

CHAPTER I

INTRODUCTION

1.1 Background

Eye is the most important of human sensory organ that play a critical role in human-environmental interaction. In 1996 and 1997, WHO Programme and the Task Force to the Partnership Committee of collaborating Non-Governmental Organizations launched The Global Initiative for the Elimination of Avoidable Blindness. The mission of this program is to eliminate the main cause of all preventable and treatable blindness by the year 2020. One of eye disease causing visual impairment that most occur is refractive error.¹

There are 4 types of refractive anomaly: hyperopia, myopia, presbyopia, and astigmatism. Myopia (or nearsightedness) is a condition where the object shadow is fall in front of retina. Clinical manifestation that makes patient really disturbed is blurred vision, and maybe worsened by headache.² Myopia is a complex disease, caused by genetic and or environment factor, or a Mendelian trait with different pattern of inheritance (autosomal dominant, autosomal recessive, X-linked).^{3,4} Myopia can be classified based on the age of onset: early-onset myopia (occur under the age of 20), early adult-onset myopia (between the ages of 20-40), and late adult-onset myopia (occur over the age of 40).^{3,5} There are some factors involved in myopia pathophysiology, such as

eyeball axial length, lens thickness, anterior chamber depth and corneal curvature.^{3,4,5}

The prevalence of children with myopia in Pondok Ranji, Jakarta, is 51 out of 89 respondent (57.3%).⁷ The highest rate of myopia in Denpasar, Bali, is in the age group 11-20 years old (25.1%).⁸ In a high school in Palembang, South Sumatera, 46.7% students were having myopia in their 15 years old age.⁹ The prevalence of myopia in Malay people who lives in Singapore were 24.6%.¹⁰

Scientists from many countries already studied many genes that assumed to play a role in myopia. A Genome Wide Association Study (GWAS) was conducted to find genes that have a strong relation to corneal curvature in Singapore citizen. This study found positive association between corneal curvature and FK506 binding protein 12-rapamycin associated protein 1 (*FRAP1*) gene on chromosome 1p36.2 and platelet-derived growth factor receptor alpha (*PDGFRA*) gene on chromosome 4q12.¹¹ This study is partly replicated by in Australian and White European populations which only found positive association with *PDGFRA* gene.^{12,13}

FRAP1 is a gene that code the FK506 binding protein 12-rapamycin associated protein 1.¹⁴ This protein regulate cell growth and proliferation. Since this protein is a family of phosphatidylinositol 3-kinase-related (PI3 kinase), it will affects the corneal tissue because corneal stroma is sensitive to growth mediators acting via PI3 kinase.¹¹ *PDGFRA* coding the PDGFRA protein that

also regulate the cell growth.¹⁵ This protein expressed mainly in the mesenchymal tissue.¹⁶

Based on database in Gene Expression Profiling In Silico (GEPIS), PDGFRA protein is expressed more in normal eye tissue (113.50 Digital Expression Unit) compare to FRAP1 protein (18.92 Digital Expression Unit).¹⁷ So, this study is focusing on *PDGFRA* gene polymorphism because its protein is expressed dominantly in eye tissue. Because of the replication studies in Australian and white Europeans found diversities in different ethnics, it may interesting to find *PDGFRA* gene polymorphism among Indonesian people.

1.2 Research Question

1.2.1 General Research Question

What kind of distribution of *PDGFRA* gene polymorphism in Indonesian people with early-onset myopia?

1.2.2 Specific Research Question

1. What kind of distribution of *PDGFRA* gene polymorphism in South Sumatera ethnic group with early-onset myopia?
2. What is the correlation between *PDGFRA* gene polymorphism and risk factors i.e parental history, near work, reading in dim light, outdoor activity, sex, and corneal curvature in early-onset myopia?

1.3 Aim of Study

1.3.1 General Aim

To identify risk factor and *PDGFRA* gene polymorphism in Indonesian people with early-onset myopia.

1.3.2 Specific Aims

1. To identify *PDGFRA* gene polymorphism in South Sumatera tribes with early-onset myopia.
2. To find the association between sex and early-onset myopia in South Sumatera tribes.
3. To find the association between family history of myopia and early-onset myopia in South Sumatera tribes.
4. To find the association between outdoor activity and early-onset myopia in South Sumatera tribes.
5. To find the association between near work activities and early-onset myopia in South Sumatera tribes.
6. To find the association between lighting while doing near work and early-onset myopia in South Sumatera tribes.
7. To find the association between corneal curvature and early-onset myopia in South Sumatera tribes.
8. To find the association between *PDGFRA* gene polymorphism and corneal curvature in South Sumatera tribes.
9. To find the association between *PDGFRA* gene polymorphism and early-onset myopia in South Sumatera tribes.

1.4 Research Benefits

1. To provide information about *PDGFRA* gene polymorphism in South Sumatera ethnic group which may differ with other ethnics.
2. To provide the information about correlation between genetic susceptibility and risk factors i.e parental history, near work, reading in dim light, outdoor activity, sex, and corneal curvature in the development of early-onset myopia in South Sumatera ethnic group.

1.5 Research Originality

This is the first study to identify *PDGFRA* gene polymorphism in South Sumatera ethnic group from Indonesia with early-onset myopia. Table 1 shows previous studies about association of *PDGFRA* gene polymorphism and corneal curvature in other ethnic groups.

Table 1. List of previous studies about *PDGFRA* gene polymorphism

No	Author	Title of Publication	Method	Result
1	Han S, Chen P, Fan Q, <i>et al.</i> (2011, Human Molecular Genetics) ¹¹	Association of variants in <i>FRAP1</i> and <i>PDGFRA</i> with corneal curvature in Asian populations from Singapore	Genome wide association studies	Identify 2 loci that were associated with corneal curvature variation: <i>FRAP1</i> on chromosome 1p36.2 and <i>PDGFRA</i> on chromosome 4q12.
2	Mishra A, Yazar S, Hewitt AW, <i>et al.</i> (2012, Investigative Ophthalmology and Visual Science) ¹²	Genetic variants near <i>PDGFRA</i> are associated with corneal curvature in Australians.	Genotyping with genome wide arrays	Meta-analysis revealed significant replication of association between rs2114039 and corneal curvature (P=0.0045) near <i>PDGFRA</i> gene.
3	Guggenheim JA, McMahon G, Kemp JP, Akhtar S, St Pourcain B, <i>et al.</i> (2013, Molecular Vision) ¹⁵	A genome-wide association study for corneal curvature identifies the platelet-derived growth factor receptor alpha gene as a quantitative trait locus for eye size in white Europeans.	Genome-wide association study.	rs6554163 genotype predicted 1.0% of variation in corneal curvature, associated with axial eye length predicting 0.6% of the normal trait variation (p=5.3×10 ⁻⁴).