UNIVERSITI PUTRA MALAYSIA

GENE POLYMORPHISMS OF ANGIOTENSIN-CONVERTING ENZYME, ANGIOTENSIN TYPE 1 RECEPTOR AND α-ADDUCIN ASSOCIATED WITH RENIN ANGIOTENSIN-ALDOSTERONE SYSTEM IN MALAYSIAN END-STAGE RENAL DISEASE PATIENTS

AISYAH BINTI ALI

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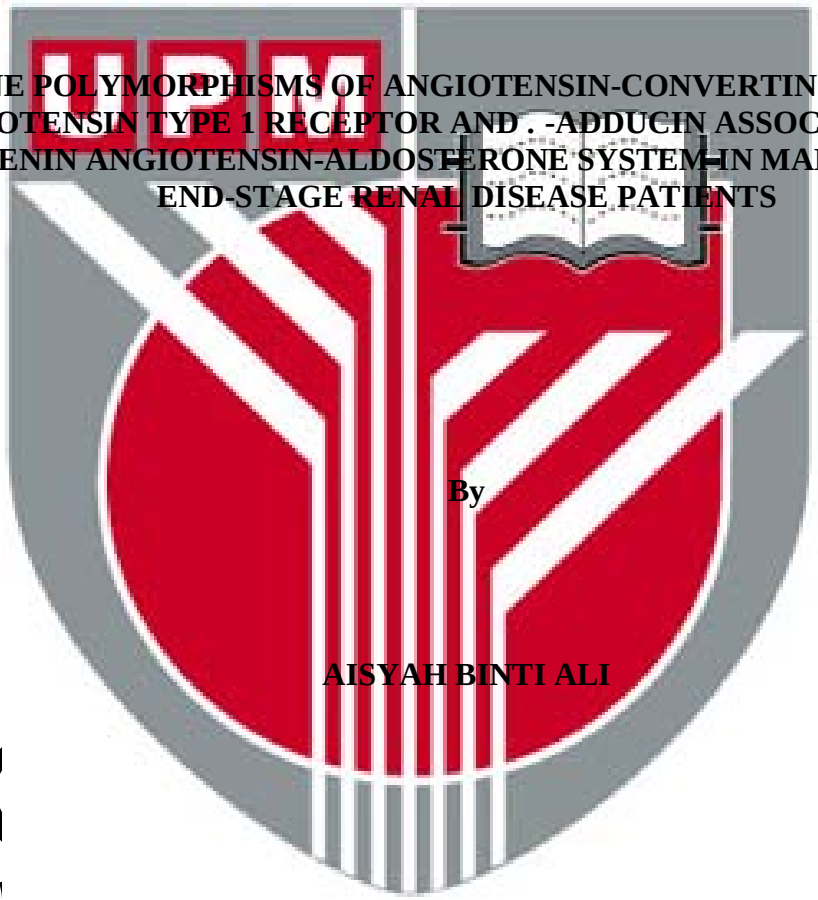

By

AISYAH BINTI ALI

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

June 2012

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DEDICATION

Dedicated to My Family, Friends and Researchers

Abstract of thesis presented to the Senate of Universiti Putra Malaysia
infulfilment of the requirement for the degree of Master of Science

GENE POLYMORPHISMS OF ANGIOTENSIN-CONVERTING ENZYME, ANGIOTENSIN TYPE 1 RECEPTOR AND . -ADDUCIN ASSOCIATED WITH RENIN ANGIOTENSIN-ALDOSTERONE SYSTEM IN MALAYSIAN END-STAGE RENAL DISEASE PATIENTS

By

AISYAH BINTI ALI

June 2012

Chairman: Professor Patimah Ismail, PhD

Faculty: Medicine and Health Sciences

Genetic Polymorphisms of renin-angiotensin aldosterone system (RAAS) genes has been extensively studied in relation to the progressive renal disease, hypertension and cardiovascular disease in various populations with conflicting results. The present study sought to determine the association of Insetion/Deletion (I/D) polymorphisms of the angiotensin converting enzyme (ACE), Gly460Trp of α-adducin and A1166C of angiotensin type 1 receptor(AT1R) of RAAS genes in Malaysian end stage renal subjects. A total of 380 subjects consisted of 190 end stage renal disease (ESRD) patients and 190 unrelated healthy individuals were recruited in this study. Genotypes of RAAS gene polymorphisms were determined using mutagenically separated PCR and PCR-RFLP method. There was significant difference ($p<0.05$) found in age, systolic blood pressure (SBP), creatinine level, triglycerides and total cholesterol between the

