

CHAPTER II

THE DYNAMICS OF HUMAN PAPILLOMAVIRUS INFECTION DISCOVERY, RELEVANCE ON SEXUALITY EDUCATION AND HUMAN PAPILLOMAVIRUS VACCINATION RECOMMENDATION

Human papillomavirus is a common sexually transmitted infection and most sexually active individuals will contract it at some point in their lives, often without symptoms. Certain types of HPV can cause serious health problems such as genital warts and cancer, especially cervical cancer. The association between HPV and cervical cancer has driven the development of sexuality education and implementation of preventive measures. Indonesia, which faces a high burden of cervical cancer, has recently expanded HPV vaccination efforts and is targeting the younger generation to integrate vaccination into mandatory vaccination to reduce cervical cancer rates from early on.

2.1 Discovery of the Human Papillomavirus Infection

The human papillomavirus (HPV) is a frequently sexually transmitted infection. Nearly all sexually active people are going to get infected at some point in their life, usually without symptoms. There are around 100 different varieties of HPV infections, the majority of which cause no symptoms and disappear naturally without treatment (WHO, 2018). However, HPV is responsible for almost all cases of wart growth up to cancer of the genital organs such as the anus, mouth and throat. HPV can

lead to serious medical problems that enhance its impact on life expectancy and quality of life, and also presents a threat to human beings.

Decades of study were required to demonstrate the specific impact of HPV on the human body, particularly with relation to cervical cancer. In the 1950s, scientists looking for potential causes of cervical cancer started looking at lifestyle factors that could be linked to the infection (zur Hausen, 2009). Researchers discovered that women who were sexually active at a younger age or who had more partners had a greater chance of cervical cancer (zur Hausen, 2009). The findings also showed a pattern of lifestyles similar to the occurrence of STIs.

HPV-related infections, such as skin and genital warts, demonstrate identical signs and have been described since ages past. Hippocrates, the founder of modern medicine, first described genital warts, skin warts, and cervical neoplasia in the 4th century BC (MAMMAS et al., 2014). Since, warts on human skin and genital have long been thought to be contagious, it wasn't until the 19th century that Antonio Domenico Rigoni-Stern, an Italian surgeon from Asiago, believed that an HPV infection could cause a cervical cancer (MAMMAS et al., 2014). In 1928, Greek scientist Dr. George N. Papanicolaou discovered malignant HPV-related infections in vaginal smears obtained from women, which led to the invention of the Pap smear test (MAMMAS et al., 2014).

Strauss and colleagues first described HPV in 1949, using an electron microscope to study samples of wart cells (Strauss et al., 1950), whereas Crawford and Crawford's 1963 study highlighted the physical characteristics of HPV DNA (Crawford

& Crawford, 1963). The significance of HPV in cervical cancer was first proposed in the 1970s by Professor Harald zur Hausen, known as the 'Father of HPV Virology' (zur Hausen, 2009). It has been proven that HPV has a role in human cancer development, resulting in a substantial percentage of non-genital malignancies as well as to the majority of cervical cancers.

Haralad zur Husen, a virologist from Germany, was intrigued about the occurrence. He had examined the cancer-causing Epstein-Barr virus, a 1930s report by American researcher Richard Shope which claimed that a certain form of Papillomavirus infection in rabbits triggered the growth of warts and eventually cancer (Lowy, 2024). Zur examined the medical cases where women with genital warts would later develop cervical cancer, he discovered the same correlation in it (Lowy, 2024). Moreover, some scientists at the time thought that this was the herpes simplex virus, a sexually transmitted infection that has been linked to genital warts and may also be the cause of cervical cancer (Jones, 1995).

Zur thus looked into the relationship between the herpes simplex virus and cervical cancer on his own journey. Yet, Zur was unable to find instances of cervical cancer malignancies, which meant he focused on HPV and published his idea in 1976 (zur Hausen, 2009). Zur's early discoveries were HPV 6 and HPV 11, which are not strongly associated with cervical cancer (zur Hausen, 2009). It wasn't until 1983 and 1984 that Zur Hausen found two strains of HPV, 16 and 18, which have a strong connection with cancer cervix (zur Hausen, 2009).

According to studies by Zur Hausen and colleagues, HPV-16 was discovered in 50% of cervical cancer cases, and HPV-18 was found in 20% of cervical cancer samples (zur Hausen, 2009). The fact that human papillomavirus infection, particularly HPV-16 and HPV-18, is linked to cervical cancer is a significant finding. Today, HPV-16 and HPV-18 account for more than 90% of cervical cancer cases caused by persistent high-risk human papillomavirus (HPV) infection. In this condition, Zur as a virologist approached for the HPV vaccine beginning in 1986 (zur Hausen, 2009).

