ABO Blood Group and Coronary Atherosclerosis in Thais at Ramathibodi Hospital

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ABSTRACT

Objective: To study the relation between ABO blood group and coronary atherosclerosis in Thais in order to preventing and reducing the death rate.

Methods: A total of 217 postmortem forensic cases with age of ≥ 20 years from the Division of Forensic Medicine, Department of Pathology, Ramathibodi Hospital were studied for the relation of ABO blood group and coronary atherosclerosis. Clotted or ethylenediaminetetraacetic acid (EDTA) bloods were used for ABO grouping by standard hemagglutination test. The disease was diagnosed by gross and microscopic examinations. The severity of the disease revealed by occlusion of either 1, 2 or 3 main branches of coronary artery and the degree of occlusion. The risk of ABO blood group in coronary atherosclerosis was expressed as Odds ratio (OR). The OR value of >1, p value of <0.05 and 95% confidence interval were considered to be statistically significant.

Results: Coronary atherosclerosis was diagnosed in 101 out of 217 cases (46.5%). The disease found in 50.9% males (86 out of 169) and 31.2% females (15 out of 48). Males had the disease more than females with OR of 2.280, p = 0.0118. Blood group A and O appeared to be risk for coronary atherosclerosis in Thais in both males and females. It was noticed that blood group A had more disease than blood group O (OR = 1.327 vs 1.094) among males whereas blood group O had more disease than blood group A (OR = 1.750 vs 1.199) among females. There were 62.4% sudden death and 37.6% non-sudden death in this study. Blood group A and O were also increased in sudden death with coronary atherosclerosis with ORs of 1.215 and 1.151, respectively (p > 0.05). It was observed that the degree of coronary artery occlusion >75% (severe) was increased in blood group A (57.9%, OR = 1.592) and blood group AB (50.0%, OR = 1.067). In addition, occlusion of 3 main coronary arteries was increased in blood group B (43.8%, OR = 1.369, p > 0.05) and blood group AB (75.0%, OR = 5.455, p = 0.0356). Furthermore, myocardial infarction frequently occurred in blood group A and blood group O with ORs of 1.270 and 1.390, respectively.

Conclusion: Blood group A and O probably be involved in coronary atherosclerosis and myocardial infarction in Thais. Blood group A was frequently observed in male while blood group O was frequently observed in female with the disease. To give health education about the risk of ABO blood group that susceptible to coronary atherosclerosis may reduce the death rate of the disease.

Keywords: ABO blood group, coronary atherosclerosis, coronary artery disease, CAD

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INTRODUCTION

Cardiovascular disease is a major cause of death in the world. Similarly, data from Health Information Unit of Thailand showed that disease of the heart (I05-I09, I20-I52) was the fourth leading cause of death with the death rate of 32.9 per 100,000 population (or 21,142 cases) in 2012 and continues rising.[1] From a study of Udnoon, et al., 44.7% of sudden unexpected deaths in Bangkok during 2003-2007 were caused by cardiovascular system (CVS) and 61.8% of CVS was coronary atherosclerosis.[2] Other CVS are coronary artery disease, coronary

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heart disease, ischaemic heart disease and myocardial infarction. The risk and prevention of cardiovascular disease were reported by WHO included age, family history with heart disease, smoking, hypertension, diabetes mellitus, hypercholesterolemia, and fundamental genetics.[3] ABO blood group is one of genetic factors related with coronary artery disease (CAD). Blood group A is increased in most people with coronary artery disease in several countries, e.g., Scottish[4], American[5], Norwegian[6], German[7], British[8], Hungarian[9], Pakistani[10], Malaysian[11] and Taiwanese[12]. Other ABO blood groups are less frequent for the disease, i.e., blood group non-O (A, B and AB) in Palestinian[13] and Italian[14], blood group B in Lithuanian[15], Swiss[16] and Indian[17], blood group AB in British[18], and blood group O in Bangladeshi[19]. In Thais, blood group A and AB were non-significantly increased in coronary atherosclerosis[20-21]. In this study, we increased the sample size and various factors were analyzed in order to have more information. The aim was to give health education to the young people (< 50 years) especially with ABO blood group that are susceptible for coronary atherosclerosis, so the death rate of the disease may reduce.

