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See and Treat: Cervical cancer prevention strategy in Indonesia with VIA-DoVIA screening and prompt treatment

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Abstract

Cervical cancer, as the second most common type of cancer in Indonesia after breast cancer, is a major problem for Indonesian women. Cervical cancer can be prevented with HPV vaccination and various screening/early detection methods, such as Pap smear, VIA (visual inspection with acetic acid) test, and HPV-DNA test. Currently, VIA test is the chosen screening method for cervical cancer in Indonesia, as it is easy, cheap, accurate, and can be implemented in all regions of the country. The VIA method was developed using VIA documentation (DoVIA) and VIA documentation telemedicine (TeleDoVIA). It is established that positive findings should be treated with cryotherapy. This serial of diagnosis using VIA screening and treatment with cryotherapy is termed See and Treat. Subsequently, it is developed into Screen and Treat. The gas supply for cryotherapy may become a challenge, which drive the search for an alternative therapeutic method, such as using TCA (trichloroacetic acid). Strategies for the prevention of cervical cancer includes implementation of HPV vaccination (90%), 70% coverage of screening, and treatment after positive findings (90%). The involvement of the authorities is crucial for the achievement of strategical target and its public implementation, by setting regulations for the success of screening coverage.

Keywords*: cervical cancer, DoVIA, see and treat, TeleDoVIA, VIA*

Abstrak

Kanker serviks menjadi masalah bagi kesehatan perempuan Indonesia, menduduki peringkat kedua setelah kanker payudara di Indonesia. Kanker serviks dapat dicegah, dengan vaksinasi HPV, upaya skrining/deteksi dini kanker serviks dengan beberapa metode skrining a.l. pap smear, tes IVA (inspeksi Visual dengan Asam Asetat), tes HPV-DNA. Saat ini untuk Indonesia dipilih metode skrining kanker serviks dengan tes IVA, karena metode ini mudah, murah, akurat, dan dapat dilaksanakan di seluruh pelosok negeri. Metode tes IVA dikembangkan dengan dokumentasi IVA (DoIVA) dan untuk konsultasi, dengan Telemedisine Dokumentasi IVA (TeleDoIVA). Telah ditetapkan temuan positif diterapi dengan krioterapai, maka rangkaian diagnosis dengan skrining IVA, dan dilakukan terapi dengan krioterapi, menjadi rangkaian See and Treat. Pengembangan nya menjadi Screen and Treat. Adanya kendala pengadaan gas untuk krioterapi, mendorong upaya mencari metode terapi lain, yaitu dengan TCA (Tri Chloro Acetic acid). Terlaksananya Vaksinasi HPV (90%), tercapainya 70% cakupan skrining, terapi pada temuan skrining positif (90%), menjadi strategi bagi upaya pencegahan kanker serviks. Dalam penerapannya di masyarakat agar pencapaian target strategi dapat tercapai, kiranya diperlukan keterlibatan peran otoritas untuk menetapkan regulasi agar cakupan skrining dapat tercapai.

Kata kunci: DoIVA, IVA, kanker serviks, see and treat, TeleDoIVA

Background

Cervical cancer is the second most prevalent cancer in Indonesian women, just after breast cancer.[1,2] A successful method for detection most commonly used in developed countries is the Pap test, which is difficult to implement in Indonesia. In the US, for example, 50 million Pap tests are conducted yearly with an estimated cost of 1.5 billion USD,[3,4] which is approximately 21 trillion IDR, the equivalent of about a third of Indonesia's Ministry of Health's expenditure in 2020.[5]

The government of Indonesia has allocated 49 million USD, approximately 704 billion IDR, as the budget for cervical cancer management in 2020.[6] In order to execute Pap tests with the aforementioned amount, the US employs 18,640 dual anatomic pathology and clinical pathology specialists and 5,729 anatomic pathologists, totaling at 24,360 anatomic pathologists with the capacity to perform Pap tests.[7] Additionally, approximately 10,000 cytotechnologists, certified associate bachelor of science, are presented to help.[8] Accounting for population differences, implementing the same resource in Indonesia requires 19,800 anatomic pathologists.[9,10] In 2016, there were only 681 anatomic pathologists in Indonesia.[11] Thus, noting the available resources and the country's unique geographic terrain, the Pap test cannot yet be performed as a routine screening program in Indonesia; an alternative method is needed.

