CHAPTER II

LITERATURE REVIEWS

This study interested to determine the hs-CRP in parallel with the risk factors for CVDs e.g. glucose, TC, TG, HDL-C, and LDL-C and furthermore the new parameters such as vascular indexes.

Cardiovascular diseases (CVDs)

CVDs are a category of the heart and blood vessels disorders. There are many risk factors involved in CVDs that can be divided into 2 groups. First, modifiable risk factors that can be changed such as insulin resistance, diabetes, dyslipidemia, hypertension, obesity, inflammation, atherosclerosis, tobacco exposure, physical inactivity, unhealthy diets, harmful use of alcohol (World Heart Federation, 2013). Second group is non-modifiable risk factors that cannot be changed. Members of the second group such as family history which first-degree blood relative has had CVDs, gender as a man is greater risk of CVDs than a pre-menopausal woman, but when past menopause, a woman's risk is equal to man. An ethnic play a part in CVDs risk factor too, people with African or Asian origin are at higher risk of CVDs than people in other part. Aging is one certain risk factor for CVDs; risk of stroke doubles every decade after age 55. (World Heart Federation, 2013)

CVDs include many diseases such as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease (PAD), rheumatic heart disease, congenital heart disease, deep vein thrombosis (DVT) and pulmonary embolism (World Health Organization, 2013), valvular heart disease which is the disease of one or more of the heart's valves (Bonow, R.O., 2006) , cardiac dysrhythmia or arrhythmia which can cause cardiac arrest cause of too slow heart beat (bradycardia) or too fast heart beat (tachycardia) (Mandel William, J., 1995) , however the major proportion which is more than 75 % of CVDs, is specifically a disease of the artery wall (American Heart Association, 2002).

There were about 63 % of 57 million people died from non-communicable disease (NCD), in 2008. CVDs and hypertension was the largest proportion, approximate 39 %, cancers 27 %, diabetes 4 %, chronic respiratory disease, digestive disease and other NCD 30 % (World Health Organization, 2010), as show in figure 1. CVDs is the number one cause of global death and be on the top of cause of death in the future. An estimated 17.3 million people died from cardiovascular disease in 2008 (World Health Organization, 2011). There were 7.3 million deaths from heart attacks and 6.2 million from stroke. If appropriate action is not taken, by 2030, an estimated 20 million people will die from cardiovascular disease every year that mainly cause from heart attacks and strokes. and around 80 % of global deaths occurred in low and middle income countries (LMIC) (World Health Organization, 2011a).

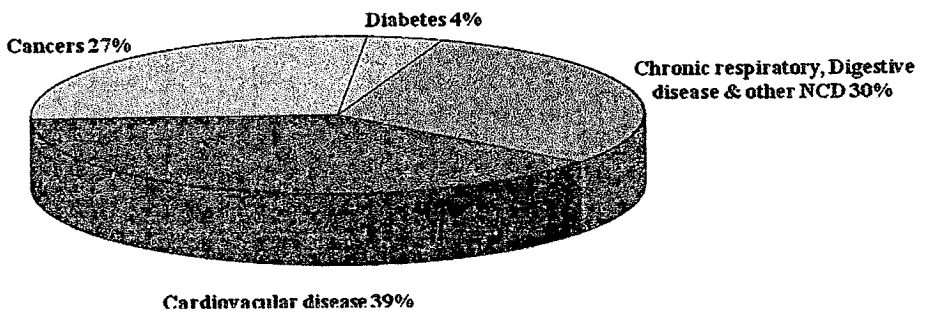

Figure 1 the percentage of non-communicable disease death globally in 2008

Risk factors for cardio vascular diseases

There are many risk factors that associate with CVDs. These factors can be classified into two groups. 1) **primary risk factor**; or non-modifiable risk factor; include aging; in men, the risk for CVDs increase after age 45 years , in women, the risk for CVDs increase after age 50-55 years (NCEP., 2004; Richard, C. Becker, 2005), gender; which in men have about 3-fold incidence, 5-fold mortality greater than in women (Pekka Jousilahti, 1999), family history; your risk increase if a first-degree blood relative (e.g. father, brother, mother, sister) has suffered from CVDs before age 55 years (in men) or 65 years (in women). If both parents have suffered from CVDs before age 55 years, your risk can rise up to 50 % compared to normal group (World

Heart Federation, 2013). 2) **secondary risk factor**, or modifiable risk factor; include insulin resistance, dyslipidemia, hypertension, obesity, inflammation, atherosclerosis, smoking, and low physical activity (NCEP., 2004)

Insulin resistance

Insulin resistance (IR) is a physiological disorder, in which cells cannot respond to the insulin hormone even though body can produces enough insulin. The cells resist to insulin and are unable to use it effectively, and cause hyperglycemia. Accordingly, beta cells in pancreas increase insulin production leading to hyperinsulinemia and is a hallmark of type 2 diabetes (DeFronzo, 1988). IR associate with many CVDs risk markers include diabetes (DeFronzo, 1988), dyslipidemia (Bonora, E., 1998), hypertension (Bonora, E., 1998; Bonora, E., 2001). Development of insulin sensitivity might be an additional objective to prevent of CVDs risk (Enzo Bonora, 2007). Several study indicated that IR can use to predict CVDs incident (Päivi Lempiäinen, 1999; Anthony, J.G., 2002) through classic risk factors such as in diabetes subject (Enzo Bonora, 2002) .

In this study assessed glucose to be the surrogate of IR and DM as one of CVD risk factors. DM describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus in clued long-term damage, dysfunction and failure of various organs (WHO, 1999). People with DM is increasing around the world because of population growth, aging, urbanization, physical inactivity (Sarah Wild, 2004). In 2013, International Diabetes Federation (IDF) estimated the number of people with DM were around 382 million people (8.3 % of adult) and is set to rise to 592 (increase by 55 %) within the year 2035. Furthermore, 80 % of all DM live in low and middle income countries, where the epidemic is frightened high rate (IDF., 2013) as show in figure 2, 3

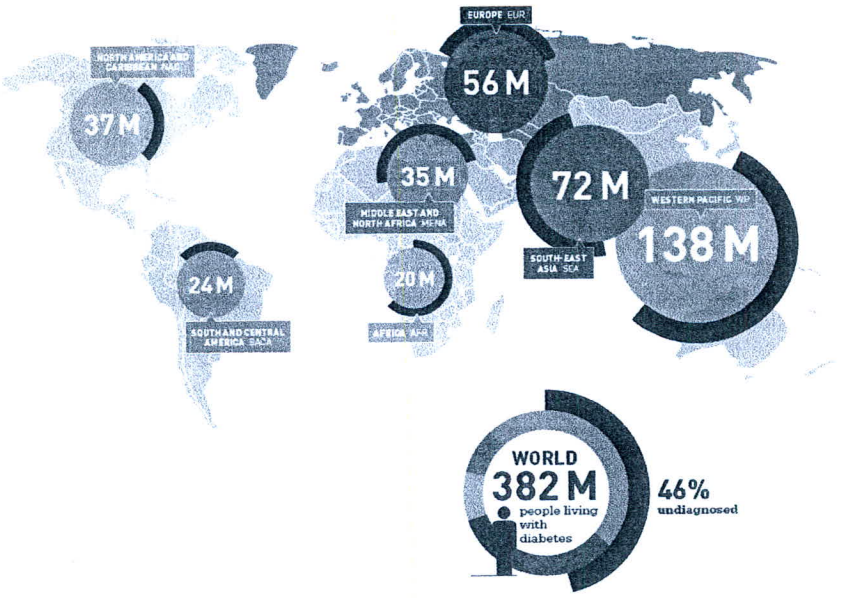

Figure 2 Number of people with diabetes by IDF Region, 2013

Source: IDF., 2013

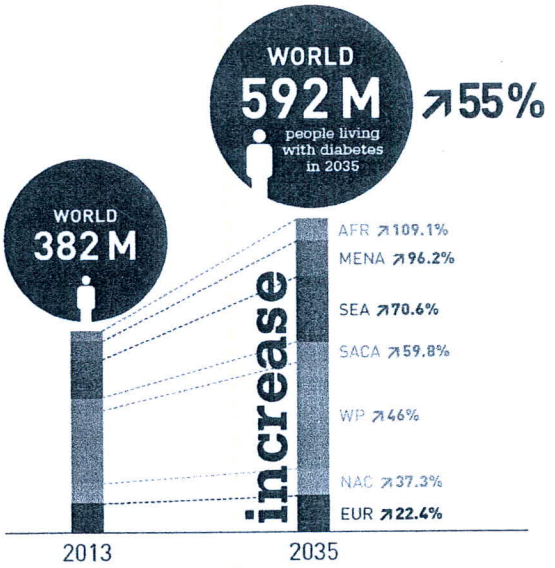

Figure 3 Increasing number of people with diabetes by IDF Region, 2013 to 2035

Source: IDF., 2013

Some evidence show that people with DM that usually have high blood pressure, high cholesterol, high blood glucose have more than two-fold risk of mortal and immortal CVD greater than non-DM (Stamler, 1993; Haffner, 1998; Asia Pacific Cohort Studies Collaboration, 2003). Moreover, the major cause of dead and disability in people with DM is CVD (Thomas, 2003; Booth, 2006; Kengne, 2007; IDF., 2013).

In summary, the prevalence of DM and IR dramatically increase around the world. It is associated with an increase risk of CVDs death and increase rate of CVDs, including CAD and congestive heart failure (CHF). Prevention and management of DM are urgent and necessary to achieve global health and reduce the burden of CVDs (M. K. Poulsen, 2010; Valentín Fuster, 2010).

Dyslipidemia

Dyslipdemia is the abnormal concentration of lipid in blood stream. The most common type are high levels of total cholesterol (TC), high levels of triglycerides (TG), high levels of low-density lipoprotein cholesterol (LDL-C), low levels of high-density lipoprotein cholesterol (HDL-C) and is the risk factor for development atherosclerosis in coronary artery disease (CAD) (Thom, T., 2006; Camila, M. Manrique, 2009; Hossein Fakhrzadeh, 2012)

NCEP ATP III specifies the interpretation of lipid levels as high risk for CVDs, if TC is more than 239 mg/dL, TG is 200 – 499 mg/dL, HDL-C is less than 40 mg/dL or LDL-C is 160 – 189 mg/dL as show in table 1

Table 1 NCEP ATP III risk interpretation for lipid levels

Test	Optimal	Borderline High risk	High risk	Very High risk
TC	< 200	200 - 239	≥ 240	
TG	< 150	150 - 199	200 - 499	≥ 500
HDL-C	≥ 60	40 - 59	< 40	
LDL-C	< 100	130 - 159	160 - 189	≥ 190

Source: NCEP., 2001; American Diabetes Association, 2006; Mosca, L., 2007

John B. Dixon and Paul E. O' Brien stated that the dyslipidemia of obesity is characterized by elevated fasting triglycerides (TG) and decreased high density lipoprotein cholesterol (HDL-C) with normal total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) concentrations. Although they found that TC and LDL-C concentrations were usually normal in obese subjects (John B. Dixon 2002, September) . LDL-C can transport cholesterol to the arteries and can be retained there by arterial proteoglycans starting the formation of plaques, the mechanism started when LDL-C infiltrated artery wall into the intima and were oxidized, induced endothelium cells releasing chemotactic proteins which attract macrophage to ingest oxidized LDL-C and became foam cells, when foam cells died and released lipid content or lipid core. Smooth muscle cell (SMC) migrated into intima and excreted collagen and elastin to form fibrous cap or plaque. Accumulation of LDL-C under fibrous cap narrowed the artery lumen. When plaque ruptures, lipid cores were release into blood stream, form the mass with platelets and other coagulation components, called blood clot or thrombus. Thrombus formation in coronary artery lumen can cause myocardial infarction. Increased levels of LDL-C are associated with atherosclerosis, and represent a strong CVDs risk factor thus heart attack, stroke, and peripheral vascular disease (Judith A. Berliner, n.d.; Wikipedia, 2008; Göran K. Hansson, 2005); because of this reason, cholesterol inside LDL lipoproteins is often called "bad" cholesterol. On the contrary, HDL-C which removes the cholesterol or harmful fat from cells and vascular wall atheroma, then transport it back to the liver for reuse or excretion, is usually known as "good" cholesterol (Toth, 2005). High blood HDL-C levels are associated with decrease CVDs evidence, Several authors call it is the protective or negative or subtract risk factor if HDL-C $\geq$ 60 mg/dL (NCEP., 2004; Paul S. Jellinger, 2012) that improve cardiovascular health (Sirtori, 2006). Triglyceride (TG) is one type of ester; consist of one glycerol and three free fatty acids. Hypertriglyceridemia; High TG level in plasma may be an independent risk for CVDs (Austin, M.A., 1998; Sarwar, N., 2007) especially in women. AACE recommends to measure TG level as a component of lipid screening because even fasting TG $\geq$ 150 mg/dL may recognize to be a risk factor for insulin resistance. If TG level is 200 mg/dL or greater than, it indicates a strong risk factor for CVDs (Paul, S. Jellinger, 2012).

