Chapter 1

Introduction

1.1 Background

Cancer has become a big public health, societal, as well as economic problem that is responsible for almost one in every six deaths (16.8%) (Bray et al., 2024). It is the second most commonly found reason of death globally. In low- and middle-Human Development Index (HDI) countries, cervical cancer is the major disease that causes death that is related to cancer (Momenimovahed et al., 2022). According to WHO (2024), in 2022, there are 660,000 cases of cervical cancer and 350,000 cases of death from cervical cancer globally. In Indonesia itself, there are 36,633 cases of cervical cancer and 21,003 cases of death in 2021. Compared to the incidence and mortality rate in 2008, the rate of cervical cancer incidence and mortality in 2021 has increased twofold (Indarti, 2023).

Various risk factors contribute to cervical cancer. However, the main reason for cervical cancer is persistent infection of HPV. Approximately 95% of cervical cancer globally are caused by the persistent infection of HPV strains that are oncogenic (Ong et al., 2023). One way to reduce the rates of cervical cancer is through vaccination. A compilation of data from 65 studies in 14 countries showed a remarkable age-dependent reduction in cervical cancer, specifically in HPV16 and HPV18 (Illah & Olaitan, 2023). However, the maximum outcomes of vaccination can only be achieved until the population that is currently vaccinated in adolescence reaches middle to late life. Hence, to prevent cervical cancer, screening is crucial (Perkins et al., 2023).

One of the most common screening methods is a pap smear, which has drastically reduce incidence and mortality rates in high-income countries. However, the incidence rates have remained stationary lately. Additionally, pap smear needs high resources and it has a risk of poor reproducibility. Since then, molecular testing to screen for cervical cancer has been used as an alternative method, which

offers better reproducibility and high-throughput benefits (Liang et al., 2020). The cobas test is one of the preferable methods to screen for cervical cancer molecularly. This test has high specificity and sensitivity and it is also efficient for sample pooling. Despite that, Cobas test has some limitations, which are the high in cost as well as the high in need for advanced laboratory equipment, making it less preferable (Mahmoud et al., 2022).

An alternative method that can be used is isothermal amplification, especially LAMP (Loop Mediated Isothermal Amplification). LAMP has long been recognized due to its constant development, cost-effective, and simplicity. One of its developments is the ability to specifically identify high-risk HPV serotypes with high specificity (Luo et al., 2011) According to Lin et al (2017), LAMP can detect multiple HPV serotypes. Isothermal amplification is a laboratory technique that has an advantage of being to operate under a constant temperature. Another advantage is that a specific polymerase is used that have the ability to directly extend primers on the double strand of a dsDNA (Boonbanjong et al., 2022).

Even though LAMP have high specificity and sensitivity, it needs a complex primer design, with the risk of altering the results. Other than that, the limit of detection for HPV identification varies depending on the HPV types (Flores-Contreras et al., 2024). With that, it is necessary to develop and optimize LAMP-based isothermal amplification for the purpose of detecting HPV in Indonesia.

1.2 Objective

This research aims to develop isothermal amplification that is based on LAMP to detect high-risk HPV serotypes. Specifically, this research aims to determine LAMP target amplification specificity and determine the limit of detection.

1.3 Hypothesis

The hypothesis for this research is a LAMP-based isothermal amplification method, including the primer design, LAMP reaction that is optimized, detection sensitivity and limit for high risk HPV18 amplification.