Cervical cancer differs from most malignancies in that its cause is well known. Harald zur Hausen was awarded a Nobel prize in 2008 for discovering that Human Papilloma Virus (HPV) is the cause of cervical cancer.[12] Its transmission widely suggests that sexual activity is a risk factor for cervical cancer.[13–15]

Cervical Cancer As A Challenge for Women's Health in Indonesia

There are several main discussion points regarding cervical cancer in Indonesia

1. Cervical cancer as a challenge for women's health
2. The need for early education for students regarding reproductive health and malignancies of the reproductive organs.
3. Direct mass education: cervical cancer prevention, early detection with VIA, Pap test, or HPV DNA test. Early detection, do not wait until a symptom appears.
4. Health professional training to raise capability and competence for cervical cancer screening.
5. Choosing an easy, affordable, accurate, and accessible screening method, such as VIA.
6. Implementation of *See and Treat.* Viable therapeutic modality includes cryotherapy, trichloroacetic acid (TCA), and cold coagulation.[16-17]
7. The need for mandatory screening regulation for married Indonesian women in areas capable of running a screening program resource-wise.

Based on the 2020 survey data of GLOBOCAN, it is estimated that there are 604,127 new cases of cervical cancer and 341,831 deaths relating to cervical cancer, most of which are from low and medium-low-income countries.[18] In Indonesia in 2020, there were 36,633 new cases of cervical cancer and 21,003 cervical cancer-related deaths. This nearly doubles from 2012, when new cases of cervical cancer were only around 20,000.[19] Cervical cancer is the second leading cause of cancer-related death in Indonesian women, just after breast cancer.[18] The high death rate in Indonesia's cervical cancer cases can be attributed to the fact that most cases (70%) are found already in the late stages.[20]

On April 21st 2015, the national movement for prevention and early detection of cancer in women (*Gerakan Nasional Pencegahan dan Deteksi Dini Kanker pada Perempuan*) was planned by First Lady Iriana Joko Widodo at Puskesmas Nanggulan public health center, Kulonprogo, Yogyakarta.[21] The execution of this program is regulated under The Minister of Health of The Republic of Indonesia Number 34 of 2015 concerning Breast Cancer and Cervical Cancer Management. Early detection using Visual Inspection with acetic acid (VIA) or pap smear and management of precancerous lesions with cryotherapy is collectively known as See and Treat.

A positive finding in screening is futile if not followed by prompt treatment. However, in a pilot national cervical cancer program, an area showed that only 30% of those who were screened positive continued to cryotherapy. Data from Faculty of Medicine, Universitas Indonesia, the Female Cancer Program (FMUI-FCP) shows that only 60% of patients who tested positive for VIA were treated.[22] Meanwhile, the World Health Organization (WHO) recommended that at least 90% of precancerous lesion cases be treated.[23]

Cryotherapy requires N_2O/CO_2 gases, which have limited availability in certain areas. Therefore, an alternative treatment method is required. One viable modality is Trichloroacetic acid (TCA), known for its cosmetic use in chemical peeling.[24] TCA is more

commonly used to treat condyloma acuminate (genital warts), but an 85% concentration of TCA can be used to treat cervical precancerous lesions. A study by Suwartono shows that 97.2% of patient with TCA treatment undergoes conversion to VIA-negative after three months. Compared to cryotherapy, there appears to be no significant difference in using TCA on VIA-positive cases.[16]