Hypertension

Hypertension characterized by Systolic blood pressure ≥ 140 mmHg and Diastolic blood pressure ≥ 90 mmHg (Brown, M.A., 2001). Kagan, et al., between 1949 and 1952, examined and followed 4,469 participants by measured BP from both arms in the seated position, weight, height, electrocardiogram, chest X-ray, Urinalysis, they examined the age-BP relationship among normal persons which excluded any known evidence of CVD and found the upward trend of BP, both mean SBP and DBP rose steadily with age in women and men, the highest age group was 50 to 54 years. They found the "white coat" BP effect; a decreasing trend of BP from the first exam which the first SBP and DBP decreased from 136.5 and 85.4 to 131.4 and 81.6 respectively in the third exam. They described this effect as the familiarity and stress decreasing with the examination procedures. They looked forward to the close relation between BP and cardiac enlargement. However, cardiac enlargement was found in all BP levels. They found that the left ventricular hypertrophy (LVH) which assessed by electrocardiograph (ECG) was a better definite indicator of hypertension than cardiac enlargement by X-ray, and found the highest coronary heart disease (CHD) event in those with LVH by ECG (Kagan A., 1959). In 1971, Kannel, et al. concluded that SBP was a better predictor of CHD in middle-aged and older persons than DBP (Stanley, S. Franklin, 2013). A recent review in 2001, found that 75 % of hypertensive disease, 54 % of stroke, 47 % of ischemic heart disease (IHD), and 25 % of other CVDs were cause of hypertension. These cause approximately 13 % of the total annual global deaths or 7.6 million deaths per year and 80 % of hypertension occurred in LMIC (Lawes Carlene M.M., 2008). Approximately, the prevalence rate of hypertension in China is 177 million people or 17.7 % and 20 % of deaths are attributable to hypertension (Yang, 2008; He, 2009). In Africa, the Demographic and Health Survey report that 12.5 % and 17.9 % of men and women respectively were hypertension (South African Department of Health, 2007), hypertensive heart disease and stroke is a major cause of CVDs burden in the region, especially black Africans (Muna, 1993; Mbewu, 2006; Mayosi, 2009)

Obesity

Obesity is an excess of total body fat that cause of abnormal body weight. Obesity is classified by location of fat into two principal types:

1. General or subcutaneous or peripheral obesity is characterized by superficial fat depots under the skin which can occur anywhere including abdomen. General obesity is defined by Body Mass Index (BMI) which developed by the Belgian polymath Adolphe Quetelet between 1830 and 1850 (Eknoyan, 2008). It is the ratio of weight to height and calculated by using this formula below:

$$BMI = \text{weight (kg)} / \text{height (m)}^2$$

The BMI is commonly used to classify health risk into 6 levels for Caucasian populations as show in table 2

Table 2 Health risk classification according to BMI

Classification	BMI (kg/m^2)	Risk of developing health problems
Underweight	15 – 18.4	Increased
Normal	18.5 – 24.9	Least
Overweight	25 – 29.9	Increased
Obese class I	30 – 34.9	High
Obese class II	35.0 – 39.9	Very high
Obese class III	≥ 40	Extremely high

Source: WHO/IOTF/IASO., 2000

In Asians, the cut-offs for overweight and obesity are shown in table 3. All cutoff point for Health risk classification in Asians are lower than in the Belgian polymath Adolphe Quetelet and focus on risk of Co-morbidities risk

Table 3 Proposed classification of weight by BMI in adult Asians

Classification	BMI (kg/m^2)	Risk of co-morbidities
Underweight	<18.5	Low (but increased risk of other clinical problems)
Normal range	18.5 – 22.9	Average
Overweight	≥ 23	
At risk	23 – 24.9	Increased
Obese class I	25 – 29.9	Moderate
Obese class II	≥ 30	Severe

Source: WHO/IOTF/IASO., 2000

2. Central obesity or abdominal obesity is characterized by a large abdomen and is the common male pattern of obesity. Central obesity is defined by waist circumference (WC) which measuring the length surround the abdomen. It is simple, inexpensive and easy measurement, requires only measuring tape, not have to calculate, but highly correlate with abdominal fat. Many organizations launch the definition of central obesity by using WC as show in table 4. The different cutoff point between organizations, make the question what is an appropriate cutoff point to use. International Diabetes Federation defines central obesity and classified by country, ethnic group, and sex as show in table 5.

Table 4 The criteria for central obesity by using waist circumference

Sex	Waist circumference (cm)				
	EGIR *	ATP III **	Modified ATP III ***	AACE ****	IDF *****
Men	≥ 94	≥ 102	≥ 90	≥ 102	Ethnic specific in table 5
Women	≥ 80	≥ 88	≥ 80	≥ 97	

EGIR; European Group for the Study of Insulin Resistance

Source: * Balkau B., 1999
** Scott M. Grundy, 2005
*** Ethiraj Dhanaraj May, 2009
**** AACE/ACE., 1998
***** IDF., 2005

Table 5 International Diabetes Federation criteria for ethnic or country-specific values for central obesity by using waist circumference

Country/Ethnic group	Sex	Waist circumference (cm)
Europid	Men	≥ 94
	Women	≥ 80
South Asian	Men	≥ 90
	Women	≥ 80
Chinese	Men	≥ 90
	Women	≥ 80
Japanese	Men	≥ 85
	Women	≥ 90

Source: IDF., 2005

An increase of abdominal fat could caused a harmful health (Vague, J., 1947). Lawrence de Koning, et.al. demonstrated that men and women who had a 1 cm increase in WC is associated with 2 % increases the risk of future CVD after adjusting for age and cohort characteristics (Lawrence de Koning, 2007). Visceral fat is the surrogate of central obesity and the harmful of fat that stored in the abdomen around internal organs such as liver, muscle, heart tissues and beta cells of the pancreas so can call this obesity as "visceral obesity". An excess of visceral fat accumulation cause abdomen stick out like an apple shape, resulting in an increase WC. This type of fat can lead adverse medical disorders such as inflammation, atherosclerosis, hypertension, and diabetes. There are the robust evidences of the association between central obesity and CVDs (Yusuf, S., 2004; Razay George, 2006). Moreover, Zhao et al. studied in nationally representative sample from the National Health and Nutrition Examination Survey (NHANES) 2005-2006, stated that WC or central obesity was correlated with an increased possibility of having high or moderate to severe depressive symptoms among overweight and obese adults (Guixiang Zhao, 2011)

WC measurement which is the simple and easy procedure seem to be the effective marker of intra-abdominal adiposity or visceral fat (figure 4) (Pouliot, M.C., 1994) and closely correlated with total amount of abdominal visceral fat (Li Xu, 2012), which associated with an increased risk of obesity-related cardiovascular disease (Samuel Klein, 2007).

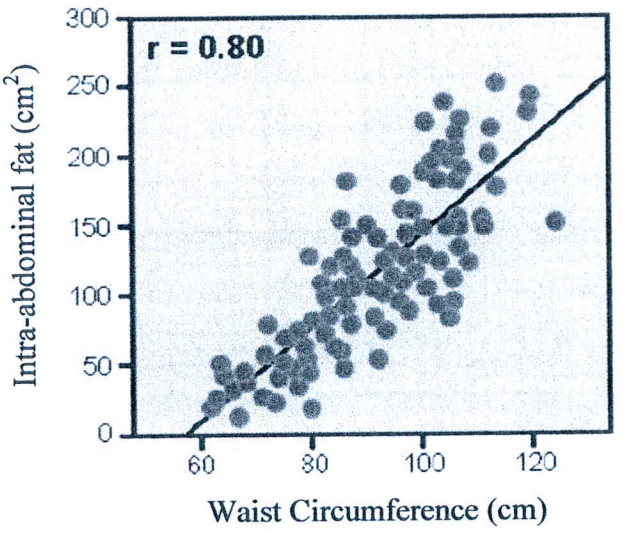

Figure 4 Relationship between waist circumference and intra-abdominal adipose tissue accumulation

Source: Pouliot M.C., 1994

Inflammation

Inflammation is central to cardiovascular disease (Libby, 2006). Current studies have clearly found that obesity also gives rise to a heightened state of inflammation. Obesity showed a positive correlation between adipose mass and expression of the proinflammatory gene tumor necrosis factor-α (TNFα) (Giacomo Ruotolo, 2003). Besides TNFα, adipose tissue produces other adipokines with well-described effects on metabolism and inflammation such as resistin, adiponectin, leptin, and monocyte chemoattractant protein-1 (MCP-1) (Yi-Hao Yu, 2005). The link between obesity and inflammation has been further illustrated by the increased plasma levels of several proinflammatory markers including cytokines and acute phase protein like C-reactive protein (CRP) in obese individuals (Trayhurn P., 2005).

CRP is an acute-phase protein found in the blood, the levels of which rise in response to inflammation. Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex (Darren Thompson, 1999) . It is a member of the pentraxin family of proteins (Pepys, M.B., 2003) which comprise of 5 polypeptide subunits. Each of them is 23 k-Da and have 2 binding sites of calcium and one binding site of phosphocholine molecule which make CRP able to recognize and bind to variety of biologic substrates (Pepys, M., 1981; Kushner, I., 1990; Gabay, C., 1999; DuClos, T., 2000) as show in figure 5.

