

**A SYSTEMATIC REVIEW FOR RATING THE ACCURACY OF VARIOUS
SCREENING METHODS USED FOR EARLY DETECTION OF CERVICAL
CANCER**

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2023

DECLARATION BY STUDENT

I hereby declare that this dissertation titled “**Analysis of effective cervical cancer screening method in India** “ is the bonafide record of my original research work. I declare that it has been submitted to any other university or institution for the award of and degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

(signature)

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Date-27th May 2023

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This is to certify that Suchismita Das, (KHPL-I-0175) has worked as “Intern” with Karkinos Healthcare Private Limited and has successfully completed the internship under the guidance of Bharat Kumar Sarvepalli.

Internship Duration: 15th March 2023 to 31st May 2023.

We wish all the best.

For Karkinos Healthcare Pvt Ltd



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Abstract

Cervical cancer is the fourth most common cancer in women worldwide, with an estimated 604,127 new cases and 342,000 deaths in 2020. About 90 % of the new cases and deaths worldwide in 2020 occurred in low and middle- income countries. The burden of cervical cancer is disproportionately borne by women in low and middle income countries, where access to screening and treatment is limited. In these countries, cervical cancer is the leading cause of cancer death among women. To eliminate cervical cancer WHO has set a goal of eliminating cervical cancer by 2030, which is 90-70-90 target. And other recommendations are ICMR, NCG, ASCO etc. some studies its noticeable that VIA is more cost effective but having false positive result. For the context of accuracy the total three screening of cervical cancer the highest sensitivity and specificity have seen in the HPV testing. Pap smear having highest specificity lowest sensitivity compared to VIA. For some case HPV vaccination is most effective with VIA screening. . HPV vaccination for preadolescent girls reduce the 62% risk from cervical cancer.

Conclusion – After evaluation on the context of accuracy and cost effectiveness HPV test should be suggested..

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Table of content

Sl no	Content	Page no
1.	Introduction	8- 15
2	Review of literature	16-20
6.	Methodology	21-23
7.	Result and Discussion	24-27
8.	Limitation	28
9.	Suggestion	29
10.	Conclusion	30
11.	Reference	31

List of figures

	Page no
A. Fig 1: Prevalence of disease in India.....	10
B. Fig 2: Prevalence of cancer in India.....	12
C. Fig 3: Prisma flow diagram of the study.....	23
D. Fig 4: Total expenditure of different screening method on the bases of 10 years.....	26

List of Abbreviation

1. ACS- American Cancer Society
2. CBA- Cost Benefit Analysis
3. CER- Cost Effective Ratio
4. CIN- Cervical Intraepithelial Neoplasia
5. HBP- Health Benefit package
6. HPV – Human Papillomavirus
7. LBC- Liquid Based Cytology
8. OOPE- Out of Pocket Expenditure
9. PFHIS-Publicly financial Health Insurance Scheme
- 10.VIA- Visual Inspection with Acetic Acid

1) Introduction –

As per WHO estimates the fourth most common cancer in women, in 2020 cervical cancer was responsible for 342,000 deaths worldwide, and estimated number of new cervical cancer cases is 604,127. Cervical cancer is a major cause of cancer mortality in women and more than a quarter of its global burden is contributed by developing countries. Cervical cancer is a significant global health burden, particularly in developing countries where access to healthcare and screening programs may be limited. The American Cancer Society advises that individuals with cervix initiation start getting screened for cervical cancer at age 25 and undergo primary human Papillomavirus testing every five years until they are 65. Individuals aged 25 to 65 years should be screened with cytology alone every 3 years or cotesting (HPV testing in combination with cytology) every 5 years if primary HPV testing is not available. The American Cancer Society (ACS) advises people over 65 who have never had cervical intraepithelial neoplasia grade 2 or a more severe form of the disease within the previous 25 years, as well as those who can demonstrate sufficient prior screening results that were negative in the previous 10 years, to stop all cervical cancer screening (qualified recommendation).

1.1. Burden of cervical cancer

Cervical cancer is the fourth most common cancer in women worldwide, with an estimated 604,127 new cases and 342,000 deaths in 2020. About 90 % of the new cases and deaths worldwide in 2020 occurred in low and middle- income countries.

The burden of cervical cancer is disproportionately borne by women in low and middle income countries, where access to screening and treatment is

limited. In these countries, cervical cancer is the leading cause of cancer death among women.

