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A COMPARATIVE ANALYSIS OF TRIGLYCERIDES LEVEL BASED ON HIGH DENSITY LIPOPROTEIN CHOLESTEROL IN THREE DISTINCT PHASES OF BLOOD PRESSURE USING MULTIPLE LOGISTIC REGRESSION

Wan Muhamad Amir W Ahmad[1], Mohamad Shafiq Mohd Ibrahim[2], NurFadhlina Abdul Halim[3], Nor Azlida Aleng[4] and Puspa Liza Ghazali[5]

[1]*School of Fisheries and Aquaculture Sciences, University Malaysia Terengganu (UMT), Kuala Terengganu,Terengganu Malaysia*
[2,3,4] *School of Informatics and Applied Mathematics, University Malaysia Terengganu (UMT),Kuala Terengganu,Terengganu Malaysia*
[5]*Faculty of Business Management and Accountancy, University of Sultan Zainal Abidin (UNISZA), Kuala Terengganu,Terengganu Malaysia*

ABSTRACT

Atherosclerosis is a common disorder which hardens the arteries due to the excessive of plaque which are made of fat, cholesterol, calcium and other substances. This study aims to examine factors that are associated directly or indirectly with triglycerides level in the distinct phases of blood pressure. Multiple logistic regression was employed in order to assess the associated factors of triglycerides level in three distinct phases of blood pressure. The statistical analysis revealed that there are partially significant differences due to the different distinct phases of blood pressure. High density lipoprotein cholesterol, total cholesterol and proconvertin were the factors which statistically significant across three distinct phases of blood pressure. This finding shows that the triglycerides might be a valuable marker for atherosclerosis in three distinct phases of blood pressure.

Keywords: Atherescleorosis, Triglycerides, Multiple Logistic Regeression, HDL Cholesterol, Total Cholesterol, Proconvertin

1. INTRODUCTION

Atherosclerosis is also known as arteriosclerotic vascular disease. It is a condition when the arteries become narrowed and hardened due to the excessive of plaque which is made of fat, cholesterol, calcium and other substances. In many epidemiologic studies by Alexander [1] and Byori et al. [2] found that, the risk factors of atherosclerosis and hypertension are still controversial and complex. This increased risk might be attributed to the heart attack, stroke, peripheral arterial disease, erectile dysfunction and kidney disease. Mostly, higher triglyceride level and low HDL cholesterol were one of the factors which attributed to the pathogenesis of coronary artery disease. Besides that, HDL cholesterol also helps to prevent the atherosclerotic cardiovascular complication by scavenges and removes LDL or bad cholesterol and act as a maintenance function for the inner walls of blood vessel. This study was continued from the previous study on high density lipoprotein cholesterol predict triglyceride level predict in three distinct phases of blood pressure by Amir and Shafiq [3] and Shafiq et al [4]. We hypothesized that a strong association between triglycerides and HDL cholesterol level might exist in three distinct phases of blood pressure which normal, borderline and hypertensive. This study was to examine the factors that are associated directly or indirectly with triglycerides in three distinct phases of blood pressure.

2. MATERIAL AND METHOD

The participants are patient diagnosed clinically with triglycerides and HDL-Cholesterol with three distinct phases of normal, borderline and hypertensive among blood pressure patients between 1st January 2009 and 31st December 2011. A total of 1000 registered patients from Hospital University Sains Malaysia (HUSM) were screened and met the inclusion and exclusion criteria (Table 1). The main outcome evaluated is the association of the triglyceride level which was evaluated by using multiple logistic regressions. The p values were two-tailed and α level of significance was set at 0.25. Mickey and Greenland [5] recommended that 0.25 level be used as a screening criterion for variable selection in logistic regression. All subjects were assigned to blood pressure level categories which are systolic blood pressure level which are normal, borderline and hypertensive. The National Institute of health [6] prescribe that Normal systolic blood pressure classification is less than 120 mmHg, borderline is 120-139 mmHg and hypertensive is more than 140 mmHg. The Power and Sample Size by Calculation (PS) software are used to calculate sample size of the analysis with significance level (α) 0.05 and the power of the study $(1-\beta)$ of 80% based on Dupont and Plummer [7] and Amir et al. [8]. Parameter involved: (i) Type 1 Error = 5.0%, (ii) Power = 80.0%, (iii) M = 1, (iv) P_0 = Based on literature review and (v) P_1 = Based on Expert Opinion. The largest size sample was 161 patients. One way

