

Cost Estimation of the New HPV/DNA Test Screening Procedure Per Person among 35 Years Old Ever-Married Women in a District of Sri Lanka

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Abstract

Background: HPV/DNA screening test has an optimum sensitivity (92.9%) to detect cervical lesions. The objective of the study was to estimate the cost of cobas 4800 HPV/DNA test in thin prep cell collection media.

Methods: The cost estimation of the HPV/DNA specimen collection was done at a randomly selected community Well Woman Clinic (WWC) in the district of Sri Lanka. Five women, who were attended WWC for HPV/DNA specimen collection in September, October, and November 2018 were randomly selected for the cost estimation.

To estimate the cost incurred in laboratory screening of the HPV/DNA specimen by cobas 4800 HPV/DNA PCR test, a reference laboratory in the district was utilized. Checklists were developed to record all instruments and consumable items used in the clinic and laboratory, while record sheets were developed to record the time taken to complete all activities associated with taking an HPV/DNA specimen by the clinic and laboratory staff.

Five HPV/DNA specimen collection procedures were randomly selected at each of three sessions and the average time per procedure was calculated. Categories of staff involved in the procedure and staff time spent on the procedure were measured and recorded on three clinic days. Staff time spent on HPV/DNA specimen screening by an HPV/DNA testing machine in the laboratory was calculated on three working days (One day per month).

Results: The total estimated cost of the HPV/DNA specimen collection procedure incurred by the government in the community WWC was Rs.2569.38 (USD 13.81), while the total estimated unit cost in the laboratory procedure for HPV/DNA screening was Rs. 50.57(USD 0.27).Therefore the total estimated cost of the HPV/DNA specimen screening procedure was Rs. 2619.95(USD 14.08). The estimated unit cost including administrative cost was Rs. 2881.95(USD 15.49).

Conclusion: Cobas HPV/DNA test is economically feasible to be incorporated into the national cervical cancer screening programme in Sri Lanka. It is necessary to further attempt alternative methods of cobas 4800 HPV/DNA test (i.e. dry swabs) to determine the most appropriate method for resource limited settings.

Keywords: HPV/DNA test; Cervical cancer; Screening; Cost estimation

Abbreviations: PCR: Polymerase Chain Reaction; WWC: Well Woman Clinic; CIN: Cervical Intraepithelial Neoplasia; DGH: District General Hospital; LBC: Liquid-Based Cytology; ERC: Ethics Review Committee; NIHS: National Institute of Health Science

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Background

Cervical cancer is the 2nd leading cause of female cancer in Sri Lanka according to the incidence rate and women at risk for cervical cancer is more than 8.4 million [1]. In Sri Lanka, annually

1721 new cases of cervical cancers are diagnosed and 690 women have died from the disease [1].

In 1998, conventional papanicolaou smear screening was included in the Well Woman Clinic (WWC) programme as a cervical cancer

screening method. After 20 years of existence of the programme, in contrast to the vigorous preventive measures, there is no marked reduction of incidence, morbidity, and mortality of cervical cancer in Sri Lanka. Other than the suboptimal sensitivity of the pap cytology [2] to detect Cervical Intraepithelial Neoplasia (CIN), another major drawback of the present programme is the low coverage. National 35 year age cohort WWC coverage for 2016 was 52.8% [3], while the recommended target coverage for the programme is 80% [4]. Therefore, the cervical cancer prevention programme needs to be reviewed with special attention.

At present, HPV/DNA screening is used as a cervical cancer screening method in some developed countries. HPV/DNA screening test is highly sensitive for high-risk types of HPV [5]. Specimen collection for the HPV/DNA screening test is easy and can be done even by primary health care workers such as public health midwives. As screening will be done by a machine, a large number of specimens can be performed per day, no observer dependence, no inter-observer variation and because of the higher sensitivity of HPV testing alone; a prolonged screening interval is appropriate [6]. The cobas 4800 HPV/DNA test sensitivity and specificity to detect \geq CIN II is 92.9% and 71% respectively [7]. It detects 14 high risk carcinogenic HPV genotypes, such as; 16, 18 and 12 pooled high risk types such as 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68.

In the estimation of costs in health care institutions, costing actual and scenario building technique methodology can be used. Costing through scenario-building technique is a feasible method when actual expenditures are not well documented or not available. Practically scenario building technique is a more feasible option and more useful when it combines with the use of actual empirical data [8].

Medical management still contributes to a major element, as the government of Sri Lanka provides health care free for service delivery. Cervical cancer-induced economic burden in Sri Lanka is consists of per patient day ward cost, radical hysterectomy, 25 doses of external beam radiotherapy [9]. Compared to medical cost allocations at endpoint disease management, early detection, and preventive measures are shown as cost effective.

The long-term cost-effectiveness of different strategies for HPV/DNA testing combined with pap smear for cervical cancer screening in Taiwan was evaluated [10]. Outcomes of the study were life expectancy, quality-adjusted life in years, lifetime costs and incremental cost-effectiveness ratios. Compared with annual pap smear screening, HPV/DNA testing followed by pap smear triage every 5 years and every 3 years were cost-effective. The objective of the study was to estimate the unit cost of a new HPV/DNA screening procedure among 35 years age cohort of ever-married women in a district of Sri Lanka.

Methods

At first preliminary survey of WWCs in the Kalutara district was conducted among 10 randomly selected WWCs of the 89 available in the district. The objective of the survey was to identify major

differences, if any between WWCs in the district. The preliminary survey revealed that the distribution and usage of facilities and function of the majority of clinics were very similar.

All WWCs in the district were listed in alphabetical order and allocated a number. The cost estimation of the HPV/DNA specimen collection was done at a randomly selected community WWC by the first author by using a lot method. The selected WWC has functioned in a separate building, which was used only to conduct community clinics. To estimate the cost incurred in laboratory screening of the HPV/DNA specimen by cobas 4800 HPV/DNA polymerase chain reaction test, the laboratory of District General Hospital (DGH) Kalutara was utilized.

Checklists were developed to record all instruments and consumable items used in the clinic for obtaining an HPV/DNA specimen and in the laboratory for specimen screening. Record sheets were developed to record the time taken to complete all activities associated with obtaining an HPV/DNA specimen by the different members in the clinic and the laboratory for specimen screening. Checklists and record sheets were developed under the guidance and supervision of expertise in health economics. Data collection instruments were pretested at another WWC in the district. Minor modifications were carried out in the clinic setup.

The study population comprised of ever-married women in 35 years of age, who have attended HPV/DNA screening at selected WWC in the district. Five women who attended WWC for HPV/DNA screening on the scheduled clinic day in September, October, and November 2018 were randomly selected for the cost estimation of HPV/DNA screening procedure per person.

Recurrent cost estimation of HPV/DNA screening procedure was carried out according to the scenario building technique [7]. The steps in scenario-building approach are a collection of information and characteristics related to an issue/situation, listing out all assumptions, and combined actual information and estimated values (expert estimates, literature based estimates... etc) to reach cost estimates.

Data collection was done by the first author and supported by a research assistant. Quantities of all consumables used for the HPV/DNA screening were recorded in the prepared datasheet. Programme recurrent cost estimation per person for HPV/DNA screening procedure consisted of two cost components. The first component is the recurrent cost incurred in obtaining HPV/DNA specimens at the community clinic with all other processing up to the transport. The second component is the recurrent cost of reading the HPV/DNA specimen by an HPV/DNA screening machine in the laboratory. Specimens from WWCs were sent to be screened at the reference laboratory in the district. Usually, specimens were hand-delivered by an individual using public transport services. Considering the differences in travel distance and the type of transport used, the transportation cost was not considered in the estimation.

The fixed capital cost of land and building was not considered in the cost assessment exercise. The reason was some community

WWCs in the district and the reference laboratory was housed within the large building and the allocated space for either clinic or laboratory was $\leq 1/20$ th of the whole building. Therefore, the cost of land and building in unit cost estimation for the HPV/DNA screening procedure was considered negligible and excluded.

One WWC clinic session per month was conducted at the selected clinic and three consecutive clinic sessions were considered for per procedure cost estimation. Five HPV/DNA specimen collection procedures were randomly selected at each of three sessions and average time per procedure was calculated. The average number for the month was considered as determinants for unit cost estimation. Categories of staff involved in the procedure and staff time spent on the procedure were measured and recorded on three clinic days. Staff time spent on HPV/DNA specimen screening by an HPV/DNA testing machine in the laboratory was calculated on three working days (one day per month). The average number screened per month was considered for the HPV/DNA screening procedure at laboratory recurrent cost estimation per person. Recurrent cost estimation for the HPV/DNA screening procedure was carried out under the supervision of an expert in health economics with extensive experience in cost estimation.

The cost of the different medical items was obtained from the medical supply division, family health bureau purchasing division and stores, and from companies dealing with medical equipment. Collected data were entered into an excel spreadsheet. Details of staff categories monthly salaries were obtained through personal communications from the ministry of health, these costs were applied to the different categories listed above and a unit cost of an HPV/DNA specimen screening procedure was calculated.

Results

Average number attended to WWC for HPV/DNA specimen collection during September, October and, November 2018 was 8 (Table 1).

Month 2018	Number of HPV/DNA specimen collection
September	7
October	9
November	8
Total	24
Average per month	8

Table 1: Average number attended to WWC for HPV/DNA specimen collection at the clinic.

The unit cost estimate for furniture and equipment in the community WWC was Rs. 61.91 while, the unit cost estimated for consumables for the HPV/DNA specimen collection in the community clinic was Rs. 2391.09 (Table 2). The HPV/DNA test kit consists of a specimen collection instrument with cell collection media called "thin prep" and reagents needs for specimen screening procedure at the laboratory and the unit prize was offered for both as a union (Rs. 2356.12). Therefore it was included under the consumables at the clinic, which needs to collect HPV/DNA specimen.

Cost item	Unit cost	Total (Rs)
Furniture and equipment		
Examination bed	1.03	
Examination lamp	2.67	
Bed screen with curtain	0.97	
Bed screen with curtain	6.25	
Plastic chairs with arms	8.83	
Wooden table	2.70	
Stationery racks	0.83	
Steel cupboard	0.83	8
Mackintosh	33.35	
Sterilizer	0.92	
Dressing drum	0.22	
Kidney tray	0.22	
Rectangular tray	0.08	
Cusco's speculum	2.89	
Bed sheets	0.12	
Plastic waste paper basket		
Total		61.91
Consumables		
Test kit with accessories (specimen collection instruments and reagents for screening per specimen)	2356.12	8
Gloves (single pair)	34.97	
Total		2391.09

Table 2: Unit cost estimation of furniture, equipment and consumables for HPV/DNA specimen collection procedure in the community WWC.

The unit cost estimation for staff services utilized for the HPV/DNA specimen collection was Rs. 110.55, while the estimated unit cost of utility and miscellaneous items required for the HPV/DNA specimen collection procedure in the community was Rs. 5.83 (Table 3). Therefore, the total estimated cost of the HPV/DNA specimen collection procedure incurred by the government in the community WWC was Rs. 2569.38 (13.81 USD).

Cost of services	Unit cost	Total (Rs)
Staff services utilized		
Medical Officer	64.57	
Public Health Midwife	45.98	
Total		110.55
Utility and miscellaneous items		
Electricity	5.83	
Water	Free of charge (From the well)	
Total		5.83

Table 3: Unit cost estimation of services utilized for HPV/DNA specimen collection procedure in the community WWC.

The estimation of the unit cost of the staff services utilized in the laboratory for HPV/DNA specimen preparation and screening procedure was Rs. 27.65, while the estimation of the unit cost of utilities and miscellaneous items required in the laboratory for a single HPV/DNA specimen screening procedure was Rs. 8.06 (Table 4).

Cost item	Unit cost	Total (Rs)
Staff services utilized		
Cyto-screener	17.43	
Supportive staff	10.22	
Total		27.65

Utilities and other items		
Water	0.15	
Electricity	7.91	
Total		8.06

Table 4: Unit cost estimation of the services utilized in the laboratory for HPV/DNA screening procedure.

The estimation of the unit cost for equipment and fixed hardware required in the laboratory for a single HPV/DNA specimen screening procedure was Rs. 12.30, while the estimation of the unit cost for consumables other than specimen screening reagents required in the laboratory for a single HPV/DNA specimen screening procedure was Rs. 1.49. The cost of the screening reagents per specimen was included under the test kit with accessories in HPV/DNA specimen collection at WWC. The estimated unit cost of furniture used for HPV/DNA specimen screening in the laboratory was 1.07 (Table 5). Therefore, the total estimated unit cost incurred by the government in the laboratory procedure for HPV/DNA screening procedure was Rs. 50.57 (0.27 USD).

Cost item	Unit cost	Total (Rs)
Equipment and fixed hardware		
cobas 4800 HPV/DNA screening machine	9.50	
Refrigerator	0.64	
LG Air condition machine	2.16	
Total		12.30
Consumables		
Gloves	1.49	
Total		1.49
Furniture		
Wooden cupboards	0.31	
Wooden tables	0.28	
Wooden rack	0.27	
Revolving chairs	0.20	
Plastic waste paper basket	0.01	
Total		1.07

Table 5: Unit cost estimation of equipment, fixed hardware, consumables and furniture in the laboratory for HPV/DNA screening procedure.

The total estimated cost of HPV/DNA specimen screening procedure incurred by the government in community clinic and laboratory was Rs. 2619.95 (2569.38+50.57) (USD 14.07), while the final estimated cost of HPV/DNA specimen screening procedure incurred by the government at community clinic and the laboratory including administrative cost was Rs. 2881.95 (2619.95 × 110/100) (USD 15.49).

Discussion

Cervical cancer is the 2nd leading cause of female cancer in Sri Lanka [1]. Hence in 1998, Sri Lanka took an initiative to include screening for cervical cancer with conventional papanicolaou (pap) smear in the WWCs. Pap smear screening per procedure cost is Rs. 308.18 [7] according to the estimation in 2009. One major drawback of the present programme is, the suboptimal sensitivity of the pap smear to detect CIN.

The sensitivity of the HPV/DNA test is high. Further, HPV/DNA

screening has lengthy screening intervals than pap smear due to its higher sensitivity and it will increase the cost-effectiveness of HPV/DNA test. Therefore estimation of per procedure cost of HPV/DNA test is very important. The scenario-building technique is considered a more feasible option for health procedure costing [11]. The unit cost incurred by the government for HPV/DNA screening procedure per person by cobas 4800 HPV/DNA polymerase chain reaction test was Rs. 2881.95 (15.49 USD), which indicated a much higher unit cost per procedure than hybrid capture 2 test, USD 6.07-6.58 [12], and clinician sampled care HPV test, USD 3.9 [13].

According to the mid-year population estimates for 2017 in Sri Lanka, the total number of 35 year age cohort women population assumed by 1% of the total population were 214440. Therefore, the country has to spend Rs. 618 million rupees annually to incorporate cobas 4800 HPV/DNA screening test with “thin prep cell collection media/Liquid-Based Cytology (LBC)” to screen all 35 year age cohort women population in Sri Lanka.

Simple inexpensive approaches for cervical cancer screening by cobas 4800 test in low-resource settings were successfully attempted in some other countries. In a study, each woman was subjected to HPV/DNA specimen collection with a swab placed into a sarstedt tube and a cytobrush placed into a “thin prep cell collection media/LBC” The rates of the agreement were reported very high (>90%) for any high-risk HPV types, HPV 16, HPV 18 and 12 high pooled risk HPV genotypes [14].

The direct medical cost of cervical pre-cancer/cancer management such as loop excision, cold knife conization, simple and radical hysterectomy varied from 61-544 USD, while direct non-medical expenditure varied from USD 0.68-3.09 for screening/diagnosis and 83-494 USD for pre-cancer treatment [13]. Therefore, cervical cancer screening is always much cost-effective than patient management.

The total inward cost of management of a patient with cervical cancer stages 1a, 1b, and IIa was Rs. 13668.50, while the cost of management for cervical cancer patients in advanced stages of the disease was Rs. 23341.76 [7]. To consider the best option in the preventive health aspect of cervical cancer, incremental cost assessment of pap smear screening (Rs. 308.18) as a national cervical cancer screening method and cervical cancer per patient management cost is a real necessity as the last cost estimation was carried out in 2009. Therefore, it's a limitation of the present cost evaluations.

This study was restricted to one WWC in Kalutara districts due to logistic constraints. The population characteristics and the public health infrastructure of the WWC favoured the generalizability of the research findings to the whole country. HPV/DNA screening test was carried out in Kalutara district as a research study, therefore the number of women coming for the test is limited to one clinic as there were 89 WWCs were dispersed throughout the district. Hence the number of samples considered for the cost estimation procedure was small (n=15).

Conclusions and Recommendations

Cobas HPV/DNA screening test in a cell collection media called “thin prep” is economically feasible to implement among 35 year age cohort of ever married women in Sri Lanka. It is better to further estimate the cost of an alternative specimen collection method (i.e. dry swabs) of cobas HPV/DNA screening test to determine the more suitable method for resource-limited settings.

Declarations

Ethics approval and consent of the participants

Ethical clearance was obtained from the Ethics Review Committee (ERC), National Institute of Health Science (NIHS), Kalutara Sri Lanka (ref number NIHS/ERC/18/06R). Informed written consent was obtained from each of the selected participants in the field during the study. Confidentiality was highly maintained while handing over individual HPV/DNA result reports. Administrative clearance to conduct the study was obtained from Provincial director of health services/western province, regional director of health services/Kalutara district, director/district general hospital Kalutara.

Consent for publication

Not applicable.

Competing interests of authors

Authors were declared that they have no competing interests.

Funding for the study

We hereby declare that the cost for specimen collection instruments with reagents (Test kits) was funded by the family health bureau, Colombo, and Sri-Lanka. There was no influence from the above-mentioned institute during the process of conducting or report writing of this research.

Authors contribution to the study

KCMP has participated in the design of the study, coordinated data collection estimated unit cost per HPV/DNA procedure, and drafted the version of the manuscript. HTCSA, DDS, and NM have participated in the design of the study. Cost estimation was carried out under the supervision of DDS. Both HTCSA, DDS, and NM were helped to draft the manuscript. All four authors were read and approved the final manuscript.

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Data and materials of the study

The datasets used to analyze in this study are available at the corresponding author on reasonable request.

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