Artificial Intelligence based analysis to evaluate for RBC cells, Pus cells and Calcium Oxalate crystals in Urine sediment slide microscopy: A pilot study in North India

Ankit Agrawal, BDS; Shelley Saxena, B.E., MBA

[*] BDS, Sevamob Ventures Limited, Lucknow, U.P, India
[**] B.E, MBA, Sevamob Ventures USA Inc

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***Abstract*- Introduction:** Microscopy is the simplest and the most important step in the diagnosis of infections (urinary tract, kidney, prostate), sexual transmitted infections (STI), kidney or bladder stones, hemophilia, interstitial cystitis, bacteremia with sepsis, prostatitis and parasites. But the microscopy requires considerable experience and is bound to have human errors. Artificial intelligence (AI) based microscopy can be an answer to this problem. AI can be used even where expert microscopists are not available. Sevamob provides artificial intelligence enabled healthcare platform to organizations. It uses deep learning for image recognition, machine learning for triaging and computer vision for object counting. AI models of various medical conditions are first trained in the software from anonymized image data procured from various sources and then tested on the test set. To determine the accuracy of AI based point-of-care screening solution for urine sedimentation, following were used: Android Smartphone / tablet with Sevamob app, tripod and a simple microscope. The system was operated by a nurse or a technician with minimal training.

Methods: 100 ml urine samples from clinically suspected infections (urinary Tract, kidney, prostate), sexual transmitted infections (STI), kidney or bladder stones, hemophilia, interstitial cystitis, bacteremia with sepsis, prostatitis, parasites and dehydration were included in the study.

Results: Out of these 196 smears, 40 had RBCs, 90 had pus cells, 38 had calcium oxalate crystals and 18 smears were negative when examined by an expert Pathologist. These smears were also analyzed by the AI system. Overall accuracy of AI was 64.06% for RBCs, 89.81% for pus cells and 87.50% for calcium oxalate crystals. The sensitivity of AI based microscopy was 58.54% for RBCs, 82.47% for pus cells and 65.31% for calcium oxalate crystals and the specificity was 94.44% for the supported conditions.

Conclusion: This shows that Sevamob's AI based microscopy system can be very useful to find RBCs, pus cells and calcium oxalate crystals in the urine samples. These indicate the likelihood of one or more of the following medical conditions - infections (urinary tract, kidney, prostate), sexual transmitted infections (STI), kidney or bladder stones, hemophilia, vigorous exercise, interstitial cystitis, bacteremia with sepsis, prostatitis, parasites or dehydration. The system has the potential to replace expert microscopists in the future. Further, the sensitivity and the specificity depends on the threshold used by the AI system.

Index Terms- RBC Cells , Pus Cells , Calcium Oxalate crystals, Artificial intelligence, Microscopy

To,
The Editor
Respected Sir,
I am submitting an original article manuscript entitled "Artificial Intelligence based analysis to evaluate for RBC cells , Pus cells and calcium Oxalate crystals in Urine sediment slide microscopy: A pilot study to know the efficacy of the software " for your consideration.

Sevamob provides artificial intelligence enabled healthcare platform to organizations. It consists of AI based triage and point-of-care screening, telehealth and popup clinics. We provide this platform to various B2B customers in India and the US.

Infections (urinary tract, kidney, prostate), sexual transmitted infections(STI), kidney or bladder stones, hemophilia, interstitial cystitis, bacteremia with sepsis, prostatitis, parasites and dehydration are common in some of these countries and due to the lack of expert microscopists, timely diagnosis is very difficult. To overcome this issue, we have developed an artificial intelligence-based system to diagnose these diseases in the sediment urine sample, simply with the help of technician or nurse and our app.

We therefore did the above-mentioned study and came out with some interesting findings which we would like to publish in your esteemed journal. These findings can be applied by the clinicians right away and may decrease the wrong diagnosis of the above-mentioned medical conditions in remote areas where expert microscopists are not available.

