# UNIVERSITI TEKNOLOGI MARA

# OXIDATIVE STRESS IN PRIMARY OPEN ANGLE GLAUCOMA: RELEVANCE OF GENETIC POLYMORPHISMS OF ANTIOXIDANT GENES AND DIFFERENTIAL METABOLITE PROFILES

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Thesis submitted in fulfillment
of the requirements for the degree of
**Master of Science**

**Faculty of Medicine**

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# AUTHOR' S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated of knowledge as reference work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Postgraduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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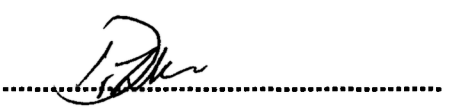
| Signature of Student | : |  |
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# ABSTRACT

Glaucoma is a common optic neuropathy. It is the second common cause of blindness. The molecular basis of primary open-angle glaucoma (POAG) is not fully understood. Thus, this study aims to examine the polymorphisms of antioxidant genes and to establish a predictive model based on the metabolite profiles using both genomics and metabolomics approaches. A total of 252 healthy volunteers and 23 POAG patients were recruited. Blood and serum samples were collected. Allele specific-PCR was developed and validated. The technique was efficient to detect genetic variations of antioxidant genes. *Manganese superoxide dismutase* polymorphism ($Val^{16}Ala$) showed higher frequency in POAG patients. Val genotype/allele was found to be significantly higher among Chinese. No polymorphisms of *catalase* (C262T) and *glutathione peroxidase* (P200L) were detected. Thirty eight different metabolites were detected by global metabolomics. Molecular feature extraction, data filtering, and statistical analysis [$p$-value <0.01 (unpaired t-test) and 2-folds change, ANOVA and PCA were able to differentiate metabolites expression between the two groups. Glycine-conjugated bile acids, palmitoylcarnitine, inosine, and β-ureidoisobutyric acid were increased in POAG patients. These metabolites indicate oxidative stress states. A predictive model using metabolites profiles was developed and validated. It discriminated each group in separate clustering. An overall predictive accuracy of 96.7% was obtained by this model. Ten features model was the best with highest sensitivity and specificity (AUC =0.999, CI 0.991-1). The model testing resulted in predictive accuracy around 0.95 (AUC= 0.985 95% CI: 0.944-1), and empirical $P$< 0.002 at 1000 times permutation test. This pilot study provides further evidence on the involvement of oxidative stress in POAG. The predictive model would be applicable after further validation. This generates new hypothesis for designing medicine and substantial improvements in patients' clinical outcomes.

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