THE ROLE OF GIGULOCHIPS-SAF$_3$ARIL IN THE PREVENTION OF CARDIOVASCULAR DISEASES

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ABSTRACT'S FORM

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ABSTRACT

The quality of life depends on the quality of the blood vessels. Many life styles, dietary regiments and other factors may affect the quality of the blood vessel. However, many preventive medical efforts can be carried out to improve it.

Based on **House to House Survey** performed in **1972, 1986** and **1992** in Indonesia revealed that cardiovascular diseases can be assumed as **11th, 3rd** and **2nd killer,** respectively.

GIGULOCHIPS-SAF$_3$ARIL (Syndrome-20) has been firstly coined by Diabetes and Nutrition Surabaya (**1992, 1993, 1994**), and it comprises 20 determinant factors for the quality of the blood vessel **GIGULOCHIPS** Syndrome-20 stands for : **Genetic, Insulin Resistance, Glucose Intolerance, Uric Acid, Lipid-Triad, Obesity, Cigarette, Hypertension, Inactivity, Platelet Aggregation, Stress, Sex, Age Fibrinogen, Factor VIIIc** and **Left Ventricle Hypertrophy.**

Hence, the quality of life will be physically determined by the quality of the blood vessel. Based on the above facts, the prevention of cardiovascular diseases can be obtained by improving the positive scores of **GIGULOCHIPS-SAF$_3$ARIL**. The preliminary data of such scoring on Diabetic Patients in Surabaya resulted that **Lipid-Triad, Obesity, Uric Acid, Platelet Aggregation, Hypertension, Insulin Resistance, Cigarette and Genetic** can be concluded as the dominant factors.

Conclusion : Health Education (dietary regiments, healthy life style, regular exercise, cessation of smoking and stop alcohol, etc.), either on Diabetic Patients or Normals to improve the score of **GIGULOCHIPS-SAF$_3$ARIL** can be assured as an obligatory in the prevention of cardiovascular diseases. **Hence, the prevalence of cardiovascular diseases can be expected at least as lower as reported in 1972.**

INTRODUCTION

According to **WHO's definition**, health is state of physical, mental, and social wellbeing. Physically the quality of life is determined by the quality of the blood vessels, and the latter depends on many factors (**GIGULOCHIPS-SAF$_3$ARIL**). Modern life styles, dietary regiments and other factors may affect the quality of blood vessels. However, we believe that many preventive medical efforts can be carried out to improve it.

Based on **house to house survey** performed in **1972, 1986,** and **1992** in Indonesia revealed that cardiovascular diseases (CVD) can be assumed as **11th, 3rd,** and **2nd killer**, respectively.

Cardiovascular disease is associated with the quality of the blood vessel, and according to **the Diabetic and Nutrition Center Surabaya (Tjokroprawiro 1994)** : the quality of the blood vessels is determined by a numerous factors which can be abbreviated as **GIGULOCHIPS-SAF$_3$ARIL (Syndrome-20).** This syndrome was firstly coined in Surabaya by **Tjokroprawiro in 1992, 1993, and 1994. GIGULOCHIPS-SAF$_3$ARIL** stands for : genetic, insulin resistance, glucose intolerance, uric acid, lipid triad, obesity, cigarette, hypertension, inactivity, platelet aggregation, stress, sex, age, fibrinogen, factor VIIIc and VII, and left ventricle hypertrophy.

Syndrome-20 can be implemented either on the diabetic patients or on the normals. If such an implementation is used for the diabetic patients, one factor can be automatically scored: **negative**. Therefore, it is easier to score several factors of Syndrome-20 in diabetic patients.

Recent developments in economic and social aspects make several changes in the behaviour and life style of people, especially in urban. These changes requently cause an atherogenic effect to the blood vessels, i.e. high cholesterol foods, alcohol, cigarette smoking, stressful life, and many others.

We do hope that through **Health Education** about the importance of several factors in **GIGULOCHIPS-SAF$_3$ARIL**, the risk factors of CVD can be lowered, and hence we will have a better quality of life as we expected. Subsequently, the prevalence of CVD as a killer in Indonesia can be suppressed as low as reported in 1972.

