

Rates of cervicitis across multiple sites in India

M Samuel, MD^I; J Swaminathan, PhD^{II}; C Sebag, BA^{III}; S Rajagopal, MD^{IV}; C Ramamurthy, MD^V; M Jagan, MD^{VI}; Sangamithirae, MD^{VI}; Aruna, MD^{VII}; K Kumari, MD^{VIII}; K Ganta, MD^{IX}; Hemalekha, MD^X; H Solomon^{II}; C Peterson, MPH^{III}; D Levitz, PhD^{II}

^I Apollo First Med, 154, Poonamallee High Rd, New Bupathy Nagar, Kilpauk, Chennai, Tamil Nadu 600031

^{II} MobileODT, Ben Avigdor 8, Tel Aviv, Israel

^V Apollo Bangalore, 154/11 Bannerghatta Road, Opp. I.I.M. Bangalore 560076

^{VII} Apollo Speciality Hospital Vanagaram, Apollo Research and Innovation, Vanagram to Ambattur Main Road Ayanambakkam, Chennai 600 095

^{IX} Apollo Hyderabad, DMRL X Roads, Kanchanbagh, Hyderabad - 500 058.

^{II} Apollo Research & Innovations, No-16&17,2nd Floor ,Krishnadeep Chambers, Apollo Annexe, No:1 Wallace Garden, Thousand lights,Chennai 600006

^{IV} Apollo Total Health, Aragonda Village, Tavanampalle Mandal, Chittoor District, Andhra Pradesh

^{VI} Apollo Tondiarpet, No.645 & 646, T.H Road, Tondiarpet, Chennai-600 081

^{VIII} Apollo Institute of Medical Sciences and Research, Apollo Health City Campus, Jubilee Hills, Hyderabad, Telangana 500033

^X Apollo Speciality Hospital Madurai, Apollo Speciality Hospitals,Lake view road , K.K.Nagar.Madurai-625020

Abstract

Objective: The presence of cervicitis in patients makes it difficult to detect cervical precancerous lesions. Data on the prevalence of cervicitis can enable appropriate policies on cervical cancer screening, since the inflammation affects the screening accuracy. While cervicitis is prevalent in India, most studies only look at individual sites. The availability of connected colposcopes enables clinicians to record the presence of cervicitis, allowing for better assessment of dysplasia. The goal is to assess variation across multiple sites in India. **Methods:** Connected colposcopes with an integrated job aid were deployed in six sites in India for visual cervical cancer screening over six months. After each screening, the provider recorded their clinical impression on the job aid (normal, precancer, cancer, cervicitis, other). Biopsies were collected when called for by the standard of care. Following the deployment, statistics from providers were tabulated. **Results:** In total, 597 patient were imaged. Patients were diagnosed with cervicitis at the following rates: 22%, 41%, 44%, 48%, 27%, and 15%. These numbers are consistent with values reported in the literature from different parts of India. **Conclusion:** Large variations in the prevalence of cervicitis were seen across sites. This has implications for health officials and policy makers.

Introduction

Cervicitis is a common condition for many women in low resource settings. Cervicitis can be of either infectious or non-infectious origin. Infectious cervicitis is most often caused by chlamydia and gonorrhea, or other micro-organisms [1]. Symptoms include bleeding between menstrual periods, pain during intercourse, and abnormal vaginal discharge. Antibiotics is the most common form of treatment.

Although generally a benign condition, cervicitis is often mentioned as a challenging factor in many visual inspection with acetic acid (VIA) programs. Specifically, many referred VIA+ cases turn out to be cervicitis instead of cervical dysplasia/cancer. But only scant statistics exist on the rates of cervicitis, particularly in low- and middle-income countries (LMICs).

In this study, we sought to assess the rates of cervicitis across southern India. To do so, we analyzed data from a pilot study in which the Enhanced Visual Assessment (EVA) System (MobileODT), a cloud-connected colposcope built around a smartphone that was compared against cytology as a cervical cancer screening tool at 6 sites. EVA data collected as part of this trial allowed for identifying patients with cervicitis, as one of the optional clinical outcomes. We utilized this data to assess the rates of cervicitis at the selected sites, and are reporting the rates here. Altogether, our data showed rates of cervicitis ranging from 15-50% across the different sites. Rates of cervicitis were markedly higher than rates of dysplasia/cancer (0-16%) at 5 of 6 sites.

Methods

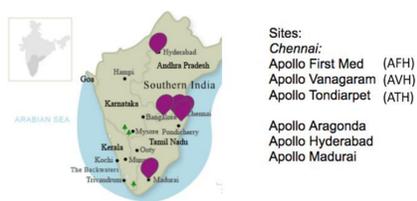


Fig 1: Map of clinical sites in trial.

The EVA System was deployed in 6 clinical sets in Southern India (Fig. 1). Of these 6 sites, 3 were in Chennai, Tamil Nadu. The 3 Chennai sites served a high income (AVH), low income (ATH), and mixed (AFH) populations. Two additional sites in Bangalore were excluded from the analysis due to slight variations in clinical protocol.



Fig 2: The EVA System's Mobile Colposcope.

At each site, patients visiting the clinic for cervical screening were recruited to participate in the trial. Patients enrolled were both imaged by EVA (Fig. 2), and had cytology co-test samples collected. Patients positive for either EVA or cytology were called back for colposcopy. When called for by the standard of care, biopsies were collected. All cytology and histopathology samples collected in this trial were processed routinely according to the standard of care.



(A) Screenshots of the key steps in the job aid.

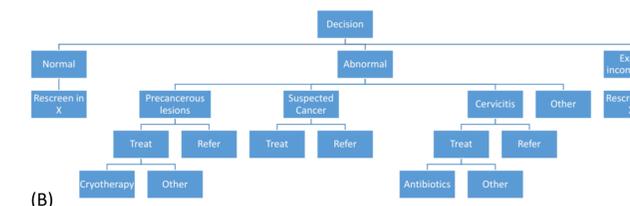


Fig 3: Decision Support Job Aid on the EVA System app. (A) Screenshots of the key steps in the job aid. (B) Full decision tree of job aid.

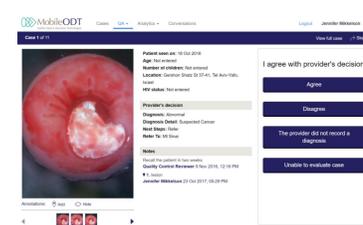
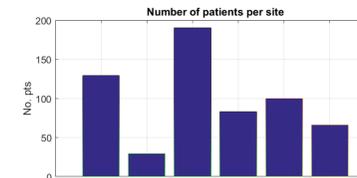


Fig 4: Screenshot of QA on EVA System.

To assess how uniformly clinical protocol was followed across the 6 sites, EVA's quality assurance (QA) feature (Fig. 4) was used. Here, an expert colposcopist reviewer monitors decisions made by clinicians at various sites for how they visually classified dysplasia. QA was performed periodically during the pilot and remote mentorship provided when needed.



Altogether, a total of N= 597 patients were enrolled at the 6 sites. The distribution of how the patients enrolled in the study across the various sites is shown in Fig. 5.

Fig 5: Distribution of patients across clinical sites.

Rates of cervicitis (as recorded on the EVA System app) and cervical dysplasia (as recorded on EVA and cytology) are shown in Fig. 6. It can be seen that overall, there was much more cervicitis than dysplasia, with cervicitis rates reaching over 40% in 3 of 6 sites. In one site (Aragonda), rates of cervicitis and dysplasia were identical.

In terms of dysplasia, the number of EVA+ patients was larger than Pap+ patients in 5 of 6 sites. In those 5 sites, EVA+ rates ranged over 9.3-16.0% (mean = 12.4%). In analyzing the cytology results, there were much fewer Pap+ patients. In total there were 20 Pap+ patients out of 597, for a total rate of 3%. This rate appears to be lower than expected for a country like India, which has the largest number of deaths from cervical cancer in the world.