Basic Concepts and Target of Cervical Cancer Prevention

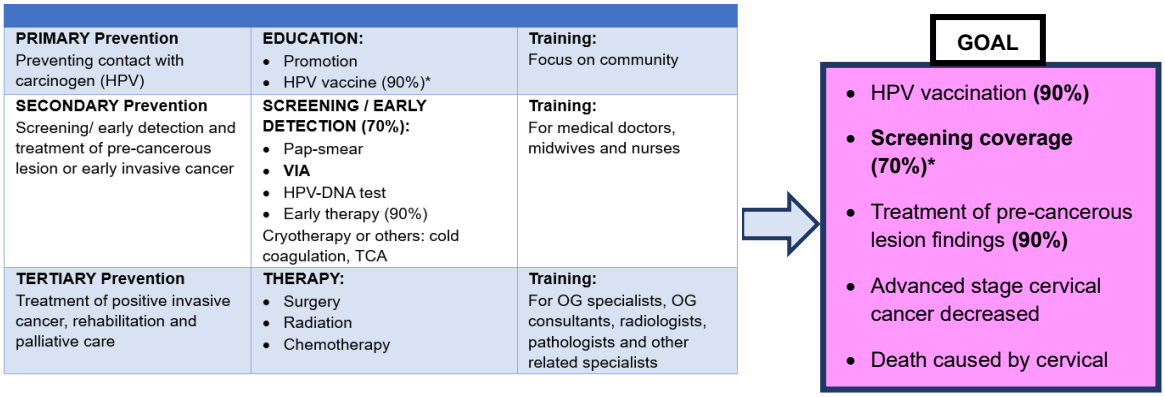

Figure 1. Concepts and Targets *) Target established by WHO for the year 2030.[25]

Purpose of Program:

Institutions responsible for cervical cancer prevention programs must have united long-term goals for Indonesia, which are adapted from WHO's target for the year 2030:[25]

1. HPV vaccination (90%)
2. Screening coverage (70%)
3. Therapy for those screened positive (90%).
   Cervical cancer has a clinical progression that starts from the precancerous lesion and ends with invasive cancer in 3 to 17 years. The broad period of time for detection gives birth to the concept of *kenalilah aku pada tahap prakanker* (Recognize Me in Precancerous Stage), as treatment is relatively easy and can reach 100% clearance in precancerous lesions.
4. Reduction of late-stage cervical cancer cases.
   Currently, most cases (70%) are in the late stages.[20]
5. Reduction of cervical cancer-related death.
6. Assurance of program sustainability.
7. Data surveillance for cervical cancer screening.
8. Building a national cervical cancer prevention network.

Developing a cervical cancer prevention strategy in Indonesia and possible solutions to challenges involved is essential. The basic concept of cervical cancer management is as follows:

1. Primary prevention.

Efforts to prevent the causative agent, HPV, from entering the target organ, the cervix. This includes health education to create healthy living habits away from possible HPV infection, such as safe sexual practices, lower promiscuous tendencies, no smoking, and consumption of nutritious foods. A brief and to-the-point message is developed for the public:

a. "All married women or engaged in sexual activity must undergo cervical cancer screening."
b. "Early detection, do not wait for a symptom."

This leads to the notion that the knowledge and education to prevent cervical cancer should be formally taught to students in secondary education within the school's curriculum. Another important primary prevention method includes the HPV vaccine, which has been available since 2006. Available vaccine variant includes the bivalent vaccine (against HPV type 16 and 18) and the quadrivalent vaccine (against HPV type 16,18, and low-risk HPV type 6 and 11). A nine-valent vaccine (against HPV type 6,11, 16, 31, 33, 45, 52, 58) has also recently made available.[26,27] In Indonesia, efforts to implement the HPV vaccine for students started with the Student Immunisation Month program (BIAS) on October 4th, 2016.

