CHAPTER I: INTRODUCTION

1.1. Background

Streptococcus pneumoniae (pneumococcus) can cause pneumonia, bacteremia, and/or meningitis toward the risk group of age and immunocompromised patients such as young children and the elderly as well as HIV patients, respectively (Wholey et al., 2016). In 2016, *S. pneumoniae* caused lower respiratory tract infection in 195 countries and estimated to be responsible for 341,029 deaths of children younger than five years. According to WHO, this bacterium causes the mortality rate of 700,000 to 1 million cases in children less than five years old with the carriage rate of *S. pneumoniae* in the human population is considered high which up to 80% of children under 5 years old. Pneumococcal bacteria is colonized in human nasopharynx, and the colonization with multiple strains simultaneously is widespread (Kjos et al., 2016). Doubtlessly, the lower respiratory infection incidence and mortality in children are mostly attributed to pneumococcal pneumonia.

Vaccines and antibiotics were considered as effective methods to combat *S. pneumoniae* and the prevention of pneumococcal infections using vaccination has been suggested (WHO, 2017). The pneumococcal vaccines are available based on the pneumococcal capsule, either as a polysaccharide-based vaccine targeting 23 serotypes (PPV23) or as conjugated vaccines targeting a limited number of serotypes, 7-valent pneumococcal conjugate vaccine or known as PCV7 (serotype 4, 6B, 9V, 24, 18C, 19F and 23F) and 13 in PCV13 (PCV7 and serotypes 1, 3, 5, 6A, 7F, and 19A) (Sime et al., 2019). Refer to Sime et al. (2019); serotype 6A is the most dominated found in sample isolates in vaccinated children which is about 5 % from 422 isolates; followed by serotype 34, 10A, 11A, 19F, 15B, 23F, and 15A. Interestingly, serotype 6A and 19F are included in the available vaccines, but still can be found in the children nasopharynx.

The reduced vaccine-type colonization from 23 serotypes might open the niche in the nasopharynx allowing for rises in the acquisition and prevalence of pneumococcal non-vaccine serotype colonization and subsequent disease (Daniels et al., 2016; Mehtälä et al., 2013). Some studies have been conducted in many vaccinated populations and showed that pneumococcal serotypes do not colonize human host independently but competitively interact with each other. These are also known as intraspecies competition could be a competition for contact sites or resources (Mehtälä et al., 2013; Wholey et al., 2016). The most potential cause of intraspecific competition is several diverse classes of pneumococcal bacteriocins which have different toxicity levels in every serotype as well as its genome.

Bacteriocin is small antimicrobial peptides synthesized to kill competing cells. Pneumococcal bacteriocin (pneumocin) production is controlled by the *blp* locus, which is stimulated by the accumulation of a peptide pheromone called BlpC (Wholey et al., 2016). *blpC* gene is different in every serotype and believed to have different effectivity and sensitivity to induce the bacteriocin activity. Afterward, the lysis of susceptible strains not only provides depredation but also allows a source of DNA for the adaptation of predators (Weiser et al., 2018).

Considering that the pneumococcal vaccine cannot cover all *S. pneumoniae* serotypes and the rising of antibiotic resistance toward *S. pneumoniae*, researchers are urged to discover and develop alternative or complementary strategies to antibiotics based on novel modes of action, such as bacteriocins produced by bacteria. Thus, in this study, *S. pneumoniae* vaccine serotypes and non-vaccine serotypes will be used to screen the *blpC* gene corresponding to the bacteriocin activity pathway and its diversity as well as determine whether serotypes contained *blpC* gene can kill the non-invasive or non-encapsulated strains.

1.2. Research Questions

1.2.1. Does every *S. pneumoniae* serotype own the *blpC* gene?

1.2.2. Is there an association between the presence of the *blpC* gene with serotype coverage in the pneumococcal vaccine?

1.2.3. Are *S. pneumoniae* serotypes containing the *blpC* gene able to kill other non-invasive serotypes using bacteriocin?

1.2.4. Does the variety of *blpC* genes affect the bacteriocin-like activity of *S. pneumoniae* serotypes?

1.3. Hypotheses

1.3.1. All *S. pneumoniae* serotypes own the *blpC* gene.

1.3.2. There is an association between the presence of the *blpC* gene with serotype coverage in the pneumococcal vaccine.

1.3.3. *Streptococcus pneumoniae* serotypes containing the *blpC* gene can kill non-invasive serotypes using bacteriocin-like activity.

1.3.4. The variety of *blpC* genes will affect the bacteriocin activity of *S. pneumoniae* serotypes.

1.4. Objectives

The study aims to:

1.4.1. Screen the presence of *blpC* gene in vaccine and non-vaccine *S. pneumoniae* serotypes.

1.4.2. Determine whether there is an association between the presence of *blpC* gene and serotype coverage in pneumococcal vaccines.

1.4.3. Identify whether *S. pneumoniae* serotypes-containing *blpC* gene have bacteriocin-like activity toward non-invasive *S. pneumoniae* serotypes.

1.4.4. Determine whether the variation of *blpC* gene affects the bacteriocin-like activity of *S. pneumoniae* serotypes.