Thanking you,

Yours Sincerely
Dr. Ankit Agarwal
Chief Medical Officer
Sevamob Ventures Limited

I. Introduction

Microscopy is the first and the foremost step in the diagnosis of infections (urinary tract, kidney, prostate), sexual transmitted infections (STI), kidney or bladder stones, hemophilia, interstitial cystitis, bacteremia with sepsis, prostatitis and parasites. The urine discharged by healthy people is ought to be clear and sterile, however certain sediments in the urine can reflect the corresponding diseases. For example, from the appearance of a great quantity of WBCs in the urine we can speculate that the patient has urinary system inflammation. A large number of RBCs, calcium oxalate crystals (CAOXs), and hyaline casts (HYALs) shows that the patient has urinary tract calculi and so on [1].[33].[34]. Therefore, microscopic examination of micro-particles in human urine analysis is one of the most important external diagnostic projects in nephrology and urology departments. Compared with the urine dry chemical method, urine sediment microscopy can directly reflect the corresponding symptoms of patients using microscopic images, and plays an irreplaceable role in urine analysis [35],[36].[1]. Also, in remote areas, due to the lack of expert microscopist, timely diagnosis at initial level is not possible, which may lead to increased morbidity. Artificial intelligence (AI) based microscopy can be an answer to overcome this problem. AI can be used even in the remotest areas where expert microscopists are not available.[3] The use of artificial intelligence in medicine is currently of great interest.[2,4,5,6] The diagnostic and predictive analysis of medical photos, for instance, photographs of skin lesions, microscopic pathological images[9-11] and radiological images are one of the clinical practice fields where artificial intelligence is expected to have a major influence.[7-14].This potential usefulness is largely due to the advances in deep learning with artificial deep neural networks (NN),which consist of a stack of multiple layers of artificial neuronal links that loosely simulates the brain's neuronal connections, and methods specialized for analysis of images, such as the convolution neural network, a particular form of deep neural network that conceptually mimics the visual pathway [12,15,17]. Adoption of artificial intelligence tools in clinical practice requires careful, meticulous confirmation of their clinical performance and utility before the adoption.[16] Based on the urgent need for data standardization and interoperability in digital microbiology, we launched a cross-departmental prospective quality improvement project to incorporate artificial intelligence digital microbiology technology and outline the resource requirements for implementation. The solution presented here empowers microbiologists and pathologist to gain an appreciation of and enable the assessment of the appropriateness of the AI system for diagnosis. We have also shown that current AI systems can aid in the timely diagnosis of infections in resource constraint setting of developing countries like India. The use of artificial intelligence-based diagnosis and data regarding the same is scarce to the best of our knowledge.

Sevamob provides artificial intelligence enabled healthcare platform to organizations. It uses deep learning for image recognition, machine learning for triaging and computer vision for object counting. AI models of various medical conditions are first trained in the software from anonymized image data procured from various sources and then tested on the test set. The software can then be used to screen for these medical conditions in new samples. The system can work fully offline in the last mile, low resource settings. We therefore planned this study with the aim to evaluate AI for identification of the above mentioned medical conditions in urine samples.

II. Methods

This study is a retrospective observational study and this study was done at three Sevamob pop-up clinics at Lucknow, Jharkhand and Rajasthan in India. Urine samples from 196 clinically suspected patients of infections (urinary tract, kidney, prostate), sexual transmitted infections (STI), kidney or bladder stones, hemophilia, interstitial cystitis, bacteremia with sepsis, prostatitis and parasites were taken to do this study. To determine the accuracy of AI based point-of-care screening solution for sediment urine sample, following were used: Android Smartphone/tablet with Sevamob app, tripod and a simple microscope. The system was operated by a nurse or a technician with minimal training. The user first prepared sediment urine samples slides of the above mentioned suspected medical conditions.

To perform the sediment urine microscopy, urine was collected from catching the mid-stream urine in the correct container (at least 50-100 ml, opening of at least 5 cm diameter) in appropriate patient preparation and manner. Once the sample of urine was properly collected, 10 to 15 ml of the well-mixed urine was poured in to a test tube and placed in a centrifuge (the test tube should always be balanced with a second test tube filled with water/another urine sample) of equal volume centrifuge the sample at low speeds of between 2,000 to 3,000 rounds per minute for about 3 to 5 minutes. The supernate was decanted (to retain about 0.2- 0.5 ml inside the tube), shaken and the supernate was retained in the test tube. A drop of the re-suspended sediment was placed on a microscopic slide by using a pipette and a cover slip was placed over the drop. It was ensured that the specimen filled the area under the coverslip without overflowing and that there were no bubbles in the specimen under the coverslip. The smear was analyzed both by an expert microscopist and by the AI based system.