2. Secondary Prevention.

Secondary prevention entails early detection in populations where HPV exposure was not prevented. This is done with screening, such as with the VIA method. The following should be accounted for in secondary prevention:

a. **Screening coverage** ideally reaches at least 70% of the target. The target for this coverage is at-risk women, i.e., those married and aged 30-50. However, the Indonesian society of oncology and gynecology (HOGI) suggests that the screening should be broadened to include 25 to 65-year-olds since the prevalence of cancer in those aged 50 years above is still high.[28,29] To achieve the targeted screening coverage, the screening method must be relatively easy to do, affordable, accessible, and applicable while still having good sensitivity and specificity.

b. **Choice of screening method.** Several methods for cervical cancer screening are known; Pap smear, HPV DNA test, visual inspection with acetic acid (VIA), and colposcopy. Historically, there was also what was known as gynoscopy (using a magnifying glass with a 2.5x power) and cervicography (using a camera equipped with a ring light). Cytology methods also vary from conventional cytology, liquid-based cytology, and examination of the cancer etiology, the HPV.

The USA spearheaded the movement toward HPV genotyping-based screening, where the majority of screeners agreed to change regulation from cytology-based to primarily based on HPV genotyping (Genotyping-HR HPV).[30] The Eurogin conference in Europe 2015 had also agreed on HPV-based screening and increasing HPV vaccination. The introduction of the HPV vaccine in the early 21st century showed that wide vaccine coverage caused a decline in HPV infection and precancerous lesions.[31]

Among all the available screening methods, VIA appears inferior at first. However, the power of looking at the cervix using VIA, combined with documentation (DoVIA), is now considered to be capable of being a confirmatory test before definitive testing in high-degree lesions. Equipment required for VIA includes speculum, light source, and 3-5% acetic acid solution. The advantage of the VIA method is the immediate result. VIA has also shown good sensitivity and specificity (94% and 95%, respectively).[32]

Conventionally, VIA does not include documentation, thus making confirmation difficult to do. Current development adds the use of camera, which is available in most person's phone nowadays. With a few tweaks, the camera can shine a light on the cervix for visual clarity and take a photo for documentation. This is known as documented VIA (DoVIA), and the documentation quality is regarded as equivalent to colposcopy.[33] With the documentation photo, it is possible to communicate and consult the finding by sending the DoVIA photo through applications such as WhatsApp messenger, creating telemedicine DoVIA (TeleDoVIA), and allowing long-ranged consultation. Our team has trained an area in Ambon, Fakfak Papua, for this method; they can send a picture from there and get answers in less than an hour, even in minutes.[34]

Documentation of visual inspection with acetic acid (DoVIA)

DoVIA reduces the possible bias from the VIA examiner and provides material for long-ranged communication and consultation. For example, a midwife or a doctor in Fakfak Papua can send a DoVIA photo to Jakarta with WhatsApp messenger applicaiton, and get an answer instantly. The entirety of this method is dubbed telemedicine documentation of VIA (TeleDoVIA). TeleDoVIA also monitors and evaluates the examiner's performance after VIA training, using long-range communication.

When screened positive, apply prompt treatment: See and treat

The protocol for a positive VIA finding is to treat in at least 90% of the cases,[29] for example, using cryotherapy. However, one issue in cryotherapy is the unavailability of N_2O or CO_2 gas. Currently, cold coagulation or trichloroacetic acid (TCA) is being considered.[24] This is the implementation of See and Treat, assuring that the positive finding in screening is not for naught. Most positive results in screening (90-95%) are caused by precancerous lesions, which are relatively easy to treat, with a recovery rate of nearly 100%. The available method in primary health care facilities in Indonesia is cryotherapy, usingN_2O or CO_2 gas to freeze the cervix. This method is simple, effective, and takes no longer than 20 minutes (3'-5'-3'). In practice, however, there are problems regarding gas availability, especially in secluded areas. With the See and Treat concept, Nuranna practices in a regional health care facility in Northern Jakarta using VIA screening followed by cryotherapy. She dubbed

this approach "Proaktivo," proactively screening with VIA and treating with cryotherapy.[32]

3. Tertiary Prevention

This stage of prevention is done in cases of confirmed invasive cancer. The prevention here refers to the prevention of death, and it is hoped that the patient's well-being can increase with adequate therapy. The therapy mainly consists of operative procedures, radiation, or combination with chemotherapy. This paper will not discuss tertiary prevention in detail.

