Introduction of Mobile Colposcopy as a Primary Screening Tool for Different Socioeconomic Populations in Urban India

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ABSTRACT

Objective: To assess the feasibility of using a mobile colposcope as a screening tool for underserved urban populations in Mumbai.

Methods: This study was conducted in hospital as well in health camps. First, visual screening was compared to standard of care cytology in a hospital-based setting. Thereafter, the technology was tested in field conditions of urban screening camps, where visual screening (Vis) using the mobile colposcope was used instead of visual inspection with acetic acid (VIA). In the hospital setting, total 321 women underwent routine cytological screening, followed by visual screening using a mobile colposcope. In the Camp, total 150 women were screened with the mobile colposcope. Clinical decisions and socioeconomic information were entered in the mobile colposcope smartphone app. The study duration was 8 months.

Results: Agreements between Vis and cytology was found in 157 cases. For dysplasia, there were 14 women who appeared Vis positive but PAP negative. Only one woman who appeared Vis negative was positive for dysplasia. For cervicitis, 29 women were Vis positive and PAP negative but 117 women were Vis negative but were positive for inflammation on PAP testing. Approximately 60% of patients who were called back for colposcopy and biopsy were lost to follow up. Use of the mobile colposcope in the screening camp allowed for improved workflow and documentation, and the experience was more positive than VIA for both patients and providers. In comparing socioeconomic level to pathology, cervicitis was common for low and middle income patients, whereas dysplasia was almost entirely observed low income patients.

Conclusion: Feasibility of visual cervical cancer screening with a mobile colposcope was demonstrated in two different clinical scenarios. Additional research is needed to find a way to mitigate the frequency of loss to follow up, which was significant in this study.

Keywords: Cervical cancer, cervicitis, cytology, cervical dysplasia, screening, low resource settings, colposcopy, digital health.
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(HPV) testing. VIA is the least expensive method, but its effectiveness is highly dependent upon provider skill level.5 Cytology is the standard of care in India, but is expensive and less sensitive.6 HPV testing is more sensitive than both methods, but still has associated costs and lab processing requirements.7 Both cytology and HPV testing use significant laboratory and human resources, and require multiple patient visits, resulting in high LTFU rates.4

Given these challenges for implementing effective screening programs in India and other Low middle income countries (LMICs), an affordable, mobile cloud-connected colposcope was developed on a smartphone platform, allowing capture of colposcopy-quality images at the time of primary screening. The device - the Enhanced Visual Assessment (EVA) System (Mobile Optical Detection Technologies (ODT)) - is a fraction of the size of a traditional colposcope. To address limitations in visual screening in low-resource settings, software was built into the EVA mobile application for workflow management and remote quality assurance. The EVA System has been successfully deployed in several LMICs, including Kenya,8,9 Haiti,10 Mexico,11 and Cambodia.12

In the present study, we assessed the feasibility of using a mobile colposcope as a screening tool for underserved urban populations in the Mumbai region.

METHODS

This feasibility study took place over an eight month period from March-October, 2017. It consisted of two components: a head-to-head comparison between visual screening using a mobile colposcope against standard of care conventional cytology (Pap smears) in an urban hospital setting, and field testing in a screening camps in an urban slum in which visual screening with EVA was compared to VIA. Both components of the feasibility study were designed as cross sectional studies, utilized the same clinical staff (mainly gynecology experts), and had the same inclusion/exclusion criteria for patient recruitment. Specifically, these criteria limited the patient age to 18-65 years, and excluded patients who were pregnant, menstruating, or had a prior hysterectomy.

Prior to screening, all the women in study were educated and sensitized about both screening methods of the study (visual screening and conventional cytology, if applicable). All women were counseled on the next steps following an examination, and providers explained data usage and risk before an informed consent was signed in Hindi and/or English, depending on the request of the patient. Approval for both study components was obtained from the Clinical Trials Registry - India (CTRI registration number–CTRI/2017/03/013660), as well as from Institutional Ethics Committee Review board.