WHAT IS GIGULOCHIPS-SAF$_3$ARIL

GIGULOCHIPS-SAF$_3$ARIL which was firstly coined by **Tjokroprawiro (1992, 1993, 1994)** comprises 20 determinant factors for the quality of blood vessel. It consists of 20 factors: Genetic, Insulin Resistance, Glucose, Uric Acid, Lipid, Cigarette, Hypertension, Inactivity, Platelet Hyperagregation, Stress, Sex, Age, Fibrinogen, Factor VIIIc - Factor VII, Free radicals, Alcohol abuse, Race, Inhibitors, and Left ventricle hypertrophy.

Eight factors of GIGULOCHIPS-SAF$_3$ARIL have been studied retrospectively in Surabaya by **Adi et al (1994).** Such a study revealed that there are eight dominant factors, f.e. Genetic, Glucose, Uric Acid, Lipid, Obesity, Cigarette, Hypertension, and Platelet Hyperagregation.

CLINICAL ASPECTS OF GIGULOCHIPS-SAF3ARIL

As mentioned above, **GIGULOCHIPS- SAF$_3$ARIL** respectively stands for :

1. Genetic (G)
2. Insulin Resistance (I)
3. Glucose (G)
4. Uric Acid (U)
5. Lipids (L)
6. Obesity (O)
7. Cigarette (C)
8. Hypertension (H)
9. Inactivity (I)
10. Platelet Hyperaggregation(P)
11. Stress (S)
12. Sex (S)
13. Age (A)
14. Fibrinogen (F)
15. Factor VIIIc, Factor VII (F)
16. Free Radicals (F)
17. Alcohol Abuse (A)
18. Race (R)
19. Inhibitors (I)
20. LVH (L)

1. Genetic

This factor can be attributed to the inheritance of risk factors such as Hypertension, Diabetes Melitus and Hyperlipidemia. Family history is one the of important factor to be considered in helping to avoid missing treatable risk factors and to do a prevention. This factor is uncorrectable.

2. Insulin Resistance

According to Continuing Medical Education (CME) by Stout (Washington University St. Louis 1993), the atherogenic effects of insulin are stimulating synthesis of lipid plaque and inhibiting its regresion, synthesis of cholesterol, increasing activity of LDL receptor.

3. Glucose

Studies in a variety of population have shown an association of hyperglicemia with clinically evidence of atherosclerotic disease suggesting a role of hyperglicemia in atherogenesis.

Hyperglicemia and atherosclerosis are metabolically associated since there is an increased prevalence of large vessel disease in known diabetics. Conversely, an increase prevalence of hyperglicemia in association with atherosclerotic disease.

4. Uric Acid

It was Gertler et.al (1951) who firstly reported that Hyperuricemia is one of risk factors for Coronary Heart Disease. Blood uric acid level higher than 6 mg/dl may lead to platelet hyperaggregation (Tjokroprawiro 1992).

5. Lipid Triad

Total Cholesterol or LDL, HDL-Cholesterol, and Triglyceride can be defined as Lipid Triad, in which the latter determines the quality of blood vessels. High cholesterol and triglyceride are important risk factors for atherosclerosis, conversely HDL cholesterol showed a strong inverse relation with atherosclerosis.

6. Obesity

Obesity is associated with Hypertriglyceridemia, hypercholesterolemia, hyperglycemia, hypertension and other metabolic cardiovascular syndromes.

7. Cigarette

The cigarette contains more 4000 components and the interactive effects of these components have been indentified as leading to the development of atherosclerosis.

8. Hipertension

High blood pressure is an important risk factor for atherosclerosis, mainly coronary heart disease and cerebrovascular disease. The reduction of diastolic levels reduces the incidence of strokes and coronary heart disease.

9. Inactivity

A moderate amount of regular exercise increases the HDL-cholesterol level and insulin sensitivity.

10. Platelet Hyperaggregatian

Platelet and endothelial cells play an important role in atherogenesis. Platelet aggregation is a preliminary process of thrombus formation and atherosclerosis.

11. Stress

Stress may induce hypothalamus and hypophise to increase the secretion of contra-insuline hormones which can accelerate the process of atherosclerosis.

12. Sex

At all ages but especially in young persons, the risk of coronary heart disease is higher in males than in females. This phenomenon may associated with the level of estrogen in the plasma.

13. Age

The cardiovascular diseases are prevalent for the people between 40-60, and the age over 40 can be assumed as one of the risk factors .

14. Fibrinogen

Fibrinogen play a major role in the formation of atherosclerosis plaque. Fibrinogen increases the blood viscosity and induces erithrocyte aggregation and also leucocyte adhesion.

15. Factor VIIIC and Factor VII

Factor VIIIc accelerate the aggregation of thrombocyte and Factor VII induce the synthesis of factor Xa which can accelerate the formation of Thrombin.

16. Free Radicals

Free radicals may cause endothelial damage and dysfunction. Free radical will oxidize LDL, and this oxidized LDL is more atherogenic and toxic to the endothelium.

17. Alcohol Abuse

This factor is associated with the increasing of triglyceride which can induce the thrombocyte aggregation, decrease the HDL-cholesterol level and cause endothelial dysfunction (Tjokroprawiro 1993).

18. Race

Race is one of the uncorrectable factor.The prevalence and mortality may vary among ethnic group.

19. Inhibitor

The inhibitors comprise Nitric Oxide, EDRF, Prostacyclin, Heparan Sulphate, Proteoglycan, Prostanoid, TGF-ß and t-PA. These factors may conteract vasoconstrictor agents such as Angiotensin, Bradykinin and Interleukin.

20. Left Ventricle Hypertrophy

Left ventricle hypertrophy will increase the risk factors of coronary heart disease. It can be reduced by ACE-Inhibitors, Calcium Channel Blockers, etc.

ILLUSTRATIVE STUDY

A retrospective study was carried out by Adi et al (1994) in 100 NIDDM patients to evaluate the correlation of each GIGULOCHIPS's components

with metabolic cardiovascular syndrome. It showed that Lipid Triad was the most dominant factor in angiopathic group, followed by Obesity, Uric acid, Stress, Platelet hyperaggregation, Hypertension, Insulin resistance, Cigarette, and Genetic, respertively.

This study showed that execellent control of GIGULOCHIPS is an obligatory to reduce the prevalence of CVD.

DISCUSSION

Nowadays there are several kinds of lifestyle and dietary regiments related to the risk factors which are listed in **SYNDROME-20**. Serious attention have to be paid in this condition especially to those who have a predipotition to get a cardiovascular diseases.

There is general agreement from an epidemiologic perspective that dislipidemia, hypertension, cigarette and blood glucose level may be the most potent factors involved in causation of atherosclerosis. People associated with poor glicemic control, dyslipidemia (abnormal lipid triad), hypertension and smoking should be considered to have more risk factors for decreasing the quality of the blood vessels.

But there are still many other factors which also play role in determining a quality of the blood vessels. The risk factors which are associated with habits and life style are :

Blood Glucose

Excellent glycemic control is very important for the diabetic patients. Prolonged hyperglycemia is believed to be the primary metabolic abnormalities responsible for the devolopment of irreversibble vascular damage. In addition it is important to control other risk factors often associated with diabetes such as hyperlipidemia, hypertension, smoking and obesity. So the

diabetic patients have to change their atherogenic life style and control their blood glocose by restriction of glucose intake.

Lipid

A clearly defined eating pattern is necessary precondition for a high population rate for CHD. It is chracterised by consuming high content of cholesterol and saturated fat.Now in Indonesia especially a young generation in big cities tends to adopt the "western style" eating such as preferring a burger or pizza to traditional cuisine such as Javanese food called pecel (contained vegetables and peanuts sauce) contains less saturated fat.

Assmann, director of institute of clinical chemistry and laboratory medicine-central laboratory of the university of Munster recommend a general lipid-lowering diet as follows.

TABLE. The principles of general lipid lowering diet (Assmann 1989)

PRINCIPLE	SOURCES
Decreased total fat intake and reduction of saturated fats	Butter, hand margarine, whole milk, cream, ice cream, hard cheese, cream cheese, visible meat fat, usual cuts of red meat and pork, duck, goose, usual sausage, pastry, usual coffee whiteners, coconut, coconut oil and palm oil-containing foods.
Increased use of high protein, low saturated fat foods.	Fish, chicken, turkey, game, veal
Increased complex carbohydrate and fruit, vegetable and cereal fibre, with some emphasis on legumes	All fresh and frozen vegetables, all fresh fruit, all unrefined cereal foods, lentils, dried beans, rice.
Moderately increased use of polyunsaturated and monounsaturated fatss.	Sunflower oil, corn oil, soybean oil and products unless hardened (hydrogenated), olive oil.
Decreased dietary cholesterol	Brain, sweethreads, kidneys, tongue; eggs (limit to 1-2 yolks per week); liver (limit to twice per month)
Moderately decreased sodium intake	Sult, sodium glutamate, cheese, tinned vegetables and meats, salt preserved foods (ham, bacon, kippers), high-salt mineral waters, many convenience foods

Beside diet, reduction of obesity are effective in reducing elevated levels of triglyceride and, to a lesser extent,cholesterol.