Answering cervical cancer challenges in Indonesia

To achieve successful screening practice, there are a few notes to remember:

1. Goal determination, which is commonly women between 30 – 50 years old (± 1/6 of the population), in accordance to WHO. However, cervical cancer can occur as soon as three years after sexual activity, and in Indonesia, cervical cancer patients aged 50 years above are plentiful. Thus, the recommended screening age is 25 – 65 years old, or ±1/3 of the population. Because the VIA screening method is relatively easy dan affordable, the broader target age range of 25-65 years is still doable.
2. Develop documentation on VIA. There may be times when VIA interpretation is hindered and subjected to bias. DoVIA can solve that and enable VIA examiners to send photos to experts with TeleDoVIA. Interpretation can then be given without concern for distance.
3. The main challenge would be raising awareness in the women population on the importance of screening so that they come to their health care centers to check themselves. Stricter regulation in the form of legislation bills and government regulation (at the hands of the house of representatives or regional house of representatives) may be needed. Implementing the regulation nationally is a bit difficult, but it can be tried on a regional level in areas with adequate healthcare resources.
4. Building a national cervical cancer prevention data network would detail the precancerous lesion finding, any given therapy, and follow-up observations. It should also be possible to know if there is a recurrent lesion or if any lesions have become invasive cancer.

Implementation of Cervical Cancer Prevention Program with the Five Pillar Model

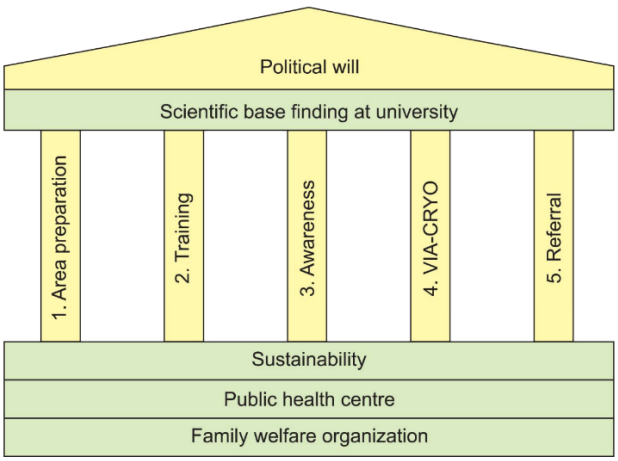

Figure 2. The Five Pillar Model for Cervical Cancer Prevention[35]

Coordination is necessary to practice cervical cancer prevention. The various activities we do with FMUI-FCP are coordinated under one model: The Five Pillar Model for Cervical Cancer Prevention.[35]

Conclusion

1. From a decade's study, it is found that the screening method applicable in Indonesia without sacrificing accuracy is VIA.
2. To increase objectivity in VIA tests, documentation on VIA (DoVIA) can be done with cell phone cameras. Furthermore, DoVIA can be used for telemedicine (TeleDoVIA).
3. A positive finding from VIA should be promptly treated. This approach is known as See and Treat. Aside from cryotherapy, the current modality in development is trichloroacetic acid (TCA).
4. A message to the public, especially to the women population:
   a. All women at risk (those who are married or have done sexual intercourse) must check themself for early detection of cervical cancer with a VIA test, Pap test, or HPV DNA test
   b. Early detection of cervical cancer should not wait for a symptom to appear.
5. The involvement of the government is essential. Strict regulation should impose mandatory periodic screening.

6. As a lecturer at Universitas Indonesia, while sailing the ocean of knowledge and life, I want to leave the following message for myself and my students: Your knowledge and your skill are essential, but your character is more. With a strong and sturdy character, keep learning and acquire valuable knowledge and skills. The most beautiful life is a beneficial one.

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