The main cause of cervical cancer is infection with the HPV. HPV is a sexually transmitted infection that is very common. Most of the people who are infected with HPV clear the infection on their own, but some people develop persistent infections that can lead to cervical cancer.

Cervical cancer is a major public health problem in India leading to high economic burden, which is disproportionately borne by the patients as out-of-pocket expenditure (OOPE). Several publicly financed health insurance schemes (PFHIs) in India cover the treatment for cervical cancer. However, the provider payment rates for health benefit packages (HBP) under these PFHIs are not based on scientific evidence. We undertook this study to estimate the cost of services provided for treatment of cervical cancer and cost of the package of care for cervical cancer in India.

Cervical cancer is a preventable disease .By getting HPV vaccination, Getting timely cervical cancer screening, women can reduce their risk of developing cervical cancer.

The World Health Organization (WHO) has set a goal of eliminating cervical cancer by 2030,

90-70-90 target –

- 90 % girls should be HPV vaccinated by age 15.
- 70 % of women should be screened by high performance test age of 35 and again by the 45.
- 90 % women with per cancer treated and 90 % of women with invasive cancer managed.

To achieve this goal, the WHO is working to increase HPV vaccination rates, improve cervical cancer screening programs, and provide access to treatment for women in developing countries.

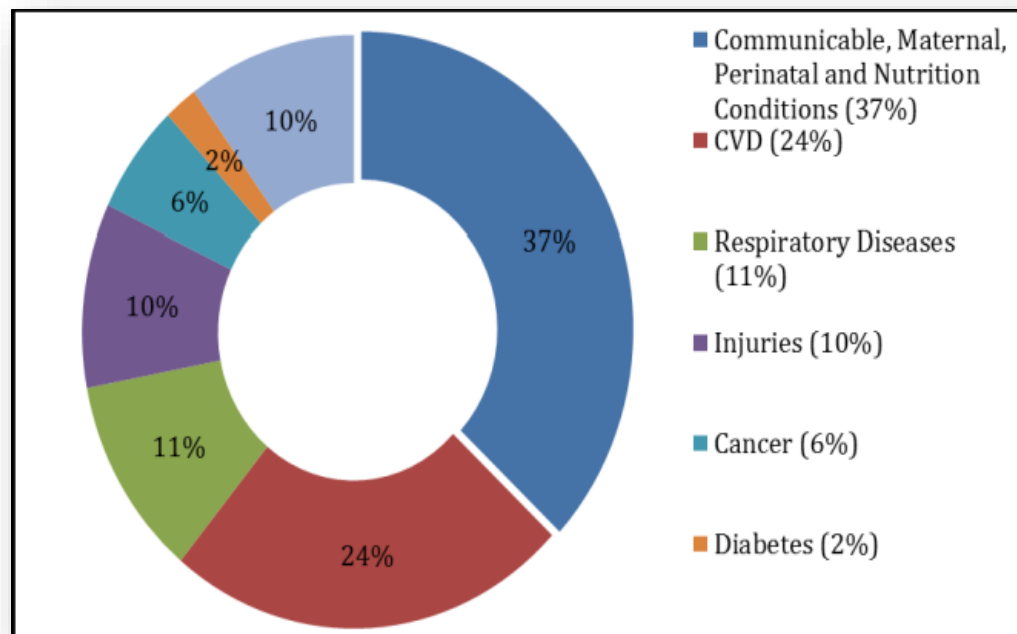


Fig 1: Prevalence of disease in India

- Based on this pictorial depiction it is seen that 37% of the diseases caused in India is due to the communicable or nutritional conditions
- Followed by major disease prevalence in India is due to Respiratory diseases
- Only 6% as of now the prevalence of cancer is present in India

HPV transmission is regulated by sexual activity and age. Almost 75% of all sexually active individuals are likely to be infected with at least one HPV type. However, the great majority of infections cure naturally, and just a few (1% of HPV infections lead to malignancy). The lifetime risk for genital HPV

is 50-80%, while the risk for genital warts is about 5%.The likelihood of having an abnormal Pap smear is 35% among women who had regular screening, 20% in CIN, and 1% in ICC. However, in women who do not receive routine screening, the risk of cervical cancer is up to 4%.The Pap test is used to detect cellular abnormalities in cervical tissue, which aids in early diagnosis. The majority of women become infected with HPV at some time in their lives, usually soon after beginning sexual activity.