The International Biological Study of Cervical Cancer group was established in 1995 to collect these data. After collecting samples from 22 different nations, researchers discovered that 93% of cervical cancer samples contained HPV (Bosch et al., 1995). Research indicates that HPV is likely to be rising as time goes on. In 1999, a team of scientists undertook extensive investigation by retesting samples. Researchers discovered that 99,7% of cervical cancers contained HPV, indicating that HPV infection is the primary cause of cervical cancer (Walboomers et al., 1999).

In the 21st century, the region with the highest occurrence of HPV among women is sub-Saharan Africa, followed by Latin America, eastern Europe and South-East Asia (Chan et al., 2019). According to further studies, low and middle-income countries had three times higher cervical cancer mortality rates than high-income countries (Hull et al., 2020). The occurrence is linked to a variety of reasons, such as inadequate availability of preventive measures, insufficient healthcare infrastructure, disparities in society, and cultural obstacles.

With the availability of advanced testing and treatment options, women and cancer patients now have a better chance of recovery. The incidence of cervical cancer is decreasing as HPV vaccination becomes more common, as Australia's comprehensive screening and vaccination strategy has been projected to eliminate cervical cancer within 15 years (Council, 2018). After decades of research by dedicated medical professionals, today's women have a better chance of avoiding or overcoming cervical cancer compared to ever before.

The correlation between HPV infection and sexual activity is substantial as HPV is predominantly spread through physical contact which is sexual activity. HPV affects the genital area, which can lead to an increased spread of the virus infecting a person without showing any noticeable symptoms. Furthermore, the issue of the younger generation being sexually active has been present for a long time; the younger a person begins sexual activity, the higher their risk of contracting HPV infection, as they might have more sexual partners over time.

2.2 The Importance of Health and Sexuality Education in Adolescents

Adolescence is a transition from childhood to adulthood that involves changes in various aspects such as biological and psychological. In such circumstances, there is a tendency to violate the norms. Adolescents suffer from a process of inability to adjust to their environment, especially when it comes to socializing. Adolescents who are satisfied in their efforts to justify and define themselves, will feel a sense of happiness and adapt easily to their environment.

On the other hand, adolescents may become defiant if all their desires are not fulfilled in accordance with what they want. As a result, adolescents will find it difficult to control themselves and have major implications for social deviations caused by biological and psychological changes. The lack of readiness of adolescents in facing these changes can lead to various behaviors such as: teenage misbehavior, drug abuse, sexually transmitted diseases, unwanted pregnancies to abortions. In order to prevent all of this, it is necessary to have formal education and a socializing environment that is expected to have an effect on adolescents, such as sexual comprehensive education.

Adolescence is defined as a transitional developmental period between childhood and adulthood that includes biological, cognitive, and social-emotional changes (National Academies of Sciences et al., 2019). The age range of adolescence commonly used is between 12 and 21 years (J. A. C. van der Zanden et al., 2020). The range of adolescence is usually divided into three, namely 12-15 years as early adolescence, 15-18 years as middle adolescence, and 18-21 years as late adolescence (J. A. C. van der Zanden et al., 2020).

Sex education in Indonesia is still quite taboo to discuss because it seems dirty, close to pornography, focused on sexual relations and often associated with adult content 18 years and over. This has led to many views, reactions and stereotypes from society if sexuality education itself is taught to children and adolescents is considered underage and excessive. Many parents are also reluctant to discuss and provide education about sex education to children even though parents have an important role for their children.

Sexuality involves a number of matters, including 1) the biological dimension, which is related to reproductive organs, how to maintain hygiene and health, 2) the psychological dimension, sexuality is related to gender role identity and how to perform its function as a sexual being, 3) the social dimension, how the environment influences the formation of views on sexual behavior choices, and 4) the cultural dimension, indicating that sexual behavior is part of the culture that exists in society (Sigusch, 2004).

Based on the 1994 international agreement in Cairo on reproductive health, which was signed by 184 countries including Indonesia, it was decided that sexual education for adolescents is necessary. One of the points of the consensus emphasizes efforts to seek and regulate sexual and reproductive health care and provide comprehensive education for adolescents. There are factors why sexual education is important to be taught early on. The first factor is when children grow into teenagers, they do not understand sex education as parents still think that talking about sex is taboo. Therefore, teenagers might feel irresponsible about sex or the health of their reproductive anatomy.

The second factor is adolescents' lack of understanding about sex and reproductive anatomy health, which then leads to searching for information that can answer their curiosity. In the social environment, content on sexuality and reproduction is offered in various media. A number of facilities such as magazines, the internet, and even television shows also contain pornographic content that leads to inappropriate consumption by adolescents. In accessing these various media, many adolescents are

not yet able to choose what is appropriate for consumption at their age and what is unnecessary. In addition, there are several reasons why it is essential to provide comprehensive sexual education to adolescents (Chavula et al., 2022):

- **Preventing improper sexual activity**

Nowadays, many adolescents engage in sexual activity before marriage. Most of them are doing this as influenced by an unhealthy environment. If they have gained knowledge of sexuality from an early age, it is hoped that adolescents can prevent sexual activity before marriage.