VISUAL SCREENING

All gynecologists who used the mobile colposcope (Fig. 1A) for screening attended a one-day training on use of the EVA System that included modules on the use of the software, job aid, and instructions of operation to capture clinically useful images of the cervix. There are three parts to using the app. First, basic patient information is collected (age, marital and socioeconomic status) directly into the EVA System mobile application that is used to operate the device. During screening, diluted 5% acetic acid was applied to the cervix, and the cervix was visualized. Both white light and green filter images of the cervix were captured for documentation. Expert gynecologists examined the cervix for signs of acetowhiteness, inflammation, and other abnormalities. After the examination, the gynecologist recorded the impression from the visualization on the decision support job aid.

The decision support job aid is a unique feature of the EVA System (Fig. 1B). It is a workflow management engine integrated into the device, which was used to document visual impression at the time of screening according to the tree in Fig. 1C. Providers recorded any abnormalities, including dysplasia and cervicitis. Patient details, images, annotations, and colposcopic impression by provider were automatically uploaded to the HIPAA-compliant image portal through an integrated SIM card.

HOSPITAL-BASED INVESTIGATION

Initially, the hospital-based setting recruited eligible patients from women who visited the clinic for routine screening over the study period. No additional outreach was conducted for hospital-based screenings. A total of N=321 patients were enrolled, and both cytology and visualization with EVA were provided according to the
study procedure. Visual screening using EVA was offered to the patient at no additional fee.

During screening procedures, the patients first underwent routine, conventional, scrape-based cytology and endocervical sample collection with dedicated brushes. Thereafter, visual screening with EVA was conducted, as described above. All women testing positive, either visually or by cytology, were asked to return for a follow up colposcopy with biopsy that was offered to the patient free of charge. Patients with cervicitis diagnosed from the visualization were prescribed antibiotics and were asked to return for a follow up screening in 1-3 months, after the infection would clear following antibiotic treatment.

All cytology and histopathology samples were sent to the hospital for routine processing and review. Pathologists documented sample adequacy presence of inflammation, and presence of abnormal cells.

FIELD TESTING
In addition to the hospital-based setting, EVA was tested under field conditions in urban screening camps. In contrast to the hospital study, patients here were recruited prior to screening camps by partner Non government organizations (NGOs) through community outreach and sensitization. Lead investigators set up eight mobile screening camps based in community centers, places of worship, and schools, where they could reach high risk, low income women, including commercial sex workers, who face extremely high risk for cervical epithelial abnormalities. Some supportive staff were junior clinicians who volunteered their time for the outreach activities within urban slums. Unlike in the hospital-based setting, here conventional cytology was not provided given the operational transport complexities. The comparison to VIA was on the operational level, in terms of ease of use and documentation.

Note that the hospital offered visual screening to its (low income) staff free of charge. However, these patients (N=38) were not offered cytology services, and as such, were grouped with the screening camp population.

DATA ANALYSIS
At the end of both study components, all cytology and histopathology results were collected and compared to visual impressions from the primary screening recorded in the EVA app. Decisions by the job aid were compared to cytology results and biopsy, as well as to age and socioeconomic status (low, middle, high, or prefer not to answer).
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A total of 420 patients were recruited to enroll in the hospital-based setting, of which 99 were excluded due to improper cytological tracking or processing of the sample. The final patient number was N=321. In the screening camp, a total of 150 patients were enrolled. Fig. 2 shows the age distribution of the hospital-based setting (Fig. 2A) and the screening camp (Fig. 2B).

Patients in the hospital-based setting were screened both visually and using standard of care cytology. The results comparing visualization to cytology is shown in Table 1.

EVA and cytology agreed on 157 total cases. In terms of disagreement, most of the diagnoses involved misclassification of cervicitis. There were 117 inflammatory smears that were not visually classified as cervicitis, and there were 29 cases of visual inflammation where the cytology was non-inflammatory. In terms of dysplasia, there were 14 cases of visual screening/Pap-cases, but only one visual screening/Pap+ case.

To determine the accuracy of EVA and cytology, both methods were compared against the histopathology golden standard. Total 34 cervical biopsy samples were sent for histopathological examination 24 from the hospital-based setting and 10 from the screening camps. Altogether, 20 biopsies processed did not yield a complete histopathological classification, 15 from the hospital-based setting, and five from the screening camps. It is assumed these were LTFU, lower than the 80% Indian standard when a referral is made to a tertiary hospital for completion of diagnosis and treatment. Within the entire data set, there were three positive biopsy-confirmed cases which were visual screening but lacked cytology assessment, one case caught by both methods, and one case missed by both methods.

