell count for supervised and core laboratory.

Conclusion: Laboratory personnel significantly affect the consistency between automated urinalysis chemical and microscopic examination results. For the reliability of the results, it is essential to reduce the unnecessary workload of laboratory personnel and increase the time they will spend on specific tests.

Keywords: Urinalysis, chemical examination, microscopic examination, laboratory personnel

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ÖZET

Amaç: İdrarın kimyasal ve mikroskobik inceleme sonuçları arasındaki tutarsızlık, sonuçların yorumlanmasını zorlaştırmaktadır. Bu çalışmada laboratuvar personelinin kimyasal ve mikroskobik idrar tetkik sonuçları arasındaki tutarlılığa etkisini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Üçüncü basamak bir hastanenin merkez ve uzaktan gözetimli laboratuvarının 2019-2020 yılları arasındaki tam idrar tetkiki sonuçları retrospektif olarak değerlendirildi. Kimyasal ve mikroskobik idrar incelemesi arasındaki tutarlılık ve laboratuvar personelinin bu uyum üzerindeki etkisi, Spearman korelasyon analizi ve Kappa uyum analizi ile incelenmiştir.

Bulgular: Merkez laboratuvar, eritrosit sayısı ile kan ve lökosit sayısı ile lökosit esteraz arasında daha yüksek tutarlılık düzeyine sahipti. Ek olarak 30'dan fazla maya hücresi varlığının, gözetimli laboratuvarda kan ve eritrosit sayıları arasındaki tutarlılığı önemli ölçüde azalttığını belirledik. Gözetimli ve merkez laboratuvar için maya hücresi sayısı kontrol edildiğinde eritrosit sayısı ile kan arasındaki korelasyonun arttığı görüldü.

Sonuç: Laboratuvar personeli otomatize idrar analizi kimyasal ve mikroskobik inceleme sonuçları arasındaki tutarlılığı önemli ölçüde etkilemektedir. Sonuçların güvenilirliği için laboratuvar personelinin gereksiz iş yükünün azaltılması ve spesifik testlere harcayacakları sürenin arttırılması gerekmektedir.

Anahtar Kelimeler: İdrar tahlili, kimyasal inceleme, mikroskobik inceleme, laboratuvar personeli

INTRODUCTION

Urinalysis, which is evaluated via physical, chemical, and microscopic examination has a vital role in the diagnosis of urinary system infections, kidney function disorders, and systemic diseases and also in monitoring disease severity (1-4). Chemical urinalysis which performed via dipstick comprise blood, leukocyte esterase (LE), nitrite, protein, glucose, bilirubin, urobilinogen, ketone, pH, and specific gravity. Urinary tract infection affects 150 million people worldwide each year (5, 6). Although Escherichia coli is the most isolated common pathogen, agents such as Enterococcus, Klebsiella, Pseudomonas, Proteus, and Candida can also be detected (5, 7, 8).

Although manual examination of urine samples has been used as the gold standard for many years, it is time-consuming, labor-intensive, subjective, and needs high experience. Besides, the manual examination has no standard procedure for urine centrifugation and has low reproducibility (9, 10).

Autoanalyzers have become widely used today for urinalysis. They have advantages such as being more standardized, having better reproducibility, and analyzing large numbers of samples in a short time. Although recent improvements in automated urine analyzers have brought extra advantages such as decreased number of unnecessary urine culture requests, guide antibiotic treatment, and reduced workload in the laboratory, the need for a manual examination of urine samples still remains (3, 11, 12).

Whole urinalysis can be commonly performed in autoanalysers, but microscopic examination alone is also available as a reflex test after chemical analysis to reduce cost (3, 13). In recent years, although urinalysis is mostly performed with automated devices, incompatibility between microscopic and chemical examination, flagged results, and results with microscopic images that cannot be distinguished require manual microscopic examination of samples (10).

Urine culture is necessary to determine the infectious agent and select the appropriate antibiotic used in treatment for urinary tract infections. However, it has disadvantages, such as the risk of contamination, prolonged result times, and a high rate of negative culture results (5, 14, 15). It is suggested that urinalysis can be used as a marker to reduce the number of urine culture requests

(3, 14). But the difference between urine analyzers' methods, mismatching of particles, factors that interfere with the chemical examination, and inexperience of laboratory personnel cause differences in the tests' sensitivities and specificities.

In this study, we aimed to evaluate the compatibility between chemical and microscopic urinalysis results of autoanalyzers located in the core and supervised laboratories, and possible effect of laboratory personnel on this.

