

DESCRIPTION OF BLOOD VISCOSITY FROM DIABETES MELLITUS OUTPATIENTS IN ENDOCRINE CLINIC, AW SJAHRIANIE HOSPITAL, 2009

Caropeboka LC¹, Kalalo LP²

¹OPD, Endocrine Division, Departement of Internal Medicine

²Departement Clinical of Pathology

Faculty of Medicine, Mulawarman University

AW Sjahranie Hospital, Samarinda

ABSTRACT

In Diabetes Mellitus (DM), the presence of chronic uncontrollable hyperglycemia, fat and protein metabolic disorder and damaged blood components generate blood haemoconcentration and hyperviscosity. Blood hyperviscosity in DM patients may influence blood stream, so that it will generate and enhance the plaque formation at venous wall and facilitate the thrombus formation. This, in turn, may lead to serious complications for example stroke, myocard infarction, vascular damages, kidney failure, retinopathy and the peripheral artery disease (PAD) occurrence. This study objective was to find the description of blood viscosity in patients with DM. This was a descriptive observational study by taking samples that meet the sample criteria, involving 105 patients DM outpatients at Endocrine Clinic, Internal Medicine Departement, AW Sjahranie Hospital, Samarinda, from September 1st to October 1st 2009. Data were obtained from the blood viscosity tests and the patients' medical record. In 105 DM patients the blood viscosity values were between 1.8-7.3 CP with average blood viscosity of 3.9 CP (SD 0.87). Blood viscosity frequency increased (>5.1 CP) in 10 patients (9.5%), blood viscosity was normal (3.5-5.1 CP) in 59 patients (56.2%), and decreased (<3.5 CP) in 36 patients (34.3%). Blood viscosity frequency increased in patients with acquired pure DM 3 people (2.9%) and DM with hypertension was found in 7 patients (6.7%). In conclusion, factors affecting blood viscosity are hematocrit, protein plasma, temperature, blood flow, blood vessel size, blood pressure, erythrocyte, and blood components. Viscosity disorder may lead to the several vital organs damage, such as kidney, heart, brain and retina.

Keywords: diabetes mellitus, blood viscosity

Correspondence: Caropeboka LC, Endocrine Division, Departement of Internal Medicine, Faculty of Medicine, Mulawarman University, AW Sjahranie Hospital, Samarinda

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome, metabolic disorder, characterized by hyperglycemia due to impaired insulin secretion, impaired insulin or both. Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction or failure of several organs, especially eyes, kidneys, nerves, heart and blood vessels. World Health Organization (WHO) has formulated earlier that DM is a collection of anatomical and chemical problems result from a number of factors that obtained absolute or relative insulin deficiency and impaired insulin function (Gustaviani 2006). Diabetic Federation estimates that the number of patients with diabetes mellitus aged over 20 will increase from 5.6 million patients in 2001 to 8.2 million by 2020 if no efforts are taken to create healthy lifestyle in the patients (Depkes RI 2005). According to a survey conducted by the World Health Organization WHO, Indonesia ranks 4th largest in the number of DM patients with a prevalence of 8.6% of the total population. From the data of the Ministry of Health

(Depkes RI), 2005, the number of hospitalized diabetic patients and diabetic outpatients ranks first of all endocrine diseases (Depkes RI 2005).

In diabetes mellitus, chronic hyperglycemia and uncontrolled and metabolic disturbance of fat, protein and disruption of blood components and haemorheologi will cause blood hemoconcentration and hyperviscosity. Hyperviscosity state of blood in patients with DM will affect the blood flow so that it will cause and accelerate the occurrence of plaque on blood vessel walls and facilitate the occurrence of thrombus. Due to the above conditions, sustainable and uncontrolled hyperviscous blood in patients with DM will accelerate the occurrence of serious complications disorders such as stroke, myocardial infarction, vascular disorders, impaired kidney and the occurrence of peripheral arterial disease (PAD). Factors influencing blood viscosity are hematocrit, plasma proteins, temperature, level of blood flow, blood vessel size, blood pressure, erythrocyte, and chemical components of blood.

The greater the percentage of cells in the blood, the greater the hematocrit, the more friction that occurs between the various layers of blood, and this friction determines the viscosity. Therefore, blood viscosity increases greatly along with increasing hematocrit (Guyton et al. 1997). Blood viscosity is also influenced by the large molecular weight protein such as fibrinogen and macroglobulin. Interaction of erythrocytes with proteins resulted in the formation of rouleaux which would increase blood viscosity (Supandiman 2003). Temperature also has a significant effect on the viscosity. When the temperature decreases, viscosity increases. Increased blood viscosity has a role in lowering blood flow (Klabunde 2007). The level of blood flow also affects the viscosity. At low level, blood flows into the cell. Adhesive interactions of cells and proteins may increase cell that can cause erythrocytes adhere to each other thereby, increasing blood viscosity (Davis 1999).

Blood flow in small vessels show much less effect than in the viscous great vessels. This effect is called the Fahraeus-Lindqvist effect. Fahraeus-Lindqvist effect is caused by the grouping of red blood cells when passing the vessels. That is, red blood cells, that normally move at random, will be lined up and moving through a vessel as a single group, thus eliminating the viscous blockade that arises internally in the vessel itself (Guyton et al. 1997).

According to the law by Hagenbach, which is corrected by Poiseulle, pressure changes in blood flow are proportional to the length of blood vessels, peripheral resistance and viscosity and inversely proportional to the diameter of blood vessels (Iffa 2007). The ability of erythrocytes to deform also affect blood viscosity. To pass the tiny blood vessels, erythrocytes should be able to change its shape. The inability to change shape of erythrocytes results in static as well as obstruction of blood flow in capillary systems, terminal arterioles and blood vessels so that blood viscosity increased (Roche 2008).

Blood lipids consist mainly of cholesterol, triglycerides, phospholipids and free fatty acids. The nature of lipid is not soluble in water, so without binding to other substances, lipids can not be transported in the blood. Lipid binds to the protein as a lipoprotein in order to be transported in the blood. High lipid levels will increase the viscosity of blood (Arsana 2007). This viscosity disorders over time will cause damage to several vital organs such as kidneys, heart, brain and retina of the eye. This damage will cause renal disorder until renal failure occurs, blockage of the coronary arteries of heart and cause coronary heart disease, brain blood vessel blockage that can lead to stroke and it also

causes blindness if there is blockage of blood vessels in the eye organ, especially the retina (Stephen 2006).

Persons with type 2 diabetes has been shown to have an increased risk of cardiovascular disorders much higher than the normal population. Vascular complications may be microvascular (eye blood vessels, kidneys and nerves) and/or macrovascular (heart blood vessels, brain and peripheral arteries). Micro- and macrovascular abnormