Editorial

Screening for Cervical and Oral Cancers in India is Feasible and Effective

Cervical and oral cancers continue to be important public health priorities in India. Annually, around 126 000 new cervical and 90 000 new oral cancer cases are diagnosed in India.[1] More than three-fourths of these cases are diagnosed at advanced stages and have a poor survival outcome, so much so that India accounts for one-quarter and one-third of the worldwide burden of cervical and oral cancers, respectively.[1] While screening has been the most effective strategy currently available to prevent and control cervical cancer,[2] the effectiveness of screening in reducing oral cancer mortality was established only recently.[3] However, there are no organized cancer screening programmes anywhere in India, even though a number of Indian research studies have addressed the feasibility and cost-effectiveness of screening options for possible wide-scale implementation.

Cervical cancer screening

In developed countries, conventional cytology screening programmes have shown a marked decline in the incidence of cervical cancer.[2,4] In less developed countries, where cervical cytology programmes were implemented, no significant reduction in disease burden has been observed. This is partly due to the poor quality of testing and programmatic deficiencies in follow up and treatment of screen-positive women, and mostly due to the considerable financial, technical and logistic inputs necessary for effective cytology programmes. In many settings, these challenges have prompted the search for programmes based on alternative cervical screening tests.

The alternative tests considered include naked-eye visual inspection with acetic acid (VIA), low level magnified visual inspection with acetic acid (VIAM), naked-eye visual inspection with Lugol iodine (VILI) and testing for oncogenic human papillomavirus (HPV) using hybrid capture II (HC II). VIA involves visualization of the cervix 1–2 minutes after application of 3%–5% dilute acetic acid. A positive VIA test is characterized by the detection of a well-defined, dense acetowhite area on the cervix close to the squamocolumnar junction (SQJ) or the external os.[5] VILI involves visualiza-tion of the cervix after application of Lugol iodine; detection of a well-defined, mustard-yellow, non-iodine uptake area on the cervix, close to the SQJ indicates a positive test.[5] The visual tests do not require a laboratory infrastructure and the results are obtained immediately following testing, allowing diagnosis and treatment to be instituted during the same or a subsequent visit.

There have been a number of cross-sectional studies in India, as part of a large multinational project, in collaboration with the Bhagwan Mahaveer Cancer Hospital and Research Centre (Jaipur), Chittaranjan National Cancer Institute (Kolkata), Tata Memorial Centre (Mumbai) and the Regional Cancer Centre (Thiruvananthapuram), which have addressed the comparative accuracy of conventional cytology—VIA, VIAM, VILI and HPV testing—in detecting high grade cervical intraepithelial neoplasia (CIN 2 and 3 lesions).[6–12] The studies followed a uniform protocol and training of the study staff. The tests were carried out by nurses, trained health workers or trained high school or university graduates. More than 31 000 women 30–64 years

of age were involved in the studies and each participant underwent colposcopy, irrespective of the screening test results, as one of the reference investigations to minimize verification bias. Biopsies were done if indicated by the colposcopic findings. The final disease status was established by histology results or by colposcopy when biopsies were not indicated. The sensitivity and specificity of screening tests in detecting high grade cervical cancer precursor lesions in the studies are given in Table I. The pooled sensitivity and specificity for cytology positivity at low grade squamous intraepithelial neoplasia (LSIL) threshold were 58% and 95%, respectively.

The results clearly suggest that, although they are less specific, VIA and VILI are as sensitive as good quality cytology and HPV testing in detecting cervical neoplasia in Indian study settings. There was a much wider range for sensitivity of cytology and HPV testing compared with the visual tests.

The efficacy of screening by VIA, cytology, or HPV testing in reducing the incidence of and mortality from cervical cancer is being investigated in a cluster randomized controlled trial in India, in collaboration with the Tata Memorial Centre (Mumbai) and the Nargis Dutt Memorial Cancer Hospital (Barshi).[13,14] This study involves 52 clusters with a total of 142 701 women, 30–59 years of age in Osmanabad district, India, randomized into 4 arms for a single round of screening by trained midwives with either VIA, cytology, HPV testing or to a control group. The women in the control group received health education on cervical cancer. Seventy-three per cent of the eligible women received screening. Test positivity rates were 14% for VIA, 7% for cytology and 10.3% for HPV testing. Test-positive women were investigated with colposcopy and biopsy, and women with CIN lesions were treated with cryotherapy or the loop electrosurgical excision procedure (LEEP). The detection rate of high grade lesions was similar in each intervention arm (0.7% for VIA, 1% for cytology and 0.9% for HPV testing; p=0.06, Mann–Whitney test). Over 85% of women with high grade lesions received treatment. The findings of the study indicate that a high level of participation and good quality cytology can be achieved in low-resource settings.