ESRD and control subjects. There was statistically significant differences ($p<0.05$) were found in I/D polymorphisms of ACE and Gly460Trp polymorphism of α-adducingene and no significant difference ($p>0.05$) was found in A1166C polymorphism of AT1R genes between the ESRD and control subjects. The findings of this study indicate that I/D polymorphisms of the ACE gene and Gly460Trp polymorphism of α-adducin gene are a useful marker and are likely to play a major role in determining genetic susceptibility to Malaysian ESRD subjects.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
Sebagai memenuhi keperluan untuk Ijazah Master Sains

POLIMORFISME GEN BAGI ENZIM PERTUKARAN ANGIOTENSIN, RESEPTOR JENIS 1 ANGIOTENSIN DAN . -ADDUCIN BERKAITAN DENGAN SISTEM RENIN ANGIOTENSIN ALDOSTERON DIKALANGAN PESAKIT BUAH PINGGANG PERINGKAT AKHIR DI MALAYSIA

Oleh

AISYAH BINTI ALI

Jun 2012

Pengerusi: **Profesor Patimah Ismail, PhD**

Fakulti: **Perubatan dan Sains Kesihatan**

Polimorfisme dalam sistem renin-angiotensin aldosteron (RAAS) telah dikaji secara meluas dengan penyakit yang berkaitan seperti penyakit kegagalan buahpinggang, penyakit darah tinggi dan penyakit jantung di pelbagai populasi dengan pelbagai keputusan yang mengelirukan. Kajian ini telah dijalankan bagi menentukan hubungan antara penambahan/pengurangan bagi gen enzim pertukaran angiotensin (ACE), polimorfisme Gly460Trp bagi gen α-adducin dan polimorfisme A1166C bagi gen Angiotensin type 1 receptor (AT1R) di kalangan pesakit buah pinggang peringkat akhir di Malaysia. Seramai 380 orang telah terlibat dalam kajian ini dimana terdiri daripada 190 orang pesakit buah pinggang peringkat akhir (ESRD) and 190 orang yang sihat sebagai kawalan. Genotip polimorfisme bagi gen RAAS telah ditentukan menggunakan kaedah tindak balas rantaian polymerase polimorfisme panjang jalur terpotong (PCR-

RFLP), tindak balas rantaian polimerase mutagenic (MS-PCR) dan tindak balas rantaian polimerase Hot-Start (Hot-Start PCR). Perbezaan signifikan telah dijumpai dalam umur, tekanan darah sistol, kretinin, trigliseride, dan jumlah kolesterol apabila dibandingkan antara pesakit buah pinggang peringkat akhir dengan yang normal. Perbezaan signifikan ($p<0.05$) telah dijumpai dalam polimorfisme penambahan/pengurangan bagi gen enzim pertukaran angiotensin dan polimorfisme Gly460Trp bagi gen α-adducin gene apabila dibandingkan antara pesakit buah pinggang peringkat akhir dengan yang normal Tiada perbezaan signifikan ($p>0.05$) dijumpai dalam polimorfisme A1166C bagi gen AT1R apabila dibandingkan dengan pesakit buah pinggang dengan yang normal. Penemuan dalam kajian ini telah menunjukkan bahawa polimorfisme penambahan/pengurangan bagi gen enzimpenukaran angiotensin dan polimorfisme Gly460Trp bagi gen α-adducin merupakan penanda yang berguna dan memainkan peranan besar dalam menentukan kestabilan genetic terhadap pesakit buah pinggang terakhir di Malaysia.

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I certify that a Thesis Examination Committee has met on 25 June 2012 to conduct the final examination of Aisyah binti Ali on her thesis entitled "Gene Polymorphisms of Angiotensin-Converting Enzyme, Angiotensin Type 1 Receptor and α-Adducin Associated with Renin Angiotensin-Aldosterone System in Malaysian End-Stage Renal Disease Patients" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

Members of the Thesis Examination Committee were as follows:

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Masters of Science. The members of the Supervisory Committee were as follows:

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DECLARATION

I declare that the thesis is my original work except for quotation and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

AISYAH BINTI ALI

Date:

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