Cervical cancer is the most frequent cancer in Indian women and the second most common cancer in women globally, owing primarily to Human Papillomavirus infection. Though there are various methods of cervical cancer prevention, vaccination is emerging as the most effective alternative, with two vaccinations now available. In India, two licenced vaccinations are available: a quadrivalent vaccine and a bivalent vaccine. Both vaccines are made using recombinant DNA technology, which creates non-infectious VLPs containing the HPV L1 protein.

So we can say , Adherence to regular screening by the vulnerable female population through monthly Pap smears has been inadequate even in industrialised nations, and ample size of screening is difficult to obtain in underdeveloped countries such as India. For that context HPV vaccination is the best method of HPV prevention.

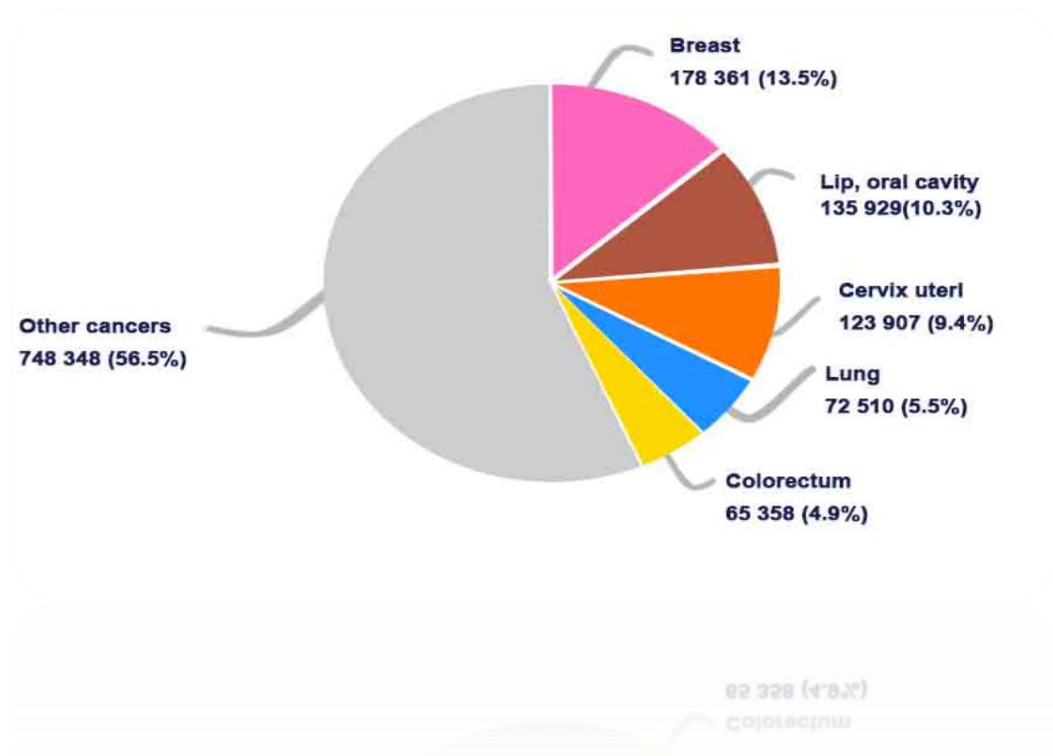


Fig 2: Prevalence of cancer in India

- This pie representation shows that new cases of cancer in India till 2022
- As per the analysis other cancers cumulatively had the number of cases of 7,48,348 which accounts for 56.5%
- After that breast cancer is the most prevailed form of cancer that do occur which stands at 13.5%
- Cervical cancer 9.4%

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India currently houses a number of research programs on cervical cancer. The Indian council of medical research established the National cancer registry program, which serves as a cancer surveillance system in India. It conducts "active" data collection by going to specialized cancer hospitals and pathology labs, both in the public and private sectors, to learn about the types and magnitude of cancer cases.