Surprisingly, there were very low rates of dysplasia detected in 2 of the 3 Chennai sites. At AVH, there was no dysplasia recorded on either EVA or cytology. This clinic services higher income women in general, which could explain the low rates of dysplasia recorded, at least in part. At ATH, all the cytology results were negative, while the EVA+ rate was 10.3%. What is surprising here is that ATH serves a lower income urban population, and have a sliding scale pay system.

As an interesting tidbit, many positive patients did not undergo the follow up colposcopy with biopsy at the sites during the study period, because of loss-to-follow-up, the need to save for the procedure, or the choice to undergo the procedure at a free government clinic. This was not the case with cervicitis patients, who were treated with antibiotics at the primary visit and did not to have a follow up visit. The loss to follow up in dysplasia cases suggests that economic decision making by patients could have affected our results. However, such economic decision making needs to be taken into consideration in order to deliver the best possible care to patients.

Conclusion

Rates of cervicitis and cervical dysplasia were recorded using the EVA System, together with cytology co-tests, at six sites in southern India. Cervicitis rates were higher than dysplasia rates (recorded on EVA or cytology) in 5 of 6 sites. In 3 of 6 sites, cervicitis rates exceeded 40%. IN contrast, dysplasia rates appeared to be low. Quality assurance on the images showed an overall 55% agreement rate of reviewers and users. A more rigorous analysis of the data is still ongoing.

Acknowledgements

This study was funded by the international finance corporation and the world bank, through an award from Tech Emerge competition.

Results and Discussion

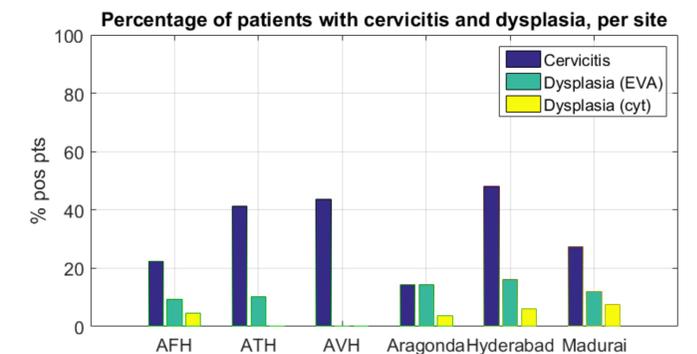


Fig 6: Distribution of patients with cervicitis and dysplasia (measured by EVA or cytology) across clinical sites. The left-most sites are all from Chennai.

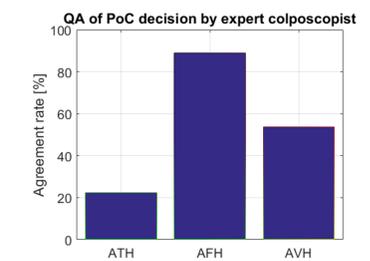


Fig 7: QA analysis on 3 Chennai clinics.

In looking at the data from Chennai hospitals more closely, the QA analysis (Fig. 7) offers additional insight. At ATH, the agreement rate was low (22%) at the onset of the trial, and so some of these negative patients could in fact be positive. This could also explain the AVH results.

Overall, the variability in QA agreement rates highlights differences in care across the sites, specifically in treatment and referral practices. The overall agreement between reviewers and PoC clinicians was 55%. We believe that standardization could further improve outcomes.

Next steps

A more detailed analysis of cases in which the reviewer disagreed with the user at the PoC is still ongoing. Specifically, we are examining how cervicitis affected false positive/negative clinical impressions of dysplasia in individual patient cases.

References

1. Kurman RJ, Ellenson LH, Ronnett BM, Eds., *Blaustein's Pathology of the Female Genital Tract, Sixth Ed.* Springer, New York (2011).
2. Peterson CW, Rose D, Mink J, Levitz D, "Real-Time Monitoring and Evaluation of a Visual-Based Cervical Cancer Screening Program Using a Decision Support Job Aid", *Diagnostics* 2016;6,20-27.