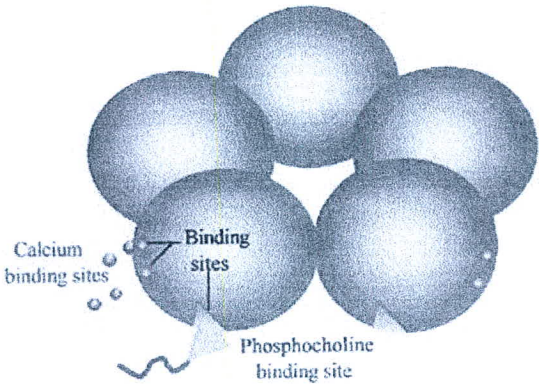

Figure 5 Pentameter structure of CRP

Source: Joan M. Hengst, 2003

CRP is commonly called high sensitivity C-reactive protein (hs-CRP) because of increasing sensitivity of methodology used in clinical laboratory in CRP measurement. hs-CRP has emerged as a strong, robust and independent risk factor for CVDs that appears to have significant clinical utility. It is a circulation acute phase reactant named initially for its capacity to bind to the C-polysaccharide of *Streptococcus pneumoniae*, and is synthesized primarily by the liver in response to IL-6 and IL-1β . As a risk assessment tool, it has several good points. It is very stable, with very little difference in values between fresh or frozen plasma and has a long half-life of up to 20 hours (Paul, M. Ridker, 2001) . It normally circulates at very low levels, but acute inflammatory processes induce marked hepatic synthesis of hs-CRP,

which can induce a 100-fold serum increase (Du Clos, T. W., 2000). The person has hs-CRP concentration higher than 3 mg/L indicates high risk of CVDs. The Center of Disease Control (CDC)/American Heart Association (AHA) classify risk of cardiovascular disease by using hs-CRP concentration and the details are in table 6 (Gary, L. Myers, 2004).

Table 6 Cardiovascular disease risk classification using hs-CRP concentration by the CDC/ AHA

Classification of CVD risk	Value (mg/L)
Low risk	< 1.00
Average risk	1.00 – 3.00
High risk	> 3.00

Source: Thomas A. Pearson, 2003

If the hs-CRP concentration is more than 10 mg/L after repeat measurement represent infection or inflammation in that person. Charuruks N. (Navapun Charuruks, 2005) examined the reference range of hs-CRP in healthy participants from 4 center regions of Thailand, showed the reference range for 279 healthy women was 1.90 mg/L (0.20 – 8.10 mg/L) which was higher than the 357 healthy Asian women (1.12 mg/L). In the United States study (Albert, M.A., 2004), mean and mode of hs-CRP was 1.80 mg/L, the mode was 0.8 mg/L respectively moreover can use this result as the reference range for hs-CRP in healthy Thai adults. Recent study suggests that CRP may direct associate with pathogenic role in atherosclerotic lesion formation. When CRP is attached to opsonin, a substance that binds to antigens and induce white blood cells come to remove CRP-opsonin complex, and this complex is bound to LDL-C, uptake of the entire aggregate by activated macrophages appears to enhance foam cell formation (Zwaka, T.P., 2001) in atherosclerosis.

Atherosclerosis

Atherosclerosis means the hardness of the arteries. It comes from the Greek words a*thero* (meaning gruel or paste) and *sclerosis* (hardness). It is a complex process of a slowly accumulation of fatty substances e.g. LDL-C and triglyceride, waste products, cellular products, calcium and other substances in the intima; an inner wall of an artery. This buildup is called atherosclerotic plaque. It begins in childhood and can progresses rapidly by middle age. The pathobiology of atherosclerotic lesions is very complicated. The atherosclerotic plaques which compost of smooth muscle cells and extracellular matrix usually be stable and asymptomatic, while, the atherosclerotic plaques which compost of foam cells (fatty material) and macrophage and extracellular matrix, seem to be weakly and easy to rupture (Finn, A.V., 2010) as show in figure 6. When the unstable plaques are ruptured, it exposes thrombogenic material (e.g. collagen) and induces thrombus formation in vascular lumen. It can be large enough to block blood vessels or detach and circulates in blood stream, causes stroke if it travels to obstruct in cerebral artery (Sims, N.R., 2009), blocks coronary artery cause myocardial infarction (Thygesen, K., 2007) and blocks peripheral vascular, then cause PVD. These are the interesting cardiovascular disorder occurrence. The vascular indexes can be used to assess vascular condition helping CVDs management.