MATERIALS AND METHODS

Our study was conducted at a university hospital's core (LAB-1) and supervised (LAB-2) biochemistry laboratories. While the LAB-1 mostly serves clinics and polyclinics, the LAB-2 serves the emergency department, and other clinics and intensive care units. Urinalysis is performed during mid-week (08.00-17.00) in the LAB-1 with a fixed laboratory personnel responsibility and 24 hours/7 days in the LAB-2 with eight laboratory personnel responsibility in 24-hour shifts through automated systems. There was no substantial change in the personnel and working conditions throughout the study. While there is at least one laboratory specialist regularly in the LAB-1, the urinalysis is carried out by laboratory personnels under the laboratory specialist's remote supervision in the LAB-2. Urinalysis was performed in both laboratories with BT URICELL 1280-1600 instruments (BT products, Izmir, Turkey) in 2019 and FUS200-H800 (DIRUI Industrial Co., China) in 2020.

The chemical urinalysis results as blood, LE and microscopic analysis results as erythrocyte, leukocyte, and yeast cell counts were obtained retrospectively. The patients' age and gender data and the clinics where urine samples were sent were recorded.

There was a routine presampling procedure for patients that recommended cleaning their external genitalia before midstream urine sampling (16). Patients urinate in the sample container (vacuum system urine container Makrolab, Konya, Turkey). Urine samples were analyzed within an hour after delivery to the laboratory. Positive and negative internal quality control practices were performed daily and external quality control practices monthly in both laboratories.

Original brand strips were used in BT (REF: 11100) and Dirui (REF: 231011501001) for chemical urinalysis. Erythrocytes, leukocytes, and yeasts were counted in each high-power field (HPF, x 400 magnification) for microscopic urinalysis. Erythrocyte and leukocyte counts were categorized into four groups as 0-5/HPF, 6-20/HPF, 21-50/HPF and >50/HPF. Yeast count was categorized as negative (0-2/HPF), trace (3-14/HPF), 1+ (15-29/HPF), 2+ (30-99/HPF), and 3+ (≥ 100/HPF). It is known that yeast cells can be recognized as erythrocytes in image-based analyzers [17, 18]. Thus, yeast cells were also categorized as <30 and >30, taking into account the threshold value of 2+, to determine yeast cells' effect on the agreement between the image-based erythrocyte count and blood.

The chemical urinalysis is performed by reflectance photometry and microscopic urinalysis by digital image-based automatic particle recognition system in both devices with a non-centrifuged sample. The agreement and correlation between blood and erythrocyte count; also, LE and leukocyte count were evaluated separately for each laboratory.

Local ethics committee approval obtained for the study (Decision number 2021/53).

Statistical analysis

Statistical analyzes were performed using IBM SPSS Statistics, Version 22.0 (SPSS Inc., Chicago, USA). Descriptive statistics of each group were reported as frequency and percentages within the group (n, %). Spearman correlation analysis and measurement of agreement analysis were

performed to examine the relationship between ordinal variables and rho correlation and kappa coefficients were reported. To exclude the confounder effect of variables, partial correlation analysis was performed. The significance limit was accepted as p <0.05.

RESULTS

The patients' distribution according to their application to the hospital and the data regarding the number of tests performed in the laboratories have been given in Table 1.

We determined that the correlation and agreement coefficients between the erythrocyte count and blood level were higher in LAB-1 for both analyzers. Likewise, LAB-1 had also higher correlation and agreement coefficients between leukocyte count and LE. We found that the lowest coherence was in the BT LAB-2 group, and the highest in the Dirui LAB-1 group (Table 2-3).

Table 1. Distributions of gender and application method of patients to the hospital.

		BT LAB-2 n (%)	BT LAB-1 n (%)	DIRUI LAB-2 n (%)	DIRUI LAB-1 n (%)
Application	Emergency	12237 (69.8)	22 (0)	6377 (63.4)	10 (0)
	Outpatient	362 (2.1)	47784 (94.6)	282 (2.8)	24163 (94.3)
	Inpatient	2611 (14.9)	2528 (5)	1552 (15.4)	1263 (4.9)
	Intensive care	2316 (13.2)	184 (0.4)	1841 (18.3)	178 (0.7)
Gender	Female	10194 (58.2)	30347 (60.1)	5529 (55)	15156 (59.2)
	Male	7332 (41.8)	20171 (39.9)	4523 (45)	10458 (40.8)

Table 2. Association and agreement between erythrocyte and blood based on analyzer.