The impact of a single round of screening by VIA on cervical cancer incidence and mortality is being investigated in another cluster randomized trial in south India in collaboration with the Christian Fellowship Community Health Centre (Ambillikai), Cancer Institute (Chennai) and the PSG Institute of Medical Sciences and Research (Coimbatore).[15] Women 30–59 years of age in 113 clusters in the Dindigul district were randomized to VIA screening by nurses (57 clusters, 48 225 women) and to a control group (56 clusters, 30 167 women); 30 577 eligible women were screened; 2939 screen-positive women (9.6%) were investigated with colposcopy by nurses and 2777 women (9.1%) by biopsy. The detection rates of lesions were 5.8% for CIN 1, 0.7% for CIN 2–3 and 0.2% for invasive cancer. Seventy-one per cent of the women with CIN 1 and 80% of those with CIN 2–3 lesions accepted cryotherapy provided by nurses and LEEP by mid-level clinicians.

TABLE I. Accuracy of cervical screening tests in detecting cervical intraepithelial neoplasia grades 2 and 3 lesions in Indian cross-sectional studies

Characteristic	Cytology at the ASCUS threshold	VIA	VIAM	VILI	HPV testing
Number of women studied	22 663	31 154	16 900	25 260	18 085
Number of studies	5	6	3	5	4
Sensitivity					
Pooled	65%	75%	64%	85%	67%
Range in individual studies	38%–81%	58%–90%	61%–71%	76%–90%	46%–81%
Specificity					
Pooled	92%	85%	87%	83%	94%
Range in individual studies	86%–98%	75%–89%	83%–90%	73%–87%	92%–95%

ASCUS atypical squamous cells of undetermined significance VIA visual inspection with acetic acid
VIAM magnified visual inspection with acetic acid VILI visual inspection with Lugol iodine
HPV human papillomavirus

Follow up is ongoing in both the studies to establish the cervical cancer incidence and mortality rates in the study arms and the final results are expected in 2007. The current findings from these two studies indicate that visual testing is a suitable alternative screening test for cervical neoplasia.

Oral cancer screening

Although visual inspection of the oral cavity has been known to be a simple, acceptable and accurate screening test for oral cancer, it was not clear if a visual inspection-based screening programme would lead to a significant reduction in oral cancer mortality. A cluster randomized controlled trial involving 192 000 subjects in 13 clusters was initiated in Thiruvananthapuram district, in collaboration with the Regional Cancer Centre (Thiruvananthapuram).[3] Apparently healthy subjects ³35 years of age in 13 municipal clusters were randomized to an intervention group (*n*=7) or to a control group (*n*=6). Subjects in the intervention group received three rounds of screening by oral visual inspection by trained health workers at 3-year intervals. Screened subjects with lesions suggestive of oral leukoplakia, submucous fibrosis or oral cancer were referred for examination by doctors. Confirmed leukoplakias were excised whenever possible, others were followed up, and those with confirmed oral cancers were referred for treatment. Data on oral cancer incidence, stage distribution, survival and mortality in the study groups were obtained from the Thiruvananthapuram population-based cancer registry, municipal death registration systems and by active house visits. Of the 96 517 eligible subjects in the intervention group, 91% were screened at least once. Of the 5145 subjects who screened positive, 63% complied with referral. Eligible subjects in the control group (*n*=95 536) received the existing standard care. Overall, 205 cases of oral cancer and 77 oral cancer deaths were recorded in the intervention group compared with 158 cases and 87 deaths in the control group, yielding a mortality rate ratio of 0.79 (95% CI: 0.51–1.22), 9 years after initiation of the screening trial.[3] Seventy oral cancer deaths occurred in users of tobacco and/or alcohol in the screened group compared with 85 deaths in controls, resulting in a mortality rate ratio of 0.66 (95% CI: 0.45–0.95).[3] These results establish the efficacy of routine oral visual screening in reducing oral cancer deaths in the high risk group of users of tobacco and/or alcohol. This study clearly establishes the beneficial role of screening in controlling oral cancer.

Conclusion

The Indian screening studies referred to above have generated vast evidence to formulate and promote public health policies for screening of cervical and oral cancers, and for organizing cancer detection and control programmes in India and other countries. The Indian study findings prove that the visual screening tests for cervical and oral cancers are affordable, simple, acceptable, feasible and accurate clinical early detection tools that can be readily used in all healthcare settings in the world, including developed and developing countries. They provide valid leads for organizing good quality cytology and HPV testing screening programmes. HPV testing is currently expensive and efforts are under way to produce rapid and affordable HPV tests. They also provide fair evidence that visual screening programmes can lead to a significant reduction in disease burden. The visual tests can be easily mastered and several training resources are now available. Medical students, nurses, interns and general practitioners should be taught these simple testing procedures and encouraged to practise them in clinical settings. For the first time, there is a real opportunity to integrate early detection of cervical and oral neoplasia in primary healthcare settings.

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