Additional data is recorded in the EVA mobile application, both in the job aid that documents the clinical decisions taken at the point of care, and in the new patient screen that records basic patient information, including socioeconomic status. Fig. 3 shows the socioeconomic makeup of the enrolled patients in both the hospital-based setting and screening camps, in terms of low- and middle-income (only one patient was high income).

At the screening camp, EVA was compared against standard naked eye visualization, though no differences in diagnosis between the two methods were noted. Patients reacted very positively to the use of the mobile colposcope.

In terms of the pathologies encountered in both components of this study, a breakdown of conditions is shown in Fig. 4, for both low income and middle income patients from the hospital based-setting, and low income patients from the screening camp (only three middle income patients participated in the camp). It can be seen that disease prevalence was approximately the

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**Table 1**

Comparison of EVA to cytology results

<table>
<thead>
<tr>
<th></th>
<th>Normal Pap</th>
<th>Inflammatory</th>
<th>ASCUS, dysplasia, cancer</th>
<th>Pap unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVA normal</td>
<td>88</td>
<td>96</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>EVA cervicitis</td>
<td>24</td>
<td>64</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>EVA dysplasia</td>
<td>5</td>
<td>9</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>EVA other</td>
<td>5</td>
<td>12</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
same between the groups (29-41%). However, dysplasia was more prevalent in the screening camp population, in comparison to patients from the hospital-based setting.

DISCUSSION

In our study, we assessed feasibility of visual screening using mobile colposcopy in two clinical settings in Mumbai, India. First, we compared visual screening to conventional cytology in a hospital-based setting, where we showed that more patients tested positive for cervical dysplasia visually than using cytology. Cervicitis was much more common than dysplasia (Table 1, Fig. 4). About two thirds of the patients called back for colposcopy and biopsy were LTFU. There were also three biopsy confirmed visual screening positive that lacked cytology results. In a screening camp setting, the EVA System allowed capture of important patient information that are difficult to capture in such settings, including age and socioeconomic status.

Our results from the hospital-based setting showed that rates of dysplasia were much lower than expected. Specifically, positive cytology rates were surprisingly low. A total of 5 patients tested positive for cytology (atypical squamous cells of unknown significant or ASCUS threshold), out of a total 321 patients, which is 1.5% of patients. In a country with such high mortality from cervical cancer, these rates appear to be surprisingly low. However, other studies from the Mumbai region showed 3% Pap screening + rate. In comparison, the total number of visual screening positive patients represented 5.6% of the total patients, which is still low, but within the expected range. The difference between 14 visual screening +/Pap - cases and one visual screening negative/Pap+ case suggests that there are probably cases where cytology is missing. Similar results have been reported previously in India. With only 3.1% of the eligible population actually getting screened, false-negative cytology poses a significant risk to the patient.

The high rates of cervicitis are particularly intriguing. About twice as many patients has in the hospital-based setting had inflammatory smears relative to visually detected cervicitis (56% versus 29%, Table 1). Such large disparities mean detecting dysplasia is much more difficult, since cervicitis can cover up dysplasia and patients need to be rescreened following antibiotics treatment. Illustrating this is the one visual screening –/Pap-, biopsy-confirmed dysplasia case, where the user wrote on the EVA app that both cervicitis and acetowhiteness were present, and they weren't sure which to mark.

Another striking finding in this study was the histopathology analysis (Table 2) where 20 of 34 patients called back for biopsy were LTFU, and importantly, 15 of those 24 cases were in the hospital-based setting. These rates of LTFU are significant, because the clinical staff reached out multiple times to the relevant patients by phone, email, and SMS, to let them know that biopsy services were offered to them at no cost, yet they were still unable to get them back to the clinic for confirmatory biopsy. These patients are predominantly low income patients (Fig. 4), which suggests that
Economic factors could have affected the LTFU rates. These high LTFU rates highlight a challenge to cervical cancer care in India, and should be looked into further, given the fact that our study compares favorably with other studies in India which had LTFU rates as high as 80%. Information recorded on the EVA app (including phone number and email) allowed clinicians to persistently call patients back to help them return for colposcopy with biopsy.