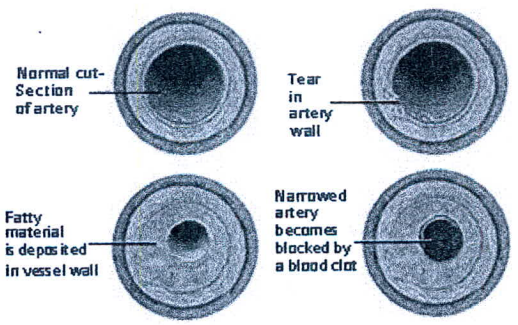

Figure 6 Atherosclerotic plaque formation

Source: Linda, J. Vorvick, 2011

Vascular Index

Ankle-Brachial Index (ABI) (Colin Medical Technology Corporation) is an index for evaluating occlusion at the extremities and brachial-Ankle Pulse Wave Velocity (PWV) is an index for evaluating stiffness. ABI and PWV can be measured by using the non-invasive procedure. ABI compares the systolic ankle blood pressure with the systolic brachial blood pressure at the same site of body part to see how well of blood flow. ABI that is lower than 0.9 show the association with occlusion in peripheral arteries, ABI that is fall down is related with severe occlusion. It has also been shown to be associated with CVDs risk factors (Yuanxi, X.U., 2007) . Previous studies have found that those with lower extremity arterial disease are 1.5 to 2 times more likely to experience a clinical CVDs event (Albert, W. Tsai, 2001). ABI > 1.40 predicts mortality with similar strength as ABI < 0.90 (Helaine, E. Resnick, 2004). The PWV measurement is based on simultaneous measuring the difference sites of blood pressure velocity of the pulse wave to travel a given distance between 2 sites of arterial system. Aortic stiffness increases with age (Avolio, A.P., 1983), hypertension (Nichols, W.W., 1990) and is also enhanced in subjects with diabetes mellitus (Lehmann, ED., 1992), end-stage of renal disease (London, G.M., 1990) and atherosclerosis (Wada, T., 1994). The baPWV value was calculated by using the following equation (Hirofumi Tomiyama, 2003)

$$\text{baPWV} = (La - Lb)/\Delta Tba$$

Note:

La is the length of the path from the suprasternal notch to the ankle

(La = 0.8129 x height of patient in centimeters + 13.328)

Lb is the length of the path from the supraternal notch to the brachium

(Lb = 0.2195 x height of patient in centimeters – 2.0734)

ΔTba is the time between the brachium and ankle

Most commonly, pulse wave velocity is measured between the carotid and femoral peripheral artery sites to provide an aortic stiffness measurement. Tomiyama H. et al. (Hirofumi Tomiyama, 2003) stated that atherogenic metabolic disorder that is

increases by aging weakly influence baPWV but significant. They evaluated the influence of age on baPWV by extracted a population of apparently healthy subjects who had no atherogenic and metabolic disorder. They consisted of more than 7000 healthy adult subjects and allowed a rather fine chronological classification at 5-year age intervals, spanning age 25 to over 70 years. The chronological evaluation of baPWV in male and female clearly demonstrated that age influences baPWV differently in both genders and the augmentation of arterial stiffness with aging is more prominent in female. PWV is a surrogate measurement of vascular damage, and a useful method to evaluate treatment benefits (Ali R. Khoshdel, 2007)

There is little information that exist the associations among hs-CRP, WC, BMI, and vascular atherosclerosis in healthy Thai adults. There are several changes in high technologies, convenience, and food in rural Thailand that impact people lifestyles include the less knowledge about risk factors in CVDs in rural Thai people. This study aims to assess obesity, central obesity, and peripheral vascular atherosclerosis and to. determine the relationship of hs-CRP, BMI, WC, peripheral vascular atherosclerosis, and other blood biochemical markers in healthy Thai adults in rural Thailand.

Previous studies of CVDs risk factors in Thais

2005- Navapun Charuruks, et al. (Navapun Charuruks, 2005) determined a reference value of hs-CRP in a healthy Thai population from 4 centers of Thailand (center; Chulalonkorn University, north; Chiang Mai University, south; Maharaj Nakornsithammarat Hospital, northeast; Maharaj Nokornrajsima Hospital) and examined the effect of time gender and age. They recommended the reference value for hs-CRP in the healthy Thai adults as 1.8 mg/L with a range of 0.2 – 7.9 mg/L, and concluded that hs-CRP concentration were no significant differences among region, time, gender and age. Therefore, the hs-CRP concentration could be determined at any time without concern.