MATERIALS AND METHODS

A total of 217 postmortem forensic cases from the Division of Forensic Medicine, Department of Pathology, Faculty of Medicine, Ramathibodi Hospital during December 2012 to April 2014 were studied for the relationship of ABO blood group and coronary atherosclerosis. The inclusion criteria were ethnic Thais and age of 20 years or older whereas the exclusion criteria were decomposed blood or excess hemolysis, no information of the dead person, and no autopsy due to Islamic religious beliefs or had a history of medical record. Coronary atherosclerosis from autopsy reports were diagnosed by gross and microscopic examinations.[22] The blockage of one or more arteries (left anterior descending artery or LAD, left circumflex artery or LCX, and right coronary artery or RCA) which supply blood to the heart was classified to be the disease group whereas no occlusion of coronary artery was classified into the control group. The details of the disease and control groups in this study have been shown in Table 1. The sample size was calculated from a formula of $n = Z^2_{\alpha/2}P(1-P)/d^2$. In this study, Z value at a confidence level of 95% is 1.96, the probability of blood group A in Thais[23] (P) is 0.21 and the probability of error accepted (d) is 0.3 X 0.21. Therefore, the sample size (n) calculated was 161. Two milliliters of clotted blood or EDTA blood stored in a refrigerator was used for the determination of ABO blood group by tube test hemagglutination method.[24] Washed red blood cells were used for cell grouping. Anti-A, anti-B and standard A cells and B cells were from the National Blood Center, Thai Red Cross Society. The relationship of ABO blood group, gender, manner of death, severity of the disease, myocardial infarction, and age in coronary atherosclerosis were analyzed using GraphPad Prism 5. The risk factor was expressed as Odds ratio (OR). The OR value of greater than 1 means ABO blood group affects the increase of coronary atherosclerosis whereas OR value of less than 1 means ABO blood group affects the decrease of coronary atherosclerosis. The p value of less than 0.05 and 95% confidence interval (CI) do not span 1.0 were considered to be statistical significance.

This document has been reviewed and approved by the Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University (MURA2013/432).

RESULTS

Coronary atherosclerosis was diagnosed in 101 out of 217 cases (46.5%). Sex, age, causes of death, and frequency of ABO blood group in the disease and control groups have been shown in Table 1. Male was increased in the disease group, i.e., M:F ratio was 5.7:1 in the disease group vs 2.5:1 in the control group. The mean age of males was also shorter than females in both disease and control groups, i.e., 50.5 years (range 20-81 years) in males with the disease vs 60.9 years (range 26-86 years) in females with the disease. The majority of the disease group had sudden death (62.4%), whereas the majority

TABLE 1. Characteristic of samples for ABO and coronary atherosclerosis study.

Characteristics of sample	Disease	Control
Sample size	101	116
Sex		
Male	86 (85.1%)	83 (71.6%)
Female	15 (14.9%)	33 (28.4%)
Ratio M : F	5.7 : 1	2.5 : 1
Age in years (range)		
Male	50.5 (20 – 81)	39.1 (20 – 69)
Female	60.9 (26 – 86)	42.8 (21 – 93)
Causes of death / underlying diseases		
Sudden or natural	63 (62.4%)	44 (37.9%)
Accident	29 (28.7%)	52 (44.8%)
Homicide	7 (6.9%)	16 (13.8%)
Suicide	2 (2.0%)	4 (3.5%)
ABO blood group		
A	19 (18.8%)	20 (17.2%)
B	32 (31.7%)	46 (39.7%)
AB	8 (7.9%)	7 (6.0%)
O	42 (41.6%)	43 (37.1%)

TABLE 2. The risk of ABO blood groups for coronary atherosclerosis in different genders and ages.

