

**UNIVERSITI TEKNOLOGI MARA**

**THE ASSOCIATION BETWEEN  
SEVERITY OF LIVER STEATOSIS,  
APNOEA AND ATHEROSCLEROSIS  
RISK IN OSA PATIENTS WITH  
NAFLD**

**DR. SAMSHOL BIN SUKAHRI**

**MMed**

**October 2018**

## AUTHOR'S DECLARATION

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

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

Name of Student : Dr. Samshol Bin Sukahri

Student I.D. No. : 2012757411

Programme : Masters in Internal Medicine – MD771

Faculty : Medicine

Thesis : The association between severity of steatosis, apnoea and atherosclerosis risk in OSA patients with NAFLD

Signature of Student : .....

Date : October 2018

## ABSTRACT

**Introduction:** Obstructive sleep apnoea (OSA) has been closely associated with non-alcoholic fatty liver disease (NAFLD). It also increases cardiovascular risk and metabolic syndrome. Carotid intima-media thickness (CIMT) is widely used as a reliable index of subclinical atherosclerosis. Thus, this study aimed to determine the relationships between severity of OSA and degree of steatosis and cardiovascular risk via CIMT measurements in a group of OSA patients.

**Methods:** This was a cross-sectional study, conducted at the Faculty of Medicine Uitm. We screened 110 subjects between 18 to 65 years of age, who were diagnosed OSA following sleep study examinations. We excluded patients with seropositive Hepatitis B or Hepatitis C, and significant alcohol intake.

**Result:** The prevalence of NAFLD was 81.8% (n= 90). Almost half of them had NAFLD Stage 1 42.7% (n= 47), 32% (n= 42) had Stage 2 and 1 had Stage 3 (0.9%). The subjects with NAFLD had significantly higher weight compared to those without NAFLD (94.77 kg  $\pm$  21.85 vs 74.67 kg  $\pm$  16.80, p < 0.001). There were statistically significantly higher mean systolic blood pressure, waist circumference, hip circumference, waist hip ratio and severity of OSA (AHI) among the NAFLD and vs the non NAFLD groups. The mean ICAM-1, Lp(a) and CIMT were significantly higher in the NAFLD group compared to the non-NAFLD group (334.53 ng/mL  $\pm$  72.86 vs 265.46 ng/mL  $\pm$  102.92, p = 0.001, 85.41 nmol/L  $\pm$  52.56 vs 23.55 nmol/L  $\pm$  23.66, p <0.001, 0.08 cm  $\pm$  0.03 vs 0.06 cm  $\pm$  0.01, p = 0.001) respectively.

Comparisons between the non-NAFLD, NAFLD 1 and NAFLD 2 groups showed significant differences in systolic blood pressure, diastolic blood pressure, BMI, waist circumference, ICAM-1 and Lp(a) indicating higher cardiovascular risks in the latter 2 groups. Similarly, patients with severe AHI had significantly higher systolic blood pressure, diastolic blood pressure, and waist circumference compared to those with mild AHI and moderate AHI. However, there were no statistically significant differences in mean CIMT values between these 3 groups (mild AHI, moderate AHI and severe AHI, respectively: 0.07 cm  $\pm$  0.02 vs 0.08 cm  $\pm$  0.03 vs 0.08 cm  $\pm$  0.02, p

## ACKNOWLEDGEMENT

Alhamdulillah, I thank God for giving me the blessings and opportunity to complete this priceless and enriching journey of Master in Medicine (Internal Medicine). My highest and deepest gratitude goes to my supervisor Dr. Fatimah Zaherah Mohamad Shah and my co-supervisors Associate Professor Dr Rohana Abdul Ghani, Dr Mohd Ahmad Izuanuddin bin Ismail, and Assoc Prof Dr Marymol Koshy, who has inspired me and has provided me endless support, ideas, and assistance in every step of this project.

I would also like to express my gratitude to the professors and lecturers of Internal Medicine department with special thanks to Dr Mohd Arif Bin Mohd Zim, Dr Bushra Johari, Dr Mazuin Mohd Razali and Dr Thuhairah. They have been more than willing to provide me the support and knowledge needed for this project.

My humble appreciation also goes to all the nurses in Respiratory and Endocrine Clinic, Medical Imaging Department staff, and medical laboratory technicians of the Universiti Teknologi MARA (UITM) who have provided me the facilities and assistance during my data collection. Without the collaboration from these individuals, the project would not have been a success and finished on time.

I have always believed that striving and working together equates to success. Therefore, my sincerest gratitude goes to all my friends and colleagues of Master in Medicine (Internal Medicine) who have provided me help in every way possible to ensure the success of this project.

Last but not least, I would like to express my love and greatest appreciation to my parents, my loving wife, my children, and my family. They have never given up on praying for my success and have given me endless support through any way possible to ensure that I progress through. This piece of work is not only a victory to myself but also specially dedicated to all of you.

# TABLE OF CONTENT

	<b>Page</b>
<b>CONFIRMATION BY PANEL OF EXAMINERS</b>	<b>ii</b>
<b>AUTHOR'S DECLARATION</b>	<b>iii</b>
<b>ABSTRACT</b>	<b>iv</b>
<b>ACKNOWLEDGEMENT</b>	<b>vii</b>
<b>TABLE OF CONTENT</b>	<b>viii</b>
<b>LIST OF TABLES</b>	<b>xii</b>
<b>LIST OF FIGURES</b>	<b>xiv</b>
<b>LIST OF SYMBOLS AND ABBREVIATIONS</b>	<b>xvi</b>
<b>CHAPTER ONE INTRODUCTION</b>	<b>1</b>
1.1 Research Background	1
1.2 Definition of Terms	3
1.2.1 Non-Alcoholic Fatty Liver Disease (NAFLD)	3
1.2.2 Significant alcohol intake	5
1.2.3 Obstructive sleep apnoea	5
1.2.4 Apnoea Hypopnoea index	5
1.2.5 Carotid Intima-Media Thickness (CIMT)	6
1.2.6 Intercellular adhesion molecule-1 (ICAM-1)	6
1.2.7 Lipoprotein (a) [Lp(a)]	7
<b>CHAPTER TWO LITERATURE REVIEW</b>	<b>8</b>
2.1 Epidemiology	8
2.1.1 Non Alcoholic Fatty Liver Disease in general population	8
2.1.2 Non Alcoholic Fatty Liver Disease and obstructive sleep apnoea (OSA) patients	9
2.1.3 Cardiovascular Disease in OSA	10
2.1.4 Carotid Intima Media Thickness as screening for subclinical atherosclerosis disease in OSA patient	10