It is suggested by Diabetic and Nutrition Center Surabaya (Tjokroprawiro, 1992) to have Ideal Lipid Triad as listed below :

a. Cholesterol < 200 mg/dl, LDL chol <130 mg/dl

b. Triglyceride <150 mg/dl

c. HDL Cholesterol > 45-55 mg/dl

Regular control of Blood lipid level and dietary management are necessary for reducing CVD incidence.

Smoking

There is an increase in smoking among young males and females a trend can be attributed to the powerful advertising influence of tobacco companies, in indonesia it can be caused by the relationship between friends, a man who never smoked will feel guilty if he refuse to smoke when he is in party for instance. Better educated people are stopping in larger numbers and fewer are beginning to smoke (It is hoped that their example will eventually extend to other educational people). Firm advice from a doctor or other well informed health professional (and maybe we, as medical students) is more effective in inducing people to stop smoking than any other technique available. Cigarette smoking affects to the progression of Atherosclerosis and cardiovascular disease through proliferation of smooth muscle cell, atherosclrosis initiation and progression, increases vasocontriction, increases glucose, serum free fatty and VLDL-choleseterol which progress the atherosclerosis.

Hypertension

Body weight and obesity show consistent association with blood pressure level so weight reduction is a good approach to this problem. Beside wight reduction, a dietary intervention and a physical activity are also important for hypertension patients. Limitation of sodium intake has been shown to reduce blood pressure, many people think that avoiding salt in their food is enough, but sometimes they still consume a food with the hidden salt such as potato chips, pop corn and pizza, so it is also important to avoid the hidden salt.Training activity that suitable for hipertensive patients are walking, hiking, jogging, cycling, swimming and cross country skiing which are included as endurance training and only recommended for mild hipertensive patients (diastolic blood pressure 90 to 105 mmHg and sisitolic blood pressure under 160 mmHg). Patients with moderate and severe hipertension should discontinue their exercise until the blood pressure can either normalised or lowered to the range of mild hipertension. Beside trying to reduce our blood pressure, early detection of hypertension is also important, it can be obtained by control our blood pressure regularly and according to diabetic and nutrition centre maintaining the blood pressure below 140/90 mmHgis good for the blood vessels.

Stress

Now people tends to have an atherogenic lifestyle such as long working hours, and lack of leisure time. A busy persons (such as bussinesmanan, doctor and bankers) in Indonesia go to work in the morning and go home late, after 21:00, many of them still wake up over the night doing the homeworks and have a very limited sleeping hour. This streesfull habits can be also happened in the students which sometimes spending

almost all of their day with studying and other activites. Limited sleeping time and stressful life is not healthy. Diabetic and Nutrition Centre (Tjokroprawiro 1992, 1993, 1994) suggest that we should sleep at least 6 hours a day to make our bodies fit and healthy to start working.

Physical Exercise

People now also to be lack of exercise, one of the reasons is their very limited time. This reasons can be overcame by choosing the exercise which just need a little time such as jogging. According to diabetic and nutrition centre an exercise of 300 kcal per day or 2000 kcal per week will have a good effect to our blood vessels (Tjokroprawiro, 1994). It can be obtained by a local jogging 3x10 minutes a day and 10 minutes jogging will be the same as 100 Kcal.So it is hoped that this advice can overcome this problem.But if we have more time we can also do other exercises. However the amount and type of exercise must be suitable with each individual condition.

Uric Acid

It is suggested to have blood uric acid level below 6 mg/dl.The production of uric acid is determined by endogenic factor and exogenic factor. Low purine dietary regiments is necessary to overcome the exogenic factor. Avoiding a high purine diet such a s alcohol, duck, sardines and nuts is suggested. Some people with endogenic disorder of uric acid production need allupurinol. Regular control of blood uric acid level is necessary in order to prevent from cardiovascular diseases.

Obesity

It is suggested to have BMI below 25, it can be obtained by low calory and low fat diets and physical exercise is obligatory to gain ideal weight.

CONCLUSION

From all the discussion above, it can be concluded that GIGULOCHIPS-SAF$_3$ARIL comprises 20 factors which theoritically and clinically have an important effect to quality of the blood vessels. It is hoped, by abbreviating the factors into GIGULOCHIPS-SAF$_3$ARIL we can remember easily such 20 risk factors for cardiovascular diseases and then make preventive efforts to suppiens the prevalence of CVD.

Firstly, GIGULOCHIPS - SAF$_3$ARIL was studied in diabetic patients. However, it can be used in the normal or healthy people in order to know their quality of blood vessels.

We should aware of some "fashionated" food and modern life styles which frequently have hidden risk factors of cardiovascular diseases. However, we can still consume such "new" foods f.e. burgers and pizza, but do not make it as a habits. Reducing stress and alter an atherogenic life style with a new healthy life style such as having a enough sleeping time, and regular exercise is important to preserve our health.

Early detection of the risk factors can obtained by regular health control, especially for those who have uncorrectable factors such as genetic, age, race and sex. It is hoped that with regular health control, we can manage the risk factors.

Based on the factors in GIGULOCHIPS-SAF$_3$ARIL, healthy life style can be summarized as follows.

1. prevent excess sugar consumption,
2. avoid purin excess (uric acid),
3. low fat diet,
4. avoid obesity,
5. cessation of smoking,
6. prevent excess sodium intake,
7. regular exercise,
8. take 6 hour sleep / day,
9. stop alcohol,
10. regular lipid triad check up (especially > 40 years old).

REFERENCES

1. **Adi S, Tjokroprawiro A, Hendromartono, Sutjahjo A, Tandra H. (1995).** Faktor-faktor Dominan dari Gigulochips (Sindroma-11) dalam Menentukan Kualitas Pembuluh Darah (Penelitian Pendahuluan pada DM TTI). Acta Medica Indonesiana. 27 (suppl.1), 133.

2. **Assmann G (1989).** Lipid Metabolism Disorders and Coronary Heart Disease. MMV Medizin Verlag GmbH, Muenchen, Munich, p. 57,26.

3. **Bierman E.L. (1987).** Atherosclerosis and Other Forms of Arteriosclerosis. In: Wilson JD, Braunwald E, Isselbacher KJ, Petersdorf RG, Martin JB, Fauci AS, Root RK, eds. Harrison's principles of Internal Medicine 1. Singapore, McGraw-Hill Co, p.1014.

4. **Ernst E, W. Koenig, G.D.O Lowe and T.W. Meade (1992).** Fibrinogen : A New Cardiovascular Risk Factor. Blackwell-MZV, Wien.

5. **Gutteridge, John M.C. and Barry Halliwell (1994).** Antioxidants in Nutrtition, Health, and Disease. Oxford University Press, Oxford, p. 124.

6. **McBride P.E. (1992).** The Health Concequences of Smoking: Cardiovascular Diseases. Med. Clinics N. America 76, p. 333.

7. **Thompson GR (1990).** A Handbook of Hyperlipidaemia. Current Science Ltd, London, p. 161.

8. **Tjokroprawiro A. (1992).** GGULIHOCHIPS Factors in Diabetes Mellitus. Pusat Diabetes dan Nutrisi RSUD Dr.Sutomo-FK Unair, Surabaya.

9. **Tjokroprawiro A. (1993).** Diabetes Mellitus : Perkembangan Mutakhir. Pusat Diabetes dan Nutrisi RSUD Dr.Sutomo-FK Unair, Surabaya.

10. **Tjokroprawiro A. (1994).** Faktor-faktor Risiko Penyakit Metabolik-Kardiovaskuler. Pusat Diabetes dan Nutrisi RSUD Dr.Sutomo-FK Unair, Surabaya.

11. **Tjokroprawiro A. (1995).** Aterosklerosis-GIGULOCHIPS-SAF$_3$ARIL. Pusat Diabetes dan Nutrisi RSUD Dr.Sutomo, Fak. Kedokteran Universitas Airlangga, Surabaya.

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