ANOVA analysis was used to test the differences among the three distinct conditions, which is normal, borderline and hypertensive. It has been shown by the previous study by Amir and Shafiq [3], the systolic blood pressure differed significantly $F((2, 997) = 3.595, p = 0.028)$ across the three distinct phases normal, borderline and hypertensive.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
a) From Malay population	a) Breast feeding or pregnant women
b) Blood pressure is divided to normal (<120), borderline (120-139) and hypertension (>140)	b) The presence of chronic disease such as kidney disease, liver disease and serious injuries
c) Any other condition which recommend by the physician	c) Any other condition which not recommended by the physician

Table 2: Sample Size Calculation

No. Variables	*P_1	P_o	M	Type 1 error	Power	Sample Size
Systolic blood pressure [9]	0.29	0.16	1	5%	80%	161
Diastolic blood pressure [9]	0.23	0.11	1	5%	80%	153
HDL-Cholesterol [9]	0.51	0.35	1	5%	80%	149
Hypertension [10]	0.54	0.38	1	5%	80%	151

3. RESULTS

The risk factors characteristics according to level systolic blood pressure in normal, borderline and hypertensive are summarized in Table 3. Patients with higher systolic blood pressure tended to have higher triglycerides level and slightly higher of HDL-cholesterol but total cholesterol with slightly decrease as the higher systolic blood pressure. They also had a higher intake of smoking pack per year; they were less physically active and also the smoker increase as the higher systolic blood pressure. They also tended to have a slightly low of body mass index, height and weight as the systolic blood pressure increases. Besides that, they also tended to higher waist and hip circumference, a higher systolic blood pressure and diastolic blood pressure. Furthermore, they also tended to a higher glucose, a higher proconvertin and a higher fibrinogen as the systolic blood pressure increases. They also tended to increase in incident coronary heart disease, family history of heart attack and diabetes as the high of systolic blood pressure. They also tended to take serum insulin and anti-hypertensive medication as the high systolic blood pressure. The taking lipid medication slightly increases and slightly decreases as the high systolic blood pressure.

Table 4 shows the variables in the final model of multiple logistic regresssion for normal systolic blood pressure. In multivariate analysis, only seven variables appeared as significant factors. It is clearly observed from the results that total cholesterol (OR = 1.025, 95% CI=1.013, 1.038), proconvertin (OR = 1.013, 95% CI=0.994, 1.033) and serum insulin (OR = 1.067, 95% CI=1.009, 1.129) has been positively associated with triglycerides level. High density lipoprotein cholesterol (OR = 0.826, 95% CI=0.771, 0.885), hip circumference (OR = 0.834, 95% CI=0.729, 0.954), glucose (OR = 0.976, 95% CI=0.938, 1.017) and incident coronary heart disease (OR = 0.237, 95% CI=0.068, 0.826), were negatively associated with triglycerides level. Garder and Altman [11] recomended that 0.25 level used as a screening criterion for variable selection in logistic regression. This is because the traditional level such as 0.05 often fails to identify variables known to be important. This logistic regression model was fit based on a non-significant Lwanga and Lemeshow [12] with p = 0.369 and good area under the curve 0.873.