For the AI analysis, the user used the smartphone app to analyze camera feed of microscopic images of various sections of the slide. The app confirmed if the sample had RBCs, pus cells or calcium oxalate crystals and even marked it on a live camera feed. The detection of RBCs, pus cells and calcium oxalate crystals was done onsite by Sevamob AI which worked fully offline on mobile and could be synced with the cloud once the network was available. The AI was previously trained to detect RBCs, pus cells and calcium oxalate crystals and it showed the percentage probability of the detected concepts. A threshold of 60% was used to consider a sample positive for a concept. The AI results were compared with those of an expert microscopist. The evaluation of true positive, true negative, false positive and false negative was done based on the result of the comparison between the expert and the AI result.

Inclusion criteria for sediment urine sample slide examination: We included 196 patients who came for routine Urine evaluation in microbiology at our site, Consent was taken from the patient/ patient attendant when they came for routine Urine in microbiology lab. Exclusion criteria: All the patients on chemotherapy and radiotherapy and women who were having periods at that time.

III. Results

We analyzed 196 sediment urine sample slides as shown in table 1. Out of these 196 smears, 40 were positive for RBC, 90 were positive for pus cells, 38 smears were positive for calcium oxalate crystals and 18 smears were negative when examined by an expert pathologist. These smears were also analyzed by AI system. The overall accuracy of AI was 64.06% for RBCs, 89.81% for pus cells and 87.50% for calcium oxalate crystals. The sensitivity of AI based microscopy was 58.54% for RBCs, 82.47% for pus cells and 65.31% for calcium oxalate crystals and the specificity was 94.44% for all the supported concepts. Based on these findings, sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratio of AI based microscopy were calculated. These are depicted in table 1, 2 ,3, 4 & 5.

Table 1. Results of the AI system

Testing Input				**Testing output (App.)**			
RBC	PUS CELL	Cal. OXALATE	Normal	RBC		PUS CELL	
				Correct	Incorrect	Correct	Incorrect
46	90	38	18	22	24	80	10

Table 2. Accuracy of each concept in the AI analysis

Accuracy RBC + Normal	60.93%
Accuracy Pus Cells + Normal	89.81%
Accuracy Calcium Oxalate crystals + Normal	91.07%

Table 3. Results of an expert microscopist

Sample	**Test**	**Positive**	**Negative**
Urine	RBC	46	18
	Pus cell	90	18
	Calcium Oxalate Crystals	38	18

Table 4: Results of AI based system as compared to the results of an expert microscopist

Module	**True Positive**	**False Negative**	**True Negative**	**False Positive**
RBC	24	22	17	1
PUS CELL	80	10	17	1
Calcium Oxalate Crystals	32	6	17	1

Table 5. Diagnostic parameters of Artificial Intelligence (AI) based system

Diagnostic parameters	**RBC**	**Pus Cell**	**Calcium Oxalate Crystals**
Sensitivity	58.54%	82.47%	65.31%
Specificity	94.44%	94.44%	94.44%
Positive Likelihood Ratio	10.54	14.85	11.76
Negative Likelihood Ratio	0.44	0.19	0.37
Disease prevalence			
Positive Predictive Value	96%	98.77%	96.97%
Negative Predictive Value	43.59%	62.96%	73.91%
Accuracy	64.06%	89.81%	87.50%

Image 1 (UR625) shows the probability of RBC Cells in an image analyzed by AI. % probability of RBCs ranged from 73% to 99% in a microscopic field.

