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STATUS OF OXIDATIVE STRESS BIOMARKERS AND LECITHIN CHOLESTEROL ACYLTRANSFERANSE (*LCAT*) GENE VARIANT IN SUBJECTS WITH LOW HDL-C CONCENTRATION

FARAH HANIS BINTI SAKRI

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CONFIRMATION BY PANEL OF EXAMINERS

I certify that a Panel of Examiners has met on 2nd November 2015 to conduct the final examination of Farah Hanis binti Sakri on her Master of Science (Medicine) thesis entitled "Status of Oxidative Stress Biomarkers and Lecithin Cholesterol Acyltransferase (*LCAT*) Gene Variant in Subjects with Low HDL-c Concentration" in accordance with Universiti Teknologi MARA Act 1976 (Akta 173). The Panel of Examiners recommends that the student be awarded the relevant degree. The Panel of Examiners was as follow:

Azian Binti Abd Latiff, PhD
Professor
Faculty of Medicine
Universiti Teknologi MARA
(Chairman)

Harbinder Jeet Singh, PhD
Professor
Faculty of Medicine
Universiti Teknologi MARA
(Internal Examiner)

Rozita Binti Rosli, MD
Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(External Examiner)

SITI HALIJJAH SHARIFF, PhD
Associate Professor
Dean
Institute of Graduate Studies
Universiti Teknologi MARA
Date: 23th February, 2016

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 unless otherwise indicated or acknowledge as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

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Name of Student	:	Farah Hanis Binti Sakri
Student I.D No.	:	2010174609
Programme	:	Master in Science (MD 780)
Faculty	:	Medicine
Title	:	Status of Oxidative Stress Biomarkers and Lecithin Cholesterol Acyltransferase (*LCAT*) Gene Variant in Subjects with HDL-c Concentration
Signature of Student	:	.....
Date	:	February 2016

ABSTRACT

Oxidative stress has been established as a key event in initiation and progression of atherosclerosis. Oxidized low density lipoprotein (ox-LDL), F_2-isoprostanes (F_2-iPs), and malondialdehyde (MDA) are biomarkers reflecting the status of oxidative stress. High-density lipoprotein cholesterol (HDL-c) is protective against atherosclerosis and coronary heart disease (CHD), but its association with oxidative stress is not well established. Studies have indicated that 40-60% of the variation of HDL-c concentration is genetically determined. Extensive literature search indicates that mutation in lecithin cholesterol acyltransferase *(LCAT)* gene is reported to be associated with lowering of HDL-c concentration. However, there is scarcity of such data amongst the Asian population particularly in a Malay-dominated community. Thus, this study aimed to a) compare the concentration of oxidative stress biomarkers between low HDL-c subjects and normal controls, b) examine the correlation and association between HDL-c and these biomarkers, c) investigate whether HDL-c concentration is an independent predictor for these biomarkers and d) determine the genetic variants of *LCAT*. A total of 207 low HDL-c subjects and 215 normal controls were recruited for the biochemical aspect of the study. For genetic studies, 70 subjects with the lowest deciles of HDL-c and 140 normal controls were selected from the recruited samples. All exons of *LCAT* were PCR amplified and sequenced in both groups. For both studies, the groups were matched for age, gender, ethnicity, smoking status, diabetes and hypertension. It was found that oxidative stress biomarkers were higher in low HDL-c group compared to normal controls. There were negative correlations and association between HDL-c concentration and some of the biomarkers. HDL-c was not an independent predictor for the biomarkers. All exons sequencing of *LCAT* gene revealed no variant found in the subjects studied. In conclusion, HDL-c concentration is strongly associated and correlated with status of oxidative stress, which in part explains the pathogenesis of atherosclerosis associated with low HDL-c. However, it is conceivable to speculate that the role of *LCAT* variation in HDL-c concentration may be minimal in our population.

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