Table 5 shows the variables in the final model of multiple logistic regresssion for borderline systolic blood pressure. In multivariate analysis, only nine variables appeared as significant factors. It is clearly observed from the results that total cholesterol (OR = 1.014, 95% CI=1.005, 1.023), waist circumference (OR = 1.108, 95% CI=1.034, 1.188), hip cirumference (OR = 1.058, 95% CI=0.964, 1.160), diastolic blood pressure (OR = 1.030, 95% CI=0.994, 1.067), glucose (OR = 1.014, 95% CI=0.996, 1.032), proconvertin (OR = 1.038, 95% CI=1.022, 1.055), serum insulin (OR = 1.053, 95% CI=1.019, 1.088) and taking lipid lowering medication (OR = 5.571, 95% CI=0.965, 32.174) has been positively associated with triglycerides level. High density lipoprotein cholesterol (OR = 0.879, 95% CI=0.844, 0.915) were negatively associated with triglycerides level. This logistic regression model was fit based on a non-significant Lwanga and Lemeshow [12] with p = 0.097 and good area under the curve 0.870.

Table 3: Clinical, Lifestyle and other characteristics according to Systolic Blood Pressure level: normal borderline and hypertensive

Variables	< 120 mm Hg, n = 232 Mean (SD)	120-139 mm Hg, n = 364 Mean (SD)	> 140 mm Hg, n = 398 Mean (SD)
Basic Data			
Height	174.03 (6.16)	174.0 (6.56)	172.46 (6.28)
Body Mass Index	25.96 (3.80)	26.54 (3.52)	26.69 (3.76)
Weight	48.71 (12.28)	50.48 (11.80)	49.58 (12.85)
Lifestyle Factors			
Kilo-calories of physical activity per week	2071.8 (2035.6)	2235.7 (2405.8)	1957.16(2015.3)
Smoking status	0.09 (0.284)	0.13 (0.33)	0.103 (0.304)
Pack years of smoking	24.58 (31.37)	24.33 (27.90)	26.88 (33.30)
Waist circumference	96.49 (10.05)	97.84 (10.07)	98.43 (10.50)
Hip circumference	100.7 (6.82)	101.55 (6.98)	101.53 (7.98)
Clinical factor			
Systolic blood pressure	110.42 (7.7)	129.56 (5.79)	157.73 (14.46)
Diastolic systolic pressure	64.07 (8.51)	71.50 (8.67)	78.82 (10.50)
Lipids			
Triglycerides	129.77 (64.82)	142.71(76.44)	147.30 (91.92)
Total cholesterol	199.36 (39.52)	198.36 (35.09)	199.97 (34.58)
HDL cholesterol	47.95 (11.71)	47.28 (12.05)	48.84 (13.58)
Biochemical			
Glucose	105.17 (18.17)	109.25 (30.16)	115.93 (36.46)
Proconvertin	110.26 (22.29)	114.0 (22.31)	117.68 (26.78)
Fibrinogen	312.83 (61.54)	315.27 (67.98)	321.31 (66.22)
Diseases			
Family history of heart attack	0.28 (0.451)	0.30 (0.461)	0.31 (0.462)
Diabetes	0.239 (0.428)	0.31 (0.46)	0.372(0.48)
Incident coronary heart disease	0.14 (0.351)	0.14 (0.348)	0.25 (0.44)
Medication			
Serum Insulin	16.11 (26.75)	15.98 (13.85)	17.52 (29.04)
Taking anti-hypertensive medication	0.24 (0.430)	0.33 (0.472)	0.44 (0.50)
Taking lipid lowering medication	0.03 (0.17)	0.04 (0.20)	0.03 (0.17)

Table 4 : Logistic regression model of the associated factors for triglycerides level (for normal systolic blood pressure)

Independent Variable	Std. Coefficient Beta (β)	S.E	Adjusted OR	95.0% CI For Adjusted OR Lower	Upper
Basic Data					
Height	-0.022	0.260	0.978	0.588	1.627
Body Mass Index	0.038	0.859	1.038	0.193	5.587
Weight	0.095	0.278	1.099	0.637	1.896
Lifestyle Factors					
Kilo-calories of physical activity per week	0.001	0.001	1.000	1.000	1.000
Smoking status	-0.421	0.826	0.656	0.130	3.312
Pack years of smoking	0.006	0.008	1.006	0.991	1.022
Waist circumference	-0.015	0.052	0.986	0.891	1.091
Hip circumference	-0.181**	0.069	0.834	0.729	0.954
Clinical factors					
Systolic blood pressure	0.024	0.032	1.024	0.961	1.091
Diastolic systolic pressure	-0.010	0.031	0.990	0.932	1.051