WHO recommendation for cervical cancer screening

Pre-cancerous lesions can be found through screening at an early stage when they are still treatable. There is limited availability to these prevention methods in low- and middle-income countries, and cervical cancer is frequently not discovered until it has progressed and symptoms appear. Additionally, may have restricted access to treatments for malignant lesions (such as cancer surgery, radiation, and chemotherapy), which would increase the mortality rate from cervical cancer. More than 95% of cases of cervical cancer are caused by the human papillomavirus (HPV)

ICMR recommendation for cervical cancer screening

ANMs and staff nurses should be there for cervical cancer screening VIA at the Primary Health Centre level. The master trainers have been selected as gynaecologists and woman medical officers who have received training in cervical cancer screening and management. A complete 10-day training programme for ANMs and staff nurses will be conducted at designated medical colleges or district hospitals, where practical skills such insertion of a speculum, performing VIA tests, and using the thermal ablation procedure should be offered. At the conclusion of the course, the student must receive at least a 70% on the knowledge evaluation and an 80% on the skill assessment. .

NCG recommendation for cervical cancer screening

For cervical cancer primary screening method if limited resources are there then VIA and for optimal resources and high resources HPV DNA should be done. For VIA Trained primary care workers, trained nurse should be there but for HPV test along with trained nurse physician should be present there. For both VIA and HPV test the targeted age group should be 30-65 yrs.

NPCDC recommendation for cervical cancer screening

National Programme for Prevention & control of cancer, Diabetes, Cardio vascular diseases and stroke promotes VIA methods for cervical screening.

ASCO recommendation for cervical cancer screening

American Society of Clinical Oncology recommends, In situations with limited resources, human papillomavirus (HPV) DNA testing is advised; in settings with more resources, visual examination with acetic acid may be sufficient. The following settings have different suggested age ranges and repetition rates: Maximum: Age 25–65, every five years; Enhanced: Age 30–65, if two consecutive negative tests at five-year intervals, then every ten years; Limited: Age 30–49, once to three times in a lifetime. Basic: Age 30–49. To identify treatment eligibility in more basic settings, ocular evaluation is performed; in other settings, genotyping with cytology or cytology alone is used to determine therapy. Women who are HIV-positive should be screened with HPV testing after diagnosis, twice as many times per lifetime as the general population. Screening is recommended at 6 weeks postpartum in basic settings; in other settings, screening is recommended at 6 months. In basic settings without mass screening, infrastructure for HPV testing, diagnosis, and treatment should be developed.

2. Literature review-

Sl no	Title , Study location	Cervical cancer technique used	Analysis	Results
1.	Cervical cancer screening in rural India: Status & current concepts	VIA, Pap Smear, HPV	The VIA methods had higher sensitivity and were less expensive than the Pap test, which had poor sensitivity but excellent specificity. HPV has higher sensitivity and specificity	In India, HPV vaccination might lead to a significant advance in the fight against cervical cancer.
2.	Burden of cervical cancer and role of screening in India	VIA , Pap Smear, HPV	All cancers women in India about in are caused by cervical cancer. The	High-quality cytology screening may not be practical for widespread application in

			pooled estimates of sensitivity and specificity of visual inspection with acetic acid (VIA), magnified VIA, visual inspection with Lugol's iodine (VILI), cytology (Pap smear), and human papillomavirus DNA the specificity and sensitivity is both High in HPV but for a huge population VIA would be comparatively better screening method	underdeveloped nations due to a lack of the essential infrastructure and quality control. Therefore, primary health care systems in resource-poor nations like India should embrace cervical cancer screening programmes based on visual screening tests like VIA/VILI.
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3.	A comparative study of cervical cancer screening methods in a rural community setting of North India	VIA , Pap Smear	VIA and Pap smear had done among the age group 30 – 59 age group women. For pap sensitivity & specificity 87.5 & 98.8 % and for VIA 50 & 95.7 %.	A comparative study of cervical cancer screening methods in a rural community setting of North India
4.	Specificity, sensitivity and cost	Pap Smear, HPV	over 10,000 women aged 30 to 69 years were randomly assigned to receive either a Pap smear or an HPV DNA test approved by the US Food and Drug Administration	As a result for HPV sensitivity & specificity are 94.6 & 94.1 % and for Pap smear 55.4 & 96.8 %.

