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Atherosclerotic Parameter Level Differences in Mongolian People Compared to Japanese People: A Brief Review of the Literature

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Objectives: In Mongolia, non-communicable disease caused morbidity and mortality related to lifestyle and metabolic diseases are increasing year after year. This review discusses the results of comparative studies related to lifestyle risk factors and the atherosclerotic parameters body mass index, glucose, insulin, and lipid level of Mongolian and Japanese people, as these are the known factors involved in metabolic and cardiovascular diseases. **Methods:** Academic literature was searched using electronic academic databases and handsearching reference lists for articles published in English and Mongolian on the topic. **Results:** The studies revealed that in comparison to Japanese subjects, a higher percentage of Mongolians smoked, and Mongolians had higher body mass index, heart rate, blood pressure, and insulin even though levels of serum total cholesterol and glucose were not different. **Conclusion:** The studies suggest that Mongolian people have higher risk of metabolic syndrome, which is a known main cause of CVDs, compared to Japanese people. On the other hand, climate, genetic and lifestyle differences might also increase non-communicable diseases in the Mongolian people.

Keywords: Atherosclerosis, Metabolic Syndrome, Glucose, Cholesterol, Body Mass Index

Introduction

The basic pathophysiologic pathway of cardiovascular disease (CVD) is atherosclerosis. CVD includes coronary heart diseases (CHD) such as angina and myocardial infarction. Hypertension (HT) nowadays is a possible world-wide cause of CHD related premature death [1]. On the other hand, lifestyle related metabolic disorders also play a role in accelerating atherosclerotic processes. The World Health Organization (WHO) reported that non-communicable diseases (NCD) such as CVD account 40% of deaths worldwide, the highest for any category of disease. The WHO expects obesity and the percentage of people with elevated blood pressure will continue to increase until 2025 [2]. Worldwide, 17.1 million people die annually from CVD, far more than the 8.8 million deaths from cancer, 3.9 million from respiratory disease, and 1.6 million from diabetes, respectively.

The rates of CVD related deaths and morbidity are different among different ethnicities, possibly because of a combination of genetic, physiological, environmental and behaviors factors. Tobacco use, physical inactivity, the harmful use of alcohol, unhealthy diets are all known to the increase risk of NCDs [3].

In this review the Japanese and Mongolian people were compared to clarify relative risk factors for atherosclerosis among the Mongolian people. CVD is a significant health burden in Mongolia, with its morbidity increasing year by year. The prevalence of metabolic syndrome is increasing in Mongolia. Enkh-Oyun et al, noted that reducing the prevalence of metabolic syndrome might help to decrease CVD in Mongolia [4]. As of 2016, in Mongolia diseases of the circulatory system increased 2 fold compared to 10 years ago (501.8 vs 1007.6 per 10,000 people) [5]. The Mongolian survey of 2009 concluded that about 1 in 4 (26.4%) of all adults, over half (58.3%) of adults 45-64 years of age have three or more common modifiable NCD risk factors [6]. The lifestyle and altitude of Mongolian people is different compared to Japanese people even though they have common racial background (Mongoloid factor) [7, 8]. There have been several comparing their reactive oxygen metabolism, dietary habits, rates of obesity and metabolic syndrome, and their lipid metabolism [9-12]. The recent studies using newer atherosclerotic parameters suggest that Mongolian people may be at higher risk for CVD than Japanese people. In our previous research, we studied the differences in cardio-ankle vascular index (CAVI) and serum high sensitive C-reactive protein (hsCRP) between Mongolian and Japanese people [13-17]. Higher levels of CAVI and CRP have been established in Mongolian people compared to Japanese people, indicating that Mongolian people are have higher risk of CVD [10, 12, 18]. Morbidity and mortality rates from CVD, levels of CAVI, and serum CRP are different for many ethnicities and are associated with their food intake, lifestyles, genetic background and environmental risk factors (e.g. altitude difference, oxidative stress). Ethnical comparative studies detect crucial features of lifestyle related diseases and are important to select suitable preventive methods.

There have been several ethnical comparative studies of CVD and its risk factors among Mongolian and Japanese population [8, 18-20]. This review aimed to clarify the atherosclerotic and metabolic risk factors of Mongolian people by reviewing the results of ethnical comparative studies to the Japanese population. Understanding where to focus preventive efforts to prevent atherosclerosis is a primary method to decrease premature deaths.

Materials and Methods

In this brief review, an overview of the current knowledge of atherosclerotic parameters comparing the Mongolian people with other countries people is provided. The academic literature was searched using electronic academic databases (PubMed, Google Scholar, Scopus, and Mongolmed) and handsearching reference lists for articles published in English and Mongolian. Studies were identified using the following keywords: comparative study, atherosclerotic parameters, non-communicable disease, differences, and lifestyle.

Results

Atherosclerosis related parameters in Japanese and Mongolian people

In one comparative study, healthy young Mongolian subjects ages 18-25 had a significantly higher percentage of meat intake and current smoking (47.0% vs. 13.0%) compared to Japanese subjects (13% vs. 2.6%) [19]. Other lifestyle factors including vegetable intake, salt intake and physical activity were not significantly different. This may be because the study participants were young, and a general data questionnaire rather than a focused questionnaire was used. A study of the residents of Murun (prefecture) in Mongolia showed a daily calorie intake 1.3 fold higher in Mongolian people than Japanese people with its resulting higher level of lifestyle related diseases [7]. This study measured reactive oxygen metabolites (ROM), and the level of ROM was 429.7±95.2 for Murun subjects, compared to 335.3±59.8 ($p<0.001$) for Japanese subjects. Furthermore, *malondialdehyde*-modified low-density lipoprotein-cholesterol and urinary *8-hydroxydeoxyguanosine* were higher.

Salt intake is one of the lifestyle related risk factors to developing hypertension [14]. In 2000, nutritional data identified an average total daily salt intake of 16.7 g in the Mongolian population and 11.2 g in Japanese population [21, 22]. Additionally, Mongolian people had higher level of oxidative stress markers including *malondialdehyde*-modified low density lipoprotein cholesterol (LDLc), urinary *8-hydroxy-*

2'-deoxyguanosine, and serum reactive oxygen metabolism compared to Japanese people [7].

Several researchers found lower levels of plasma n-3 polyunsaturated fatty acid (n-3 PUFA) in Mongolian people which related to higher risk of CVD. N-3 PUFA is found in fish which is consumed in larger amounts by Japanese people. The lower level of n-3 PUFA is negatively related to triglyceride (TG) in Mongolian people while higher n-3 PUFA is associated with lower HDL-c and TG in Japanese people and lower systolic blood pressure in Korean people [23].

Recently, there has been a collision between traditional and westernized lifestyles in the urban areas of Mongolia. The previous studies showed Mongolian people may have higher risk of cardiovascular events related to their lifestyle [8, 9].

One of the health crucial issues to prevent CVD is the detection of atherosclerotic alterations among asymptomatic subjects. There have been a few comparative studies which included healthy young aged 18-25 years subjects. In recent study new atherosclerotic parameters, CAVI and ABI were measured for the first time in Mongolian subjects. Modern high-quality scientific techniques may help to find new important information which has not been detected previously. Previous research has shown that body mass index (BMI), heart rate (HR), diastolic blood pressure (DBP), CAVI and ABI levels were significantly higher, and TC and glucose levels were significantly lower in Mongolian subjects compared to Japanese subjects [18,19]. Similar results were found in Mongolians between the ages of 30 and 60 compared to Japanese subjects and Korean subjects [12].

Interestingly healthy young Mongolians have significantly higher measurements of CAVI and ABI than Japanese subjects. Researchers explained the higher measurements of CAVI and ABI in Mongolian subjects may be related to their hematocrit, oxidative stress, and peripheral resistance which are hypoxia-related effects that occur at higher altitudes [24, 25]. Mongolia is a landlocked country located 1580 m above sea level which is higher in altitude than Japan (Tochigi prefecture; 50 m). The highest altitude in Mongolia is 2180 m above sea level (Gobi-Altai) and lowest is 625 m above sea level (Selenge). CVD risk factors such as elevated blood pressure and hematocrit are known to increase with altitude [25]. Although, the rising CAVI measurements showed decreasing vascular elasticity, the Mongolian subjects were young. Therefore, future study is needed to clarify the impact of higher CAVI measurements in young Mongolian subjects. Additionally, this study correlated CAVI and ABI with other atherosclerotic parameters between Mongolian and Japanese subjects [19].