Lipid					
Total cholesterol	0.025**	0.006	1.025	1.013	1.038
HDL cholesterol	-0.191**	0.035	0.826	0.771	0.885
Biochemical					
Glucose	-0.024**	0.021	0.976	0.938	1.017
Proconvertin	0.013**	0.010	1.013	0.994	1.033
Fibrinogen	-0.003	0.004	0.997	0.990	1.004
Diseases					
Family history of heart attack	-0.553	0.495	0.575	0.218	1.518
Diabetes	0.835	1.050	2.305	0.294	18.049
Incident coronary heart disease	-1.439**	0.636	0.237	0.068	0.826
Medication					
Serum Insulin	0.065**	0.029	1.067	1.009	1.129
Taking anti-hypertensive medication	0.450	0.508	1.568	0.580	4.241
Taking lipid lowering medication	-2.816	1.403	0.060	0.04	0.936
Hosmer and Lemeshow Test	p-value 0.369				
Area under the Curve	0.873 (95% CI: 0.828,0.919)				

Table 5 : Logistic regression model of the associated factors for triglycerides level (for borderline systolic blood pressure)

Independent Variable	Std. Coefficient Beta (β)	S.E	Adjusted OR	95.0% CI For Adjusted OR	
				Lower	Upper
Basic Data					
Height	-0.055	0.187	0.947	0.656	1.367
Body Mass Index	-0.288	0.603	0.749	0.230	2.442
Weight	-0.024	0.196	0.977	0.665	1.434
Lifestyle Factors					
Kilo-calories of physical activity per week	0.001	0.001	1.000	1.000	1.000
Smoking status	-0.198	0.534	0.820	0.288	2.336
Pack years of smoking	-0.004	0.006	0.996	0.984	1.007
Waist circumference	0.103**	0.036	1.108	1.034	1.188
Hip circumference	0.056**	0.047	1.058	0.964	1.160
Clinical factors					
Systolic blood pressure	-0.009	0.026	0.991	0.941	1.044
Diastolic blood pressure	0.029**	0.018	1.030	0.994	1.067
Lipid					
Total cholesterol	0.014**	0.005	1.014	1.005	1.023
HDL cholesterol	-0.130**	0.021	0.879	0.844	0.915
Biochemical					
Glucose	0.013**	0.009	1.014	0.996	1.032
Proconvertin	0.038**	0.008	1.038	1.022	1.055
Fibrinogen	-0.003	0.003	0.997	0.992	1.002
Diseases					
Family history of heart attack	0.172	0.318	1.188	0.636	2.217
Diabetes	0.030	0.643	1.030	0.292	3.630
Incident coronary heart disease	0.123	0.440	1.131	0.478	2.678
Medication					
Serum Insulin	0.052**	0.017	1.053	1.019	1.088
Taking anti-hypertensive medication	0.055	0.315	1.056	0.570	1.959
Taking lipid lowering medication	1.718**	0.895	5.571	0.965	32.174
Hosmer and Lemeshow Test	p-value 0.097				
Area under the Curve	0.870 (95% CI: 0.831,0.909)				

Table 6 : Logistic regression model of the associated factors for triglycerides level (for hypertensive systolic blood pressure)