5.	Cervical Cancer Screening in Resource-Constrained Countries: Current Status and Future Directions	VIA, HPV	With careful monitoring of test positive and detection rates and standard testing, VIA proved a helpful substitute for HPV testing in low-resource settings. Among the all three modalities VIA is the most cost effective compared to the HPV test.	With the introduction of HPV vaccine, cervical cancer primary prevention also appears to be a strong prospect. For underdeveloped nations, vaccine accessibility and acceptance, however, remain a problem. It is also necessary to assess any potential future impacts of vaccination on various screening strategies.
6.	The IARC perspective on cervical cancer screening		The capability to reduce of cancer risk is week in VIA method. Additionally,	Some times VIA unable to detect the precancerous cells then HPV is

			standardised interpretation criteria still need to be established, and sufficient training is required to execute VIA screening.	the most convenient test.
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5. Methodology

5.1.Research question

- 1) What is the most accurate screening method for the early detection of cervical cancer?
- 2) How public and private sectors are taking initiative to increase the screening methods for the people of India

5.2.Objectives

- 1) To analyse the different methods used to screen for the early detection of the cervical cancer
- 2) To determine the various methods used by the public and private sectors for the early detection of cervical cancer

5.3. Selection of Study

From the year 2014 to 2023, the publishing window was taken into consideration. There are 17,800 records recognized through information database which incorporates google scholar, science direct, research gate, pubmed, cancer.gov, nih.gov to get to the distributed work India and globally.

Source & Selection of Data

Cervical cancer, screening test, cervical screening test, cervical elimination, cancer testing, Pap smear, Visual Inspection with Acetic Acid, vaginal smear, Human papilloma virus (HPV), HPV

testing, effectiveness of result these are some of the search phrases utilised during the process .There are 16,900 reports were collected through information database which incorporates google scholar, science direct, research gate, pubmed, cancer.gov, nih.gov, nejm.org to get to the distributed work. After removing 8997 duplicate articles get 7903 articles. Then read title and abstract and after all kind of sorting like eliminate the irrelevant , similar, non full text article finally got 17 articles. Those 17 papers were chosen for in-depth investigation and were ranked according to their suitability.