In 1965, serum TC levels in healthy young Mongolian subjects were compared to Czechoslovak people (age 19-23 and the Mongolian subjects had lower TC [12, 26]. This result was confirmed in other studies that included Japanase and Korean populations [12]. Some data showed low density lipoprotein cholesterol (LDL-c) level is lower in Mongolian people than in people from other Asian countries. However a physiologic pathway was not clearly explained.

Carotid atherosclerosis is assessed by carotid IMT using non-invasive ultrasound and this is widely useful in clinical practice. Carotid IMT is also a surrogate marker for CVD used in the preventive in the field of preventive cardiology. Carotid IMT in Mongolian subjects was greater (median [interquartile range]; 0.63 [0.49-0.86]) and strongly associated with age when indirectly compared other ethnic studies results [27]. Furthermore, carotid IMT related parameters were different in Mongolian people compared other Asians [28, 29].

There have a few comparative studies on atherosclerotic parameters between Japanese and Mongolian patients. An ethnicity-based disease study attempted to compare atherosclerotic parameters between hospital-based Mongolian and Japanese populations with hypertension and/or DM [17]. Significantly higher BMI, HR, DBP and CAVI, significantly lower TC and glucose were found in Mongolian patients compared with Japanese patients and this was consistent with the previous studies of healthy young Mongolian subjects. Comparing Mongolian subjects to Japanese subjects 20-25 years of age, their BMI was 21.4 [19.8-23.3] vs 20.5 [19.3-22.3], TC was 3.99 [3.55-4.38] vs 4.40 [4.04-5.06], and glucose was 4.22 [3.55-4.38] vs 4.88 [4.61-5.16]. Comparing Mongolian and Japanese people with hypertension and diabetes mellitus over age 40, their BMI was 27.5 [24.0-31.0] vs 23.7 [21.5-26.3], HR was 67.5 [59.0-78.0] vs 64.0 [58.0-71.0], SBP was 147.0 [134.0-164.0] vs 128.0 [119.0-138.0], glucose was 83.0 [5.7-14.9] vs 107.5 [9.4-14.4] (Table 1). Additionally, CRP, carotid IMT and insulin were significantly higher in Mongolian patients than in Japanese patients. Higher serum CRP levels were seen with increased metabolic syndrome risk factors in both Japanese people and Mongolian people [19]. These higher atherosclerotic

Table 1. Atherosclerotic parameter levels in Mongolian and Japanese people

#	Authors	Parameters	Mongolian	Japanese
1.	Uurtuya S et al. 2009	Current smoking,%	13.0	2.6
2.	Uurtuya S et al. 2010		26.3	17.9
3.	Sanders PW, 2009	Total dairy salt intake	16.7g	11.2g
4.	Uurtuya S et al. 2009	Meat intake, (yes)	47.0%	13.0%
5.	Fujihara Y et al. 2017		7.39±3.19	1.45±1.83
6.	Shiwaku K et al. 2005		41% (men)	92% (men)
			81% (women)	45% (women)
7.	Komatsu F et al. 2009	Consumed kcal per day	2534 kcal	2121 kcal
8.	Uurtuya S et al. 2009	Heart rate, bpm	65.0(61.0-70.0)	57.0 (50.3-65.0)
9.	Uurtuya S et al. 2010		67.5(59.0-78.0)	64.0 (58.0-71.0)
10.	Uurtuya S et al. 2009	BMI, kg/m^2	21.4(19.8-23.3)	20.5 (19.3-22.3)
11.	Uurtuya S et al. 2010		27.5[24.0-31.0]	23.7 [21.5-26.3]
12.	Shiwaku K et al. 2005		26.2±4.2 (men)	23.2±3.1 (men)
			25.5±4.6 (women)	22.6±3.4 (women)
13.	Fujihara Y et al. 2017		27.0±5.6	23.4±3.9
14.	Komatsu F et al. 2009	TC, mg/dL	6.5% (men) high	1.3% (men)
			14.7% (women)	0.8% (women)
15.	Uurtuya S et al. 2009		3.99(3.55-4.38)	4.40(4.04-5.06)
16.	Uurtuya S et al. 2010		180.0[160.3-194.8]	186.6 [172.0-199.5]
17.	Shiwaku K et al. 2005		186±39 (men)	205±38 (men)
			176±33 (women)	205±35 (women)
18.	Shiwaku K et al. 2005	TG, mg/dL	123±104 (men)	131±90 (men)
			88±54 (women)	91±52 (women)
19.	Shiwaku K et al. 2005	LDL, mg/dL	113±35 (men)	125±35 (men)
			103±31 (women)	128±31 (women)
20.	Shiwaku K et al. 2005	HDL, mg/dL	50±12 (men)	54±16 (men)
			55±12 (women)	58±14 (women)
21.	Uurtuya S et al. 2009	Glucose, mg/dL	4.22(3.90-4.50)	4.88(4.61-5.16)
22.	Uurtuya S et al. 2010		83.0[75.3-113.3]	107.5[94.0-144.0]
23.	Shiwaku K et al. 2005		101±40 (men)	100±25(men)
			96±19 (women)	90±20 (women)
24.	Uurtuya S et al. 2009	SBP, mm Hg	114.0[108-121.8]	111.0[105.0-120.8]
25.	Uurtuya S et al. 2010		147.0[134.0-164.0]	128.0[119.0-138.0]
26.	Fujihara Y et al. 2017		150.8±26.2	144.0±19.2
27.	Uurtuya S et al. 2010	CAVI	8.8±1.2	8.1±1.1
28.	Uurtuya S et al. 2009	IMT, mm	0.44[0.38-0.50]	0.42[0.37-0.47]
29.	Uurtuya S et al. 2010		0.84[0.67-1.51]	0.70[0.60-0.89]
30.	Uurtuya S et al. 2009	CRP, mg/dL	0.04[0.02-0.08]	0.03[0.01-0.05]
31.	Uurtuya S et al. 2010		0.19[0.09-0.42]	0.05[0.03-0.12]
32.	Komatsu F et al. 2006	ROM	429.7±95.2	335.7±59.8

(median [interquartile range]), (mean ± SD), BMI-body mass index, TC-total cholesterol, TG-triglyceride, LDL-low density lipoprotein, HDL-high density lipoprotein, SBP-systolic blood pressure, CAVI-cardio-ankle vascular index, IMT-intima-media thickness, CRP-C-reactive protein, ROM-reactive oxygen metabolites

parameters in Mongolian patients may indicate that the Mongolian patients have more vascular stiffness.

Discussion

The 2016 WHO statistical data reports that the life expectancy of Mongolian people is approximately 14.0 years less than Japanese people despite their genetic similarities [4, 30, 31]. According to the latest WHO data published in 2015 life, the life expectancy for males in Mongolia is 64.7 years, for females is 73.2 years, and when combined the expectancy is 68.8 years giving it life expectancy rank of 122. In Mongolia, the top 5 causes of death are CHD, stroke, liver cancer, and lung disease [32]. Mongolian morbidity data in 2009 compared to 2001 report the top leading causes of morbidity were diseases of the respiratory, digestive, genitor-urinary, circularity system and injury/poisoning and these increased 25-40% [33]. Since 1991, the mortality rate due to diseases of the circulatory system has been increasing and has become the leading health issue in Mongolia [33]. Statistical data shows that morbidity and mortality rates of NCD such as CVD have been rapidly increasing in Mongolia. The WHO 2009 data reported age-standardized death rate per 100 000 people in Mongolia for stroke was 185.60, for CHD was 92.82, for DM was 2.05 and for HT was 50.98, respectively [32]. These data showed that the mortality rate of stroke, CHD and HT was 3-5-fold higher in Mongolia than Japan. Among inpatients, ischemic heart disease accounted for 19.2% of the diseases of the circularity system in 2000, 25.7% in 2004, 30.1% in 2008 [8]. Even in 2009, the mortality rate caused by stroke, CHD and HT was a significant cause of mortality for Mongolia despite the lower levels of TC compared to Korean and Japanese people [12]. Japanese people have the highest life expectancy in the world and have been maintained this rank for over 20 years [34]. According to the latest WHO data published in 2015, the life expectancy for males in Japan is 80.5 years, for females are 86.8 years yielding a total life expectancy of 83.7. The top 5 causes of death in Japan are stroke, influenza, and pneumonia, CHD, lung cancer, and suicide [35]. The main features of CVD in Japan are a high stroke rate and low CHD mortality rate compared to other industrialized countries. However their TC and smoking rates are high [35]. In 1965, age-adjusted all-stroke mortality rate in Japan was the highest in the world after which the mortality rate gradually decreased until 1990 [23]. Since 1970, the mortality rate due to CHD also decreased with more people having heart failure in Japan than in the United States [23]. According to the 2009 WHO data for Japan, the age-standardized death rate per 100 000 people for stroke was 42.20, for CHD was 32.14, for DM 4.53 and for HT 1.74 respectively [32]. Controlling HT and reducing smoking are the main ways used to reduce stroke and CHD in Japan [22]. Compared to 1965, in 1990 the prevalence of HT in Japan decreased by 17%, and the prevalence of smoking decreased by 43.2% in men and 17.5% in women, respectively. Currently Japan still has high levels of TC, however the mortality rate for CVD has decreased compared to CHD. Therefore, research comparing these diseases in Mongolia and Japan is helpful to clarify the impact of the disease, to predict premature deaths, and to consider the ethical issues surrounding treating and preventing this disease.

Higher levels of CVD risk factors in the Mongolian population such as smoking and higher BMI were identified in all comparative studies. This included apparently healthy subjects, young people and patients. The components of cigarette smoke such as nicotine are accelerating factors of atherosclerosis due to their pathophysiologic affect injuring endothelial cells, inhibiting prostacyclin and increasing LDLc level. Interestingly, Mongolian patients have similar levels of insulin resistance compared to Japanese patients while having higher insulin and lower glucose levels. Schindler et al, report that chronic inflammation and insulin resistance increase with body weight and this is related to impairment of endothelial dependent coronary vasomotion in overweight individuals [36]. One possible explanation for this affect is the differences in environmental factors such as altitude. The lowering effect of high altitude on plasma glucose has also been reported in previous study [37]. Fujihara et al, found that BMI, DBP, and intake of meat were statistically higher in Mongolian women however the Mongolian study participants were younger than the Japanese. The researchers concluded that hypertension was a significant contributing factor for atherosclerosis in Ulaanbaatar participants, but not in Uku Island participants [38].

Researchers confirmed that atherosclerotic parameters such as higher CAVI and CRP in Mongolian patients were not associated with elevated blood pressure. However, there have been several studies in Mongolia which show that blood pressure increases with altitude in the different regions of the country [23]. Additionally, some different and unknown genetic

polymorphisms may play a role on atherosclerosis. However, the genetic backgrounds of Japanese and Mongolian people are similar. These factors are thought to merit further investigation to elucidate the differences between the Japanese and Mongolian people, otherwise some potentially important unknown factors might remain unknown.

Perspective strategy of atherosclerosis in Mongolian people

Previous studies have shown different CAVI measurements in countries with different ethnicities. The higher CAVI measurements in young Mongolian subjects may not suggest that their arteries were stiffer than Japanese subjects. A previous study suggested that the CAVI measurements and lower level of glucose may be dependent on environment factors such altitude difference. But this is not clear. The highest altitude where people live in Mongolia is 2180 m above sea level (Gobi-Altai) and lowest is 625m above sea level (Selenge) in Mongolia. The CAVI level may be different among Mongolian residents who live at different altitudes. Further studies are needed between Japanese and Mongolian to identify the effect of lifestyle differences, meat intake, fruit intake, vegetable intake, salt intake and physical activity on CAVI. Comparative studies on arterial stiffness are required to understand pathophysiologic effects and features of higher levels of blood pressure, IMT, HR, BMI, CAVI, and CRP in countries with different ethnicities.

A limitation of this review was that there were few papers with direct comparisons of atherosclerotic parameters in Mongolian and other populations and this limited the data from which conclusions could be drawn.

Conclusions

Higher levels of atherosclerotic parameters in young healthy Mongolian people and patients with HT and DM indicate that Mongolian people are at high risk to have increasing morbidity and mortality rates due to CVD in the future. Furthermore, the reasons for lower levels of HDL and glucose in Mongolians is not clear. Therefore, more research is needed to clarify the atherosclerotic parameters and arterial wall stiffness, and their association with environmental risk factors including altitude and climate on the lifespan of the Mongolian people. Further comparative studies are crucial to identify risk factors based on their lifestyle.

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