- **Aware of changes during puberty**

Many of the physical changes occur in teenagers when they start puberty. This often makes the youngsters unprepared and confused because of the changes. In girls experiencing menstruation for the first time or boys having nocturnal dreams for the first time. In order to accept these changes easily, parents need to provide knowledge about sexuality from an early age.

- **Understanding of the risk of sexually transmitted diseases**

Introduced about common sexually transmitted diseases, how the diseases that through sexual activity and how to prevent it. Especially adolescents, should be aware of it. Hence, they will not easily engage in casual or promiscuous sex which lead to unpleasant things such as sexually transmitted disease.

- **Has knowledge of boundaries with the opposite gender**

Education on sexuality helps individuals understand the importance of personal space and boundaries. It highlights the need to respect others' comfort levels and personal boundaries, fostering an environment where everyone feels safe. In addition, adolescents who live in a positive environment, born and raised in a religious family generally understand the rules that must be followed and implemented in their lives. Such as how to behave with the opposite gender and implement these boundaries in order to avoid promiscuous sexual behavior that can harm themselves.

However, it is important to acknowledge that sexuality education is a sensitive topic that requires advocacy to relevant regulatory authorities and public education on the importance of adolescent sex education. For this purpose, it is essential to understand the cultural norms surrounding sexuality in order for the education to be accepted. Sexuality education needs to be viewed comprehensively, acknowledging the various dimensions faced by adolescents that may also influence whether or not they decide to engage in risky sex.

In Indonesia, adolescent knowledge of reproductive health is relatively low, with 13% of adolescent women not aware of their physical changes and 47,9% not aware of when a woman's fertile period is (Andriati Reny Harwati, 2006). What is concerning is that adolescents' knowledge about the most important ways of avoiding HIV infection is still limited. According to the Ministry of Health Indonesia, in 2010 showed that 47.8% of AIDS cases by age were also occupied by the young age group

of 20-29 years. This shows that high-risk sexual behavior occurs in adolescence. Therefore, the low knowledge makes sexual and reproductive health education an important thing to provide.

In conclusion, reproductive and sexuality education should be considered as part of the educational process, whether it's at school or part of socializing at school, university or in the local society that aims to strengthen the basics of knowledge and personality development. Providing comprehensive sexuality education is an opportunity for adolescents to improve their understanding, knowledge, attitudes, and positive behaviors about sexuality and health, as well as to strengthen their sexual reproductive capabilities.

2.3 Human Papillomavirus Vaccination Policies and Recommendations in the World and Indonesia

In Indonesia, cervical cancer is the second leading cause of death and one of the biggest health financing burdens in the country stated by WHO. In 2018, the rate of cervical cancer in Indonesia was 179 per 100.000 women (Kemenkes RI, 2023). In 2021, there were 36.633 cases of cervical cancer in Indonesia with an escalating mortality rate (Kemenkes RI, 2023). Based on The health ministry in Indonesia, the cause is diverse but mostly caused by Human Papillomavirus infection, around 95%.

According to WHO, Indonesia accounts for 5.8% of the global occurrence of cervical cancer. HPV vaccine recommendations for women from the Association of Indonesian Internal Medicine Specialists in 2017 revealed that the HPV vaccine can be

carried out in the form of bivalent or quadrivalent which has been widely distributed in Indonesia. The most effective vaccine can be provided to women aged 9-26 years, stated by WHO.

The government of Indonesia is dedicated to preventing mortality caused by vaccine-preventable diseases in order to achieve the 2030 SDGs, stated by WHO. The government is committed to developing an innovative system that is a priority for the Ministry of Health in improving health services in Indonesia, by expanding health care services and also focusing on preventive promotion efforts, one of which is by introducing new types of vaccines added to the national vaccination program, including HPV vaccines.

In Indonesia, HPV vaccination has been carried out in several provinces such as DKI Jakarta, DIY Yogyakarta, East Java, Central Java, Bali, North Sulawesi. However, the deployment was carried out simultaneously in 2024 to all provinces in Indonesia to conduct HPV vaccination. This vaccine is primarily given to girls in grades 5 and 6 of elementary school or ages 11 to 12 for those who are not in school. Vaccination for school-going children is carried out through the monthly program of vaccination for school children (Kemenkes RI, 2023). The HPV vaccine is considered to be most efficient if given before sexual activity, as there is no opportunity to be infected with the HPV virus. Hence, the government has included this vaccine in the mandatory vaccination schedule for students aged 15 years and below (Kemenkes RI, 2023). In addition, the Indonesian Ministry of Health outlines the recommended age groups for HPV vaccination as follows (Kemenkes RI, 2023):

- Adolescent aged 15-20 years for 3 doses.
- Adults aged 20-26 years for 3 doses.
- Adults aged 27-45 years old for 3 doses. However, it is important for these age categories to seek medical professionals prior to receiving the vaccine.