Independent Variable	Std. Coefficient Beta (β)	S.E	Adjusted OR	95.0% CI For Adjusted OR	
				Lower	Upper
Basic Data					
Height	0.282**	0.186	1.325	0.920	1.908
Body Mass Index	0.909**	0.594	2.482	0.775	7.944
Weight	-0.338**	0.194	0.713	0.488	1.043
Lifestyle Factors					
Kilo-calories of physical activity per week	0.001	0.001	1.000	1.000	1.000
Smoking status	-0.328	0.528	0.720	0.256	2.027
Pack years of smoking	0.006**	0.005	1.006	0.997	1.016
Waist circumference	0.063**	0.033	1.066	0.999	1.137
Hip circumference	-0.047	0.040	0.954	0.882	1.032
Clinical factors					
Systolic blood pressure	0.001	0.010	1.001	0.981	1.022
Diastolic systolic pressure	-0.005	0.015	0.995	0.967	1.024
Lipid					
Total cholesterol	0.023**	0.005	1.023	1.014	1.032
HDL cholesterol	-0.130**	0.018	0.878	0.847	0.909
Biochemical					
Glucose	0.003	0.005	1.003	0.992	1.014
Proconvertin	0.029**	0.006	1.030	1.017	1.042
Fibrinogen	-0.002	0.002	0.998	0.993	1.002
Diseases					
Family history of heart attack	0.179	0.303	1.197	0.661	2.167
Diabetes	0.548	0.494	1.729	0.657	4.552
Incident coronary heart disease	-0.028	0.328	0.973	0.512	1.848
Medication					
Serum Insulin	0.003	0.006	1.003	0.993	1.014
Taking anti-hypertensive medication	1.086**	0.299	2.961	1.648	5.322
Taking lipid lowering medication	1.355**	0.764	3.878	0.868	17.332
Hosmer and Lemeshow Test	p-value 0.113				
Area under the Curve	0.880 (95% CI: 0.847,0.914)				

Table 6 shows the variables in the final model of multiple logistic regresssion for borderline systolic blood pressure. In multivariate analysis, only ten variables appeared as significant factors. It is clearly observed from the results that total cholesterol (OR = 1.023, 95% CI=1.014, 1.032), height (OR = 1.325, 95% CI=0.920, 1.908), body mass index (OR = 2.482, 95% CI=0.775, 7.944), pack years of smoking (OR = 1.006, 95% CI=0.997, 1.016), waist circumference (OR = 1.066, 95% CI=0.999, 1.137), proconvertin (OR = 1.030, 95% CI=1.017, 1.042), taking anti-hypertensive medication (OR = 2.961, 95% CI=1.648, 5.322) and taking lipid lowering medication (OR = 3.878, 95% CI=0.868, 17.332) has been positively associated with triglycerides level. High density lipoprotein cholesterol (OR = 0.878, 95% CI=0.847, 0.909) and weight (OR = 0.713, 95% CI=0.488, 1.043) were negatively associated with triglycerides level. This logistic regression model was fit based on a non-significant Lwanga and Lemeshow [12] with p = 0.113 and good area under the curve 0.880.

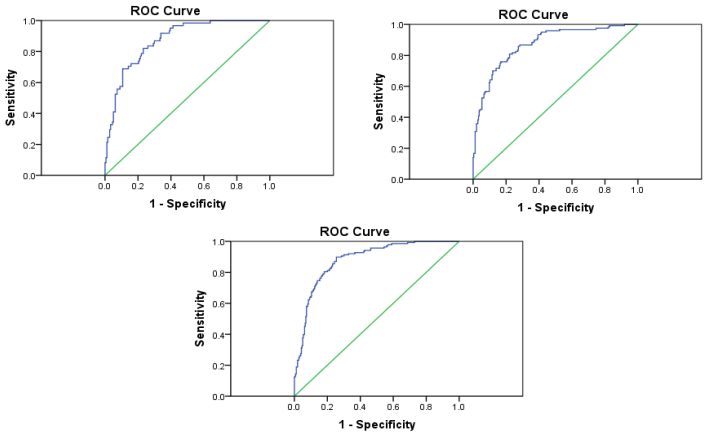

Figure: 1(a), 1(b) and 1(c)

The ROC curve is a fundamental tool for diagnostic test evaluation. It's a graphical plot of the sensitivity which measure of the overall performance of a diagnostic test. ROC curve value between 0 and 1, since the x axes and y axes have value ranging from 0 to 1. The closer the area is to 1.0, the better test is where else the area closer to 0.5 were not so good. Beside that, the larger the area, the better the diagnostic test achieved. Based on Figure 1(a,b,c) the area under the curve is 0.873 (0.828,0.919), 0.870 (0.831,0.909), 0.880 (0.847,0.914) with 95% confidence interval. Moreover, the area under the curve is significantly different from 0.05 since *p*-value is 0.000, meaning that the logistic regression classifies the group significantly better than by chance. Since, the model can accurately discriminate 87.3%, 87.0% and 88.0% of the cases.