			Erythrocyte count					Spearman Correlation		Measure of Agreement	
Analyzer			**0-5**	**6-20**	**21-50**	**> 50**	**Total**	**rho**	**p**	**Kappa**	**p**
LAB-2/BT	**Blood**	Negative	9839	700	97	50	10686	0.72	<0.001	0.47	<0.001
		+	1371	763	189	136	2459				
		++	437	452	258	401	1548				
		+++	337	421	452	1623	2833				
LAB-1/BT	**Blood**	Negative	42203	420	23	0	42646	0.74	<0.001	0.54	<0.001
		+	2693	1511	325	83	4612				
		++	329	749	446	718	2242				
		+++	20	51	90	857	1018				
LAB-2/DIRUI	**Blood**	Negative	4386	726	156	70	5338	0.76	<0.001	0.50	<0.001
		+	645	629	223	110	1607				
		++	167	373	309	244	1093				
		+++	29	164	322	1499	2014				
LAB-1/DIRUI	**Blood**	Negative	18312	554	24	5	18895	0.78	<0.001	0.58	<0.001
		+	1602	1467	282	58	3409				
		++	245	795	383	170	1593				
		+++	54	224	293	1146	1717				

Table 3. Association and agreement between Leukocyte count and LE based on analyzers.

Analyzer			Leukocyte count					Spearman Correlation		Measure of Agreement	
			0-5	6-20	21-50	> 50	Total	rho	p	Kappa	p
LAB-2/BT	LE	Negative	10327	1916	351	215	12809	0.72	<0.001	0.43	<0.001
		+	460	818	473	366	2117				
		++	41	221	368	825	1455				
		+++	55	49	105	936	1145				
LAB-1/BT	LE	Negative	38134	2403	121	13	40671	0.84	<0.001	0.61	<0.001
		+	697	3017	1248	372	5334				
		++	38	638	1070	1374	3120				
		+++	5	31	130	1227	1393				
LAB-2/DIRUI	LE	Negative	6384	855	171	81	7491	0.75	<0.001	0.51	<0.001
		+	154	160	85	32	431				
		++	105	219	148	113	585				
		+++	61	203	262	1019	1545				
LAB-1/DIRUI	LE	Negative	18926	918	27	6	19877	0.87	<0.001	0.64	<0.001
		+	396	1048	397	94	1935				
		++	102	670	658	383	1813				
		+++	25	211	407	1346	1989				

LE: Leukocyte Esterase

Yeast groups were compared to assess possible yeast interference on the erythrocyte count. Accordingly, we determined that in the group with yeast cell count >30, the agreement level and the correlation between erythrocyte count and blood decreased significantly in the LAB-2 (Table 4.). It was seen that the correlation between erythrocyte count and blood increased when controlling for yeast in LAB-2 (rho: 0.765; p <0.001) and LAB-1 (rho: 0.812; p <0.001).

Table 4. The effect of yeast cells on the agreement between RBC and blood.

LAB-2 vs LAB-1				Erythrocyte		Spearman Correlation		Measure of Agreement	
				0-5	>5	rho	p	Kappa	p
LAB-2	Yeast <30	Hb	Negative	13129	2763	0.629	<0.001	0.628	<0.001
			Positive	2167	9057				
	Yeast >30	Hb	Negative	78	54	0.456	<0.001	0.456	<0.001
			Positive	47	283				
LAB-1	Yeast <30	Hb	Negative	58867	2608	0.768	<0.001	0.768	<0.001
			Positive	2799	11665				
	Yeast >30	Hb	Negative	55	11	0.85	<0.001	0.845	<0.001
			Positive	2	125				

DISCUSSION

Whole urinalysis consists of physical examination, evaluation of chemical properties, and microscopic examination of urine sediment manually or employing autoanalysers. Manual microscopic examination has disadvantages compared to autoanalysers such as more time consuming, professional and well-trained personnel need, workload excess (9, 12). In addition, factors such as failure to fully apply standard procedures during preparing urine sediment and lysis of cells during centrifugation may negatively affect the analysis process (12).

Although implementing autoanalysers remarkably accelerates the analysis process, it is known that microscopic examination is insufficient in the presence of particles such as casts, crystals, yeasts and requires the assessment of a significant part of the samples on the device or manual inspection in some samples. Studies have shown that 4-49% of autoanalyzer results require manual examination (10, 17-19). Urine autoanalysers require manual assessment due to discrepancies encountered during both chemical and microscopic analyses. Therefore flagged results must be examined manually by experienced and well-trained personnel (10).