The screening camps represent another clinical scenario in which visual screening using EVA was piloted. Such camps serve a different patient population (Fig. 3), and represent different field conditions relative to a stationary hospital clinic. Cytology and biopsy are not as readily available, given the resources and infrastructure they require. Because of the camps' physical condition and overall patient volume, proper record keeping is quite challenging. Anecdotally, it was much was easier to use EVA for documentation of patient information than existing methods (hand-written records or information typed on a laptop). And the information stored by the app allowed for much more rapid data analysis following the deployment.

On a qualitative level, feedback from providers showed they felt the device, in comparison to naked-eye visualization, reduced the time of the exam because less “looking” had to be done. Moreover, the digitized data capture improved documentation of the results at the community level, increased trust among patients due to the ability to see the images from the examination and increased the patient’s sense of empowerment and ownership over her body.

The socioeconomic makeup of the patients enrolled in the study (Fig. 3) was similar to expected levels – the hospital clinic had a large majority (89.4%) of middle income women, some (8.8%) low income women. In contrast, the screening camp population was predominantly lower income. Our socioeconomic data shows two key findings: first, that dysplasia was much more common in low income patients than middle income patients, and second, that cervicitis rates are much higher than dysplasia rates. Both of these results are in general agreement with the previous reports in the literature. Moreover, the numbers from a similarly designed multi-center trial in six sites in southern India showed very similar results, with recorded cervicitis rates being much higher than dysplasia.

While formal cost effectiveness data was not collected in this study, given the high cost of consumables and laboratory testing costs associated with cytology, it is assumed that mobile colposcopy is more cost effective given the device’s ten year lifespan and ability to screen up to 50 patients per day with the same consumable as VIA, the lowest cost method of screening today. However, like cytology, the examination does require a higher level of expertise to not only collect specimens but also distinguish the difference between cervical infections and cervical dysplasia.

There were several limitations to the current study. First, the screening technologies tested in the hospital-based setting were limited to cytology and EVA; an improved comparison would have included HPV testing as well. HPV testing, with its high negative predictive value, would allow better assessment of false negatives, which was not possible under the current protocol. The screening camp effort should separate the provider using EVA from the provider performing VIA, to better document the differences between the two methods. And finally, a behavioral health economist should be consulted on how to incentivize patients to return for follow up check-ups, although this a challenging task all on its own.

One possible way to reduce LTFU rates would be to utilize a single visit approach method, where a follow up

<table>
<thead>
<tr>
<th>Biopsy Analysis</th>
<th>Biopsy Positive</th>
<th>Biopsy Negative</th>
<th>Biopsy Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>vis+/PAP+</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>vis+/PAP-</td>
<td>2</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>vis+/NO PAP (hospital)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>vis-/NO PAP (hospital)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>vis-/PAP-</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>vis+/NO PAP (camp)</td>
<td>2</td>
<td>3</td>
<td>5</td>
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</table>
colposcopy with biopsy can be performed immediately after screening. Further investigation should be done using this approach to better assess clinical accuracy of the EVA System, utilizing new real-time consultation features, to conduct confirmatory biopsy at the primary screening. No technology available today has both high negative predictive value and fast response time needed for a single-visit approach. Two technologies under development that could potentially enable implementing this are point of care HPV testing and automated visual evaluation (AVE).20 Until then, there will be a compromise between accuracy and time/cost.

CONCLUSION

In conclusion, in this study we assessed feasibility of visual cervical cancer screening using a mobile colposcope in urban clinical settings in India. In the hospital based settings, visual screening detected less cases of cervicitis than conventional cytology. However, more cases of dysplasia were identified at the primary screening from visualization than conventional cytology. Histopathology results revealed very high LTFU rates. Under field conditions in a screening camp, visual screening using EVA allowed for capturing more pertinent information about the (underserved) patient population, and overall there was a more positive experience for both the provider and the patient.

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LIST OF ALL ABBREVIATIONS AND ACRONYMS

Add one table of acronym given in the manuscript.

DISCLOSURE STATEMENT

CS and DL are employees of Mobile ODT and own stock in the company. Additionally DL sits on Mobile ODT Board of Directors.

REFERENCES