4. DISCUSSION

The study examined the factors that associated directly or indirectly with triglycerides among blood pressure patients. This analysis only a preliminary overview of the problem associated with the relationship with triglycerides level using multiple logistic regression models method. Findings from the present study found that there are several factors which are significantly across the three distinct phases of blood pressure: normal, borderline and hypertensive (Table 4, Table 5 and Table 6). Total cholesterol, HDL cholesterol and proconvertin were main significant factors across the three different blood pressure phases. Our previous finding also support with this finding result which were same three factors significantly across the three distinct phases Amir & Shafiq [3]. However, our another previous study does not support with this finding which body mass index, weight and hip circumference were the main significant factor across the three distinct phases of blood pressure [4]. Egger et al. [13] reported that, total cholesterol remained statistically significant ($p < 0.05$) as a risk factor in all models. Another study by Bonna and Thelle [14] also reported that total cholesterol was increased significantly as the systolic blood pressure increased in both sexes.

Present study, shows that a negative association relation was found between triglycerides and HDL cholesterol along the three distinct phases of blood pressure. Our study also supported by Lindeberg et al. [15] which reported that a negative association was found between triglycerides and HDL cholesterol in Kitava and Sweden. On contrast finding on Swedish subjects, triglycerides and HDL cholesterol were not associated with waist circumference, glucose, BMI, insulin or systolic blood pressure in the Kitavans. Furthermore, triglycerides were negatively associated with HDL cholesterol and positively associated with non-HDL cholesterol. Present study also shows that body mass index for hypertensive blood pressure is significant. According to the Tesfaye et al. [16], risk of hypertension based on Ethiopia (OR = 2.47, 95% CI (1.42, 4.29)) and Vietnam (OR = 2.67, 95% CI (1.75, 4.08)) significantly high on body mass index. It also reported by Amir et al. [17] that body mass index is strongly associated with HDL cholesterol and diabetes mellitus among heart disease patients. Our previous study by Shafiq et al. [4] also reported that, body mass index was significant for normotensive where for borderline and hypertensive was not significant.

Beside that, present study serum insulin for normotensive and borderline was statistically significant where for hypertensive blood pressure was not significant. Previous studies by Lucas et al. [18] reported that the insulin was significant to blood pressure and play a major role in the regulation of blood pressure. It also reported by Falkner et al. [19] which insulin also significant in borderline blood pressure and there is a relation between insulin and blood pressure. Another study by Boyko et al. [20] reported that the insulin levels were higher in hypertensive subject and significant positive correlation was found between insulin level and blood pressure. Our previous study by Shafiq et al. [4] also reported that serum insulin was significant in borderline and hypertensive blood pressure. Present study, glucose was significant for normotensive and borderline blood pressure however does not significant for hypertensive blood pressure.

Our previous study by Amir and Shafiq [3] also reported that glucose was significant in borderline blood pressure. The previous report by Boyko et al. [20] also reported that normal blood pressure have less often had fasting blood glucose odd ratios (OR 0.4, 95% Cl: 0.26-0.75). Henry et al. [21] reported in the presence of moderate systolic hypertension can identify subject with glucose level which support our finding result. In conclusion, this study demonstrated that triglycerides level is strongly associated with the HDL cholesterol level among normal, borderline and hypertensive systolic blood pressure. Hence, triglycerides level might be a valuable marker to be monitored in normal, borderline and hypertensive systolic blood pressure.

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