In our study, in which we evaluated the agreement between the chemical and the microscopic urinalysis results of two different autoanalyzers, we observed that the correlation between the core laboratory results was higher. Although analyzer applications and long-term periodic maintenance are made by the same technical service, and our laboratory personnel go through similar training processes, the consistency was higher in the core laboratory. The fact that laboratory staff routinely dealt with a single instrument and spent more time on instrument images was contributed to the high agreement in the core laboratory.

Although, our primary goal was not to compare device performances, we have seen a higher compliance rate for the Dirui analyzer in both laboratory results. While there was one personnel appointed only for the urine analyzer in the core laboratory, a total of 8 personnel, two on each shift, in the supervised laboratory for the urine analyzer, hemogram, biochemistry, coagulation, immunoassay, and blood gas analyzers. Each result was carefully could examined regardless of flags in core laboratory. On the other hand, personnel in a remote supervised laboratory cannot devote that much time to urine analyzers at the same frequency. These may be some of the reasons for poor compliance.

In studies evaluating the harmony between chemical and microscopic urinalysis, varying levels of correlation between erythrocyte count and blood, leukocyte count and LE, bacteria and nitrite were mentioned (10). Correlation rates include 85.6-93.3% between erythrocyte count and blood, 91.6-96.1% between leukocyte count and LE were reported (10, 20). Although our study's compliance rates are lower than the studies mentioned, both the different cut-off values, and the compliance criteria used and the variability in the laboratories' organization can explain this difference.

It is well known that urine analyzers can misclassify yeast cells as erythrocytes (10, 21, 22). For this reason, the microscopic images of these samples should be examined and, if necessary, manual microscopic examination should be done. We observed that yeast cells significantly reduced the correlation between the erythrocyte count and blood level in urine samples, especially in the supervised laboratory. This finding supports that the process of evaluating urinalysis under supervised laboratory conditions was not very satisfactory.

It has been reported that urine specific gravity, antibiotics, mismatching of epithelial cells as leukocytes, high concentrations of glucose or protein may be the reasons for the incoherence between the leukocyte count

and LE (16, 23). We observed that the core laboratory compliance was better than the supervised laboratory for both devices. The diversity of the urine samples might have a contribution.

Nitrite is formed due to the conversion of nitrate compounds in the diet by enzymes in bacteria. For this transformation to occur, sufficient nitrate compounds must be taken with the diet, the urine must wait for a particular time in the bladder (up to 4 hours), and the bacteria must have the enzyme that can transform (16, 24).

Increasing the number of patients day by day, requesting laboratory tests from asymptomatic patients due to malpractice concerns, and continuous expansion of test panels contributed to the increase in laboratories' workload. The request for the patients' test results to be concluded in a shorter time puts time pressure on the laboratories. This immoderate workload on the laboratory personnel creates an obstacle to allocating sufficient time for each sample. This situation decreases the evaluation time allocated to each test. Although urine analyzers lead to shortening of turnaround time, problems related to analysis necessitate examining a significant part of the samples by the laboratory personnel concerning the methods used. Despite regular on-the-device training, not enough time to fully evaluate each test becomes one of the reasons for the lack of consistency between analysis results.

While there are studies in the literature in which the compatibility of urine analyzers is compared with manual examination and the consistency between chemical and microscopic urinalysis is evaluated, there is no study investigating the effect of laboratory personnel on this discrepancy to our knowledge (2, 11, 12, 23, 25).

Including a large number of samples and the fact that there were no significant changes during the working period, are our study's advantages. Due to the nature of retrospective studies, patients were not asked about their symptoms. Assessing device compliance for symptomatic patients may result in increased compliance rates (14, 26).

The discrepancy between the chemical and the microscopic urinalysis results is a common situation that makes it difficult for the laboratory specialists to decide whether the tests will be approved and for the clinician to interpret the results. In some studies, it is recommended to perform the urinalysis in steps, first chemical examination, if there is an abnormal finding in the chemical examination, microscopic examination, and culture tests as reflex tests (3, 13, 14). As seen in our study, besides interfering conditions, user performance is an essential factor affecting the consistency between chemical examination and microscopic examination. We suggest that chemical and microscopic examination are complementary and should not be used interchangeably. Both analyses should be performed for all urine samples.

CONCLUSION

It should be noted that the compatibility between chemical and microscopic examination in urine analyzers highly depends on the laboratory personnel. In order to prevent this, user dependency should be reduced with technological improvements. Laboratory personnel should be assigned, especially considering excessive workload of the emergency polyclinic. For the reliability of the results it is necessary to reduce the unnecessary workload of laboratory personnel and increase the time they will spend on tests.

Conflict of interest

None.

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