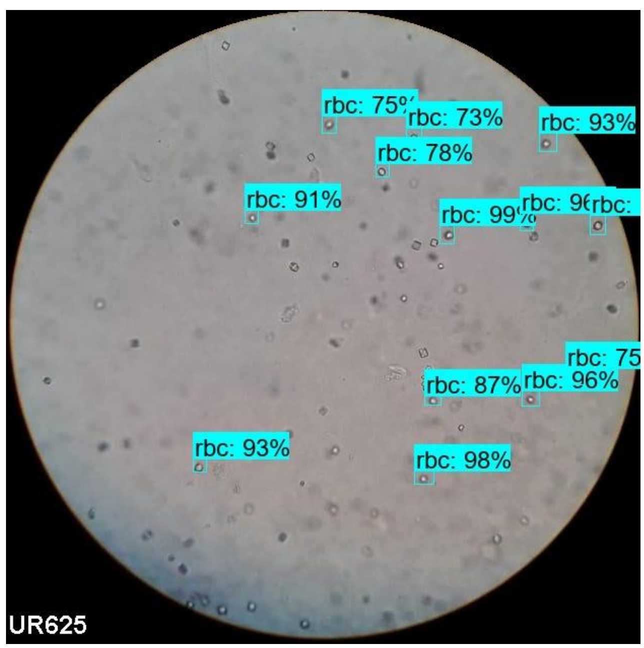


Image 2(UR573) shows the probability of Pus Cells in an image analyzed by AI. % probability of Pus Cells ranged from 55 % to 99% in a microscopic field

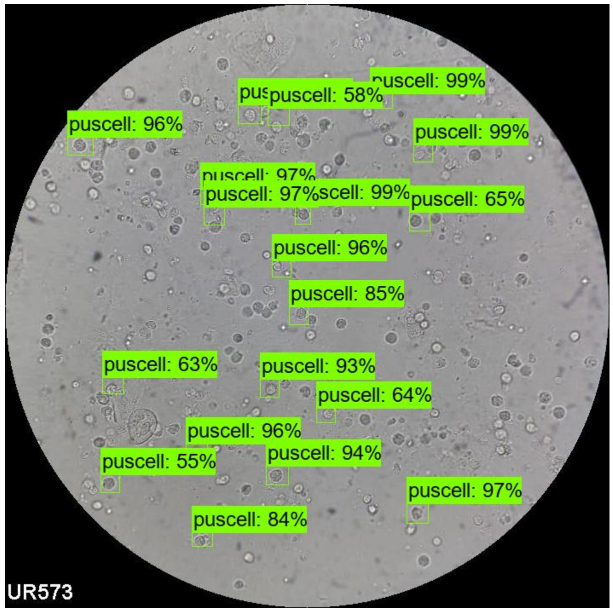


Image 3 (UR625) shows th probability of Calcium Oxalate crystals in an image analyzed by AI. % probability ranged from 71% to 99% in a microscopic field.

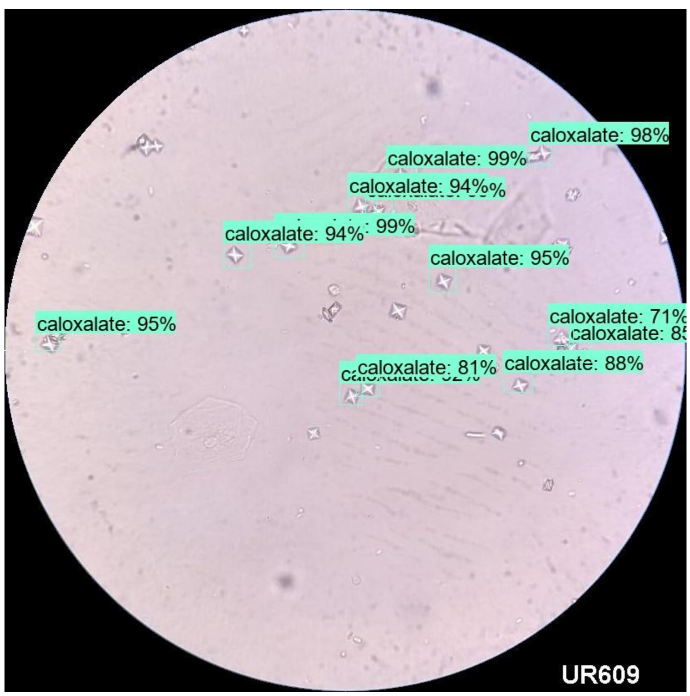
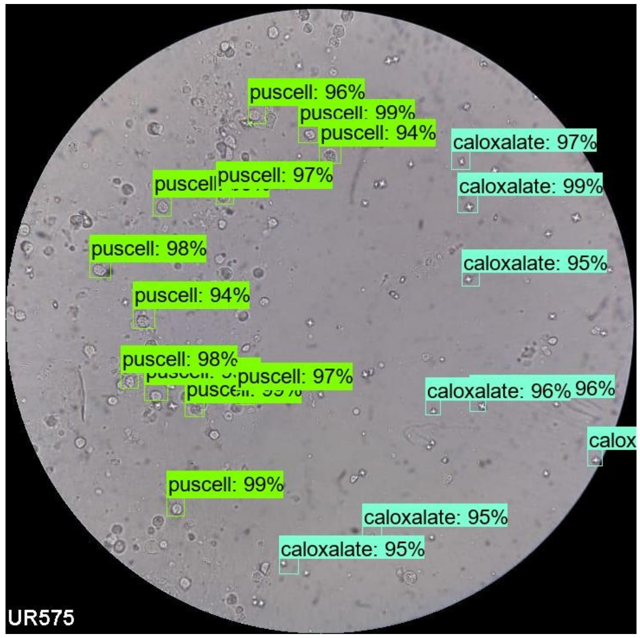