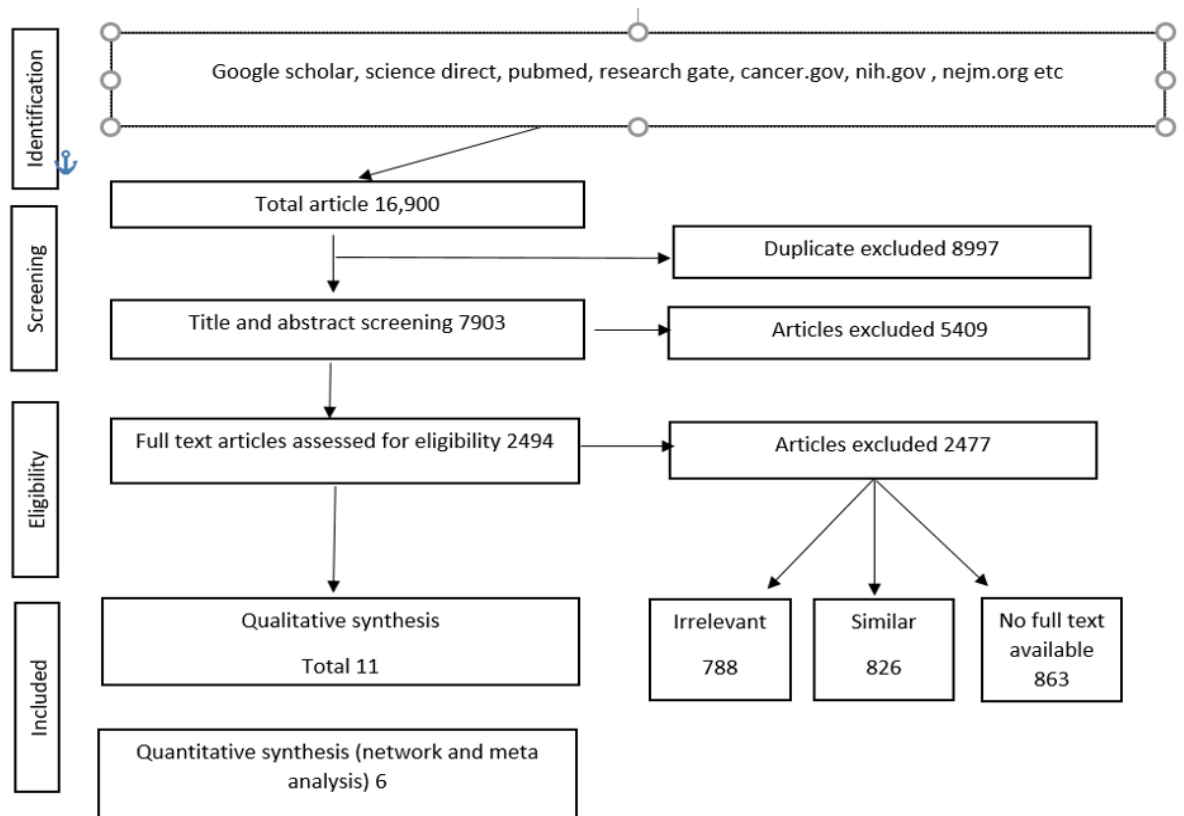
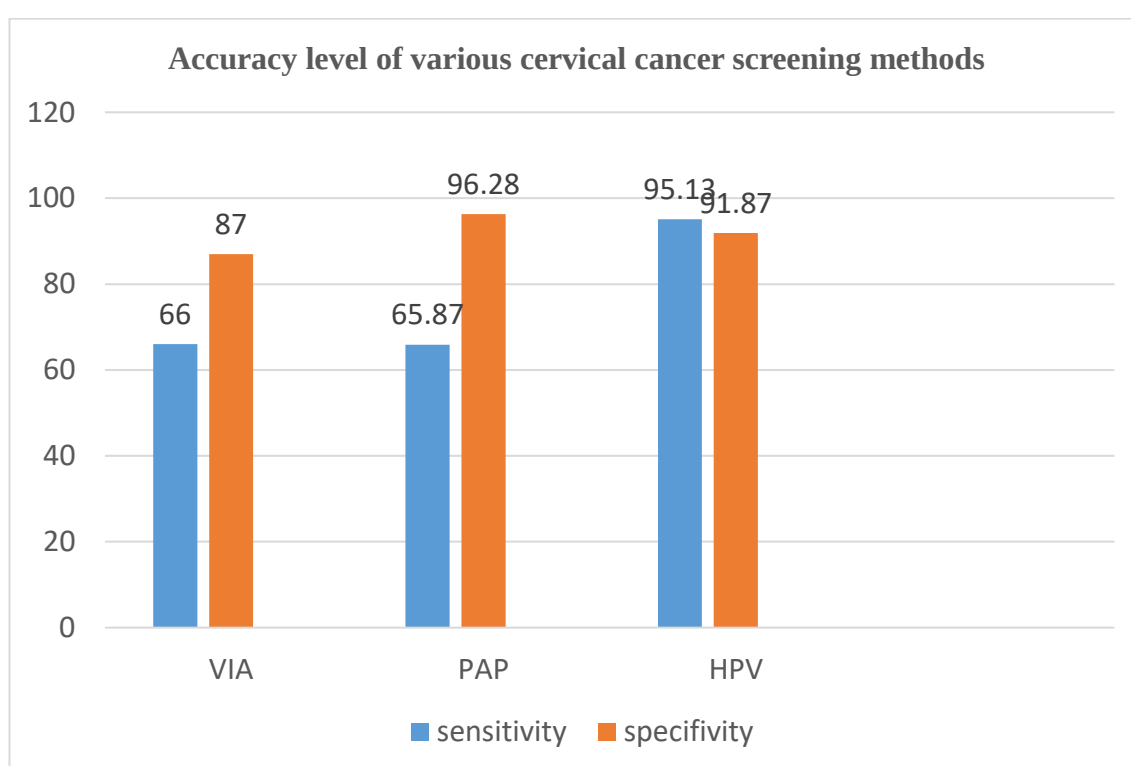


Fig 3: Prisma flow diagram of the study

6.Result and Discussion –

For cervical cancer screening, the Pap smear test and visual detection tests were compared in order to determine the best approach for low-resource environments. It was seen that the VIA methods had higher sensitivity and were less expensive than the Pap test, which had poor sensitivity but excellent specificity. As WHO recommendation the accuracy chart is following:



Accuracy of a test meaning its ability to differentiate the patient and health cases correctly. Sensitivity is the ability of a test to correctly identify patient with a disease (true positive).

Specificity is the ability of a test to correctly identify patient without a disease (false positive).

HPV has higher sensitivity and specificity compared to the VIA & Pap Smear.

From some research study, Pap smear and HPV testing combined testing is now recommended for women because at 5-year intervals in women aged 20 to 70 might reduce cervical cancer mortality by more than 90% compared to no screening.