The ministry of health in Indonesia, tries to accelerate the reduction of cervical cancer mortality, it is required to achieve HPV vaccination of at least 90%. For this reason, support from policy makers, related cross-sectors and all components of society is essential for this program to succeed. In 2022, a Joint Decree of 4 Ministers was issued, namely 1) Minister of Education, Culture, Research and Technology; 2) Minister of Health; 3) Minister of Religious Affairs, and 4) Minister of Home Affairs of the Republic of Indonesia on the implementation of improving the health status of students where primary schools or other similar forms need to ensure the complete vaccination status of each student, including HPV vaccination.

Therefore, the role of local governments and the education sector is essential for the implementation of early HPV vaccination integrated with a program of vaccination for school children as one of the School Health Efforts. Collaboration with health professionals, civil society organizations, the private sector and health development partners can support the acceleration of health transformation in order to achieve high and equal vaccination coverage that can further strengthen the national vaccination program.

WHO appreciates Indonesia's efforts to introduce HPV vaccination nationally, considering that cervical cancer is still the fourth most common cancer in women in

the world and second in Indonesia. Globally, 90% percent of cases occur in low- and middle-income countries such as Indonesia stated by WHO. “HPV vaccination, combined with screening, is the most cost-effective way to prevent cervical cancer. WHO encourages all countries to introduce HPV vaccination and ensure 90% of girls receive it before age 15 by 2030” said Dr. N. Paranietharan, WHO Representative to Indonesia.

In Indonesia, there are two types of commercially available HPV vaccines: bivalent and quadrivalent. The quadrivalent vaccine protects against four HPV types (6, 11, 16 and 18) and the bivalent vaccine protects against two HPV types 16 and 18. Recently introduced nonavalent vaccines in countries such as the United States protect against five HPV types 31, 33, 45, 52 and 58. All three available vaccines (bivalent, quadrivalent and nonavalent) are administered intramuscularly in several countries. Data from several clinical studies among young women aged 15-26 years showed highly favorable immunogenicity patterns for all vaccines tested (Indonesia & International, 2008).

The Centers for Disease Control Prevention (CDC) and Advisory Committee on Immunization Practices (ACIP) has developed recommendations regarding all HPV vaccinations in the United States. The current ACIP recommendations for HPV vaccination are:

- HPV vaccination is regularly recommended at 11 or 12 years of age. Vaccination can be started at 9 years old and can be advised for everyone up to 26 years' old who was not adequately vaccinated previously.

- Although the HPV vaccine is approved by the Food and Drug Administration (FDA) to be given up to 45 years old, HPV vaccination is not recommended for all adults aged 27 to 45 years. According to the Advisory Committee on Immunization Practices (ACIP), they recommend that those ages should discuss with medical professionals earlier whether HPV vaccination is appropriate for them. Since, HPV vaccination in this age range provides less benefit as more people have been exposed to the virus.
- Individuals who are pregnant. HPV vaccination should be postponed after pregnancy, but a pregnancy test is not required before vaccination.

According to WHO, an estimated 620.000 new cancer cases in women and 70.000 new cancer cases in men were caused by HPV in 2019, globally. Cervical cancer is the fourth leading cause of cancer and death in women in 2022, with 660.000 new cases and approximately 350.000 deaths worldwide, stated by WHO. According to UNICEF, nearly 60% of cervical cancer cases occur in countries that have not introduced HPV vaccination. UNICEF stated they will target the 20 highest-burden countries by introducing the HPV vaccine in the next two to three years. UNICEF and GAVI, the vaccine alliance that supports this effort, made a policy that vaccination should be a mandatory vaccination to reduce the prevalence. The 5 countries to be highlighted in the near future are India, Nigeria, Bangladesh, Angola and Mali.

However, with the vaccine distribution policy, early detection such as Pap Smear or VIA still needs to be done at least once every 3 years (Kemenkes RI, 2023). As well as pregnant women in Indonesia, it is necessary to discuss with medical

professionals referring to the ACIP policy that pregnant women should postpone the HPV vaccine, until the birth process is complete. Both the government in Indonesia and health organizations in the world have made comprehensive recommendations and policies regarding the administration of the HPV vaccine. It is hoped that the HPV vaccine will be a solution to the reduction of cervical cancer in Indonesia and in the world. Especially in Indonesia itself, with the mandatory HPV vaccine policy, it is highly expected to decrease the rate of cervical cancer and the mortality rate of women in the future.