Image 4 (UR575) shows the probability of Pus Cells and Calcium Oxalate in an image analyzed by AI.



IV. Discussion

In the present pilot study, we have analyzed 196 sediment urine samples for presence of RBC cells, pus cells and calcium oxalate crystals and correlated with AI system. The sensitivity and specificity were found to be good. This shows that this particular AI system may be very useful for detection of presence of these concepts and can replace the requirement of an expert microscopist in future. The sensitivity and the specificity of AI also depends on the threshold set for the AI system used. In our study this threshold was set at 60% and this was decided after training and internal lab testing of samples at different thresholds of 5% intervals (50%-80%). We found optimal sensitivity and specificity at 60% threshold only. It should be noted that this idea is called self-adjusting neural networks that adjust themselves to a boundary to that the input data and their outcome must convert. To our understanding the meaning of a self-learning classification system adjusts the "rules" to a given final outcome. At higher threshold, there were too many false negatives. At lower threshold, there were too many false positives. It finds appropriate that the implementation of an automated diagnosis or pre-screening system consists of several modules that should work independently from each other. This approach of a control and an evaluation of the objective image quality is necessary so that one can easily evaluate the results of AI and microscopy. The system has used various enhancement techniques. The shape features extraction technique had been implemented to extract various shape features and finally for classification, the support vector machine was used as a pattern recognition tool to classify the objects as RBC cells, pus cells or calcium oxalate crystals.

As per the best of our knowledge, such AI based pilot study has never been done before in India or elsewhere in the world. Few automated microscopy systems have been used in the past, but they were not based on artificial intelligence. The traditional automatic recognition methods, as the main methods of urine sediment images recognition, mainly relied on artificial feature extraction and the classification. Sun et al. [18] proposed a new detector named aggregate channel features plus (ACF) detector which is based on aggregate channel features (ACF) for urine sediment detection. Sun et al. [19] adopted ACF, which are variant and discriminative, combining improved soft-cascade and a boost classifier for RBCs detection in urine sediment micrograph. Zheng et al. [37] successfully used AI for histopathology examination to segment colon gland, breast tissue, as well as nuclei as reported by different authors in their study [25-32].

The limitation of our study is the small sample size. A larger sample size study is further required to validate our system.

V. Conclusion

In this pilot study, automated AI based identification of RBC cells, pus cells and calcium oxalate crystals has been done. This AI based software method reduces fatigue and screening time by providing images on the screen and avoiding visual inspection of microscopic. The system has an acceptable degree of accuracy, specificity and sensitivity.

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AUTHORS

First Author – Dr. Ankit Agarwal, BDS, Sevamob Ventures Limited, Lucknow, U.P, India, Phone: +91-7408417918, Email ID: dr.ankitagarwal06@sevamob.com

Second Author – Shelley Saxena, B.E, MBA, Sevamob Ventures USA Inc, Email ID: saxenas@sevamob.com