ABO / Gender / Age	Disease	Control	OR	p value	95% CI
ABO					
Males (n = 169)	86	83			
A (n = 30)	17	13	1.327	0.310	0.599 - 2.938
B (n = 59)	26	33	0.657	0.128	0.347 - 1.241
AB (n = 13)	8	5	1.600	0.306	0.501 - 5.108
O (n = 67)	35	32	1.094	0.449	0.590 - 2.027
Females (n = 48)	15	33			
A (n = 9)	2	7	0.571	0.415	0.104 - 3.150
B (n = 19)	6	13	1.026	0.606	0.295 - 3.570
AB (n = 2)	0	2	0.406	0.468	0.018 - 8.999
O (n = 18)	7	11	1.750	0.285	0.503 - 6.086
Age					
Males (n = 169)	86	83			
≤ 50 yrs (n = 112)	44	68	0.231	< 0.0001	0.115 - 0.466
> 50 yrs (n = 57)	42	15	4.327	< 0.0001	2.146 - 8.724
Females (n = 48)	15	33			
≤ 50 yrs (n = 28)	4	24	0.136	0.004	0.034 - 0.541
> 50 yrs (n = 20)	11	9	7.333	0.004	1.850 - 29.08

of the control group had accident (44.8%). The frequencies of ABO blood groups in the disease and control groups were almost similar although blood group A, AB and O were slightly increased in the disease group.

The risk of ABO blood groups for coronary atherosclerosis in different genders and ages have been shown in Table 2. Blood groups A, AB and O were increased in males with OR of 1.327, 1.600 and 1.094, respectively whereas blood group B

and O were increased in females with OR of 1.026 and 1.750, respectively. However, there was no statistical significance. The prevalence of coronary atherosclerosis was significantly increased in the age of more than 50 years old. Females had higher risk for the disease (OR = 7.333, p = 0.004, 95% CI = 1.850 – 29.080) than males (OR = 4.327, p < 0.0001, 95% CI = 2.146 – 8.724).

Among 101 postmortem cases with coronary atherosclerosis, the ABO blood groups and various risk factors (manner of death, coronary artery occlusion, myocardial infarction and ages) were analysed (Table 3). Blood group A had higher sudden death (OR = 2.656) followed by blood group B (OR = 1.008). Coronary artery occlusion > 75% was also observed in blood group A (OR = 1.592) and blood group AB (OR = 1.067). It was noticed that the results from autopsy by gross and microscopic examinations revealed 3 main artery occlusions (LAD, LCX and RCA) frequently occurred in blood group AB (OR = 5.455, p = 0.036, 95% CI = 1.041 – 28.58) and blood group B (OR = 1.369). In addition, myocardial infarction (MI) was frequently observed in coronary atherosclerosis with blood group O (OR = 1.390) and blood group A (OR = 1.270). Finally, coronary atherosclerosis with age of less than 50 years was found in blood group A, B and O with ORs of 1.672, 1.156 and 1.006, respectively.

DISCUSSION

Cardiovascular disease is an awful cause of death especially in working age group. Several activities are established by both government and non-government organizations in order to decrease certain cardiovascular risks, but the outcome has not reached satisfaction. The ABO blood group is one of the genetic factor related to cardiovascular disease and the technique to detect is simple and less expensive. The management of the disease requires intensive investigations and ABO blood group would be one of the possibilities.

Male and age of more than 50 years are susceptible to coronary atherosclerosis (Table 1 and 2). The result was similar to other ethnicities. In this study, coronary atherosclerosis frequently occurred in female older than 50 years (OR = 7.333 in female vs OR = 4.327 in male with the same age) which may be due to menopause and lack of hormone estrogen.[22]

The relations of ABO blood group and coronary atherosclerosis in Thais have been summarized in Table 4 (data from Table 2-3).

Blood group A: Male, < 50 yrs, sudden death, occlusion > 75% and MI

Blood group B: Female, < 50 yrs, sudden death, 3 main coronary artery occlusion

Blood group AB: Male, occlusion > 75%, 3 main coronary artery occlusion

Blood group O: Male and female, < 50 yrs and MI

Our study was similar to many reports that blood group A is associated with CAD.[4,8-12] Anvari et al, studied 10,621 Iranian patients awaiting for coronary artery bypass graft surgery and found that blood group A was increased in male patients whereas blood group O was increased in female patients, and blood group B was less susceptible for hyperlipidemia compared to other blood groups.[25] Similar to our study that blood group A is increased in male with the disease, blood group O is increased in female with the disease, and blood group B is less harmful although 3 main coronary arteries occlusion was detected. Our study is also similar to Biswas et al,[19] that blood group O was increased risk for CAD in Bangladesh and Meade et al,[18] that blood group AB was increased in British male patients with ischaemic heart disease.

The role of ABO blood group in the occurrence of coronary atherosclerosis is still unclear. A disintegrin and metalloproteinase with a thrombospondin type 1 motif 13 (ADAMTS13) is a gene on the same chromosome as ABO blood group (chromosome 9) which provides instructions for making an enzyme that is involved in blood clotting by sealing off after injury. The relationship between ABO histo-blood group, von Willebrand factor (vWF), factor VIII and ADAMTS13 was reported to be involved in the mechanism of proteolysis, rate of vWF synthesis by endothelial cells and plasma vWF clearance rate.[26-27] Since the subjects to be studied in this study were postmortem cases, there was no other laboratory examinations supported except coronary artery occlusion.

TABLE 3. Distribution of ABO blood groups in 101 postmortem cases with coronary atherosclerosis and various risk factors.

ABO	Manner of death		OR	p value	95% CI
	Sudden (n = 63)	Non-sudden (n = 38)			
A	15	4	2.656	0.079	0.810 - 8.710
B	20	12	1.008	0.583	0.424 - 2.395
AB	3	5	0.330	0.129	0.074 -1.469
O	25	17	0.813	0.385	0.360 - 1.836
ABO	**Coronary artery occlusion**		**OR**	**p value**	**95% CI**
	> 75% (n = 49)	≤ 75% (n = 52)			
A	11	8	1.592	0.257	0.580 - 4.367
B	14	18	0.756	0.331	0.325 - 1.756
AB	4	4	1.067	0.608	0.251 - 4.523
O	20	22	0.940	0.520	0.426 - 2.077
ABO	**Coronary artery occlusion**		**OR**	**p value**	**95% CI**
	3 main arteries (n = 39)	1-2 main arteries (n = 62)			
A	6	13	0.685	0.335	0.237 - 1.985
B	14	18	1.369	0.306	0.583 - 3.215
AB	6	2	5.455	0.036	1.041 - 28.58
O	13	29	0.569	0.130	0.248 - 1.308
ABO	**Myocardial infarction**		**OR**	**p value**	**95% CI**
	Present (n = 23)	Absent (n = 78)			
A	5	14	1.270	0.444	0.403 - 4.000
B	6	26	0.706	0.350	0.249 - 2.004
AB	1	7	0.461	0.417	0.054 - 3.957
O	11	31	1.390	0.324	0.545 - 3.542
ABO	**Age**		**OR**	**p value**	**95% CI**
	≤ 50 yrs (n = 48)	> 50 yrs (n = 53)			
A	11	8	1.672	0.227	0.609 - 4.589
B	16	16	1.156	0.450	0.499 - 2.676
AB	1	7	0.140	0.041	0.016 - 1.182
O	20	22	1.006	0.573	0.456 - 2.223

TABLE 4. Summarized the risk of ABO blood groups for coronary atherosclerosis with other risk factors in Thais.

Risk Factors	A	B	AB	O
Male	OR = 1.327	OR < 1	OR = 1.600	OR = 1.094
Female	OR < 1	OR = 1.026	OR < 1	OR = 1.750
Age ≤ 50 yrs	OR = 1.672	OR = 1.156	OR < 1	OR = 1.006
Sudden death	OR = 2.656	OR = 1.008	OR < 1	OR < 1
Coronary occlusion >75%	OR = 1.592	OR < 1	OR =1.067	OR < 1
3 main coronary arteries occlusion	OR < 1	OR = 1.369	OR = 5.455	OR < 1
Myocardial infarction	OR = 1.270	OR < 1	OR < 1	OR = 1.390

In conclusion, blood group A and O probably are involved in coronary atherosclerosis and myocardial infarction in Thais. Blood group A was frequently observed in male while blood group O was frequently observed in female with the disease. Although the p value was greater than 0.05, these findings may warn us to be aware about ABO blood group. Further investigation in living patients including their behavior in daily life may be necessary to clarify the mechanism of ABO blood group in the development of the disease especially in young age group (< 50 years). To give health education about the risk of ABO blood group which is susceptible to coronary atherosclerosis may reduce the death rate of the disease.

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