2006-Wanvisa Boonlert, et al. (Wanvisa Boonlert, 2006) showed the data from the mobile medical unit (MMU) for people health and occupation development at Naresuan University that serve 10 provinces at lower Northern Thailand from January 2004 to December 2005, they analyzed the test glucose, TC, and TG at or near the site

of patient care and found that 10.7 % of 2,141 participants had glucose higher than 110 mg/dL, 5.0 % higher than 125 mg/dL, 17.8 % had TC higher than 250 mg/dL and 32.0 % had TG higher than 150 mg/dL and also help medical staff in local areas to educate people in health care prevention for DM and CVDs.

2007-Kanokwan Srisupornkornkool, et al. (Kanokwan Srisupronkornkool, 2007) assessed metabolic syndrome (MetS) from central obesity and blood pressure that either be the risks of CVDs among Naresuan University personnel base on NCEP-ATP III criteria and found that 17 % central obesity, 8 % of high blood pressure (blood pressure high than 130/85 mmHg). However, they suggested to further assessing MetS from lipid and glucose level to confirm the results of this study.

2008-Kanokwan Srisupornkornkool, et al. (Kanokwan Srisupornkornkool, 2008) assessed occult prevalence of MetS in 288 healthy staff of Naresuan University and found that the prevalence of MetS was 6.0 % overall, 3.1 % of women, and 2.9 % of men, more than 70 % of the subjects had normal WC, BP, glucose, TG, and HDL-C meeting NCEP-ATP criteria. The prevalence of central obesity, high blood pressure, hyperglycemia, hypercholesterolemia, hypertriglyceridemia, and low HDL-C were 51.1 %, 20.3 %, 5.7 %, 45.3 %, and 17.2 %, respectively.

2009-W. Aekplakorn1 and L. Mo-suwan (W. Aekplakorn, 2009) documented the reviewed article about prevalence of obesity in Thailand. They stated that the increasing rate of obesity in Thailand was terrifying, as in other countries with fast growing economy. According to the National Health Examination Surveys I, II, III which were done in 1994, 1997 and 2004. BMI in Thai adults' age $\geq$ 18 years increased from 22.0 kg/m^2 to 22.7 kg/m^2 and 23.2 kg/m^2 from 1994, 1997 and 2004 respectively. These mean that the distribution of weight and BMI in Thai adults trend to raise up. If use BMI cutoff point at $\geq$ 25 kg/m^2 (WHO/IOTF/IASO., 2000), the prevalence of obesity were 18.2 % , 24.0 %, 28.1 % in 1991, 19997 and 2004 respectively. Meanwhile, using BMI cutoff point at $\geq$ 30 kg/m^2 (WHO., 2000), the prevalence of obesity were 3.5 % , 5.8 %, 6.9 % in 1991, 1997 and 2004 respectively. When defined central obesity by using WC, if WC $\geq$ 80 cm in women and $\geq$ 90 cm in men. The prevalence of central obesity in women were double raising from 14.3 % in 1997 to 36.3 % in 2004, while central obesity in men were 14.3 % and 15.7 % in 1997 and 2004 (Porapakkham, Y., 2006; Aekplakorn, W., 2007).

2010-Andrew J. Hillman, Vitool Lohsoonthorn, Orrawadee Hanvivatvong, Wiroj Jiamjarasrangsi, Somrat Lertmaharit, Michelle A.Williams (Andrew J. Hillman, 2010) investigated the association of hs-CRP levels and MetS among Thai adults. Their participants were 451 men and 940 women in annual health examination at King Chulalongkorn Memorial Hospital between December 2006 and February 2007. A modified version of NCEP ATP III criteria was used to define MetS. They found that the median of hs-CRP in men with MetS was significantly higher than those without MetS (1.50 mg/L vs 0.80 mg/L, $p < 0.001$), and the median of hs-CRP in women with MetS was higher than those without MetS (3.10 mg/L vs 0.70 mg/L, $p < 0.001$). Among men without MetS, the hs-CRP levels were positively associated with adiposity (WC, $r = 0.415$; BMI, $r = 0.308$; Body fat percentage, $r = 0.422$), whereas no similar association among men with MetS. Among women with and without MetS, measures of adiposity were positively and significantly correlated with hs-CRP levels. Among women without MetS, SBP ($r = 0.227$), DBP ($r = 0.197$), Age ($r = 0.188$), TG ($r = 0.370$) and uric acid ($r = 0.299$) were positively correlated with hs-CRP levels.

After adjusting for confounding (e.g. age, educational attainment, smoking), men with hs-CRP levels > 3.0 mg/L had a 5.45 fold increased risk of MetS as compared with men who had hs-CRP levels < 1.0 mg/L.