In some of study, In contrast to screening alone, vaccination would be more effective when paired with existing screening, and the combined strategy would result in a 69% decrease at a cost. VIA every three years in women aged 30-49 has 10% coverage rate. HPV vaccination of preadolescent girls at 70% coverage would result in a 62% lifetime risk reduction for cervical cancer.

The HPV testing in cervical cancer screening programmes are becoming more and more popular around the world, however they are currently too expensive to be used at the population level in developing country settings. The lifetime risk of cervical cancer would be reduced by 34-50% in women who underwent three lifetime screenings between the ages of 35 and 45. We have seen cost is associated with with various screening tests, their technical specifications, the equipment needed in laboratories, and the viability of the programme etc. These results are in line with a prior investigation into the affordability of cervical cancer prevention. We have seen Rapid HPV-DNA testing is the most effective course of action. Other screening techniques were dominated by quick HPV-DNA because to its cheaper cost per test and higher sensitivity than traditional cytology. The results also take into account the extra costs and advantages of fewer visits, as well as the savings on time, money, and transportation, as well as the decreased loss to follow-up. A quick HPV-DNA test-based method obviously offers high value for the resources spent with a cost-effectiveness ratio.

In contrast to screening alone, vaccination would be more effective when paired with existing screening, and the combined strategy would result in a 69% decrease at a cost.

Some times the cost differs in various screening test technical requirements of tests, laboratory infrastructure and programme feasibility settings.

As long term result the suggestion would go for HPV testing because if we can see next 10 years which method having accuracy and cost effectiveness both.

Screening test	Price (INR)	Frequency	In 10 years	Total cost in 10 years
VIA	300-350/-	1 times in 3 years	3 times	Around 1100/-
Pap Smear	550-600/-	1 times in 3 years	3 times	Around 1800 /-
HPV	1000/-	1 – 2 times in 10 years	1-2 times	1000-2000/-

Fig 4: Total expenditure of different screening method on the bases of 10 years.

According to that research , Sensitivity and Specificity of VIA has 66 % and 87%. The average price in market 300-350 /- and It should be done 1 times in 3 years. So on the bases of 10 years it should be done 3 times. So for that case total cost should be around 1100/- .VIA should be done .

Sensitivity and Specificity of Pap Smear has 65.87 % and 96.28%. The average price in market 550-600/- and It should be done 1 times in 3 years So on the bases of 10 years it should be done 3 times. So for that case total cost should be around 1800/-.

Sensitivity and Specificity of HPV testing has 65.87 % and 96.28%. Total accuracy is high compared to the VIA and Pap Smear test. The average price in market 1000 /- and It should be done 1 or 2 times times in 10 years So on the bases of 10 years it should be done most probably 1 times. So for that case total cost should be around 1000 Or 2000/-.

As a lone term accuracy HPV can be effective.

7.Limitation

As a limitation we have seen not only the economic constraints but also constraints on human resources or infrastructure are common in many resources poor setting. There are numerous factors including socio cultural preference will influence the country decision to implement particular screening strategy. There are so many places ,several cervical cancer screening programme are still under the planning and early implementation stage as they are trying to figure it out which screening procedure are efficient and affordable in a specific environment.

Lack of equipment, lack of decentralizing the programme, lack of proper training to the workers and also awareness and education all those are the contributing factors. For contesting some times doctors remained unsure of the value of concurrent HPV settings.

Suggestion

- In the context of accuracy and cost effectiveness HPV should suggested
- Government should include cervical cancer screening test in their health scheme

Example-

Under Chiranjeevi Yojna (for Rajasthan) , the eligible candidate can receive benefit of 5 lakhs, Swastha Sathi (for Westbengal) its 1.5 lakh , government should improve those procedures and include those screening tests in those scheme. So that it can be a major part of early detection of cervical cancer.

8. Conclusion

Cervical cancer is a huge public health issue which represent the second most frequent and fatal cancer among women. Experience from developed countries demonstrates that cervical cancer incidence and death are reduced by more than half when screening is done. However, in developing nations like India, where facilities and trained manpower are few, executing the required screening method presents both a financial and a health system feasibility problem. This research has clear review of effectiveness and accuracy level of the screening methods of cervical cancer—VIA, Pap tests, and HPV DNA tests. VIA is Some times studies show that VIA at a frequency of every five years is the most economically advantageous technique for or some times we have seen VIA will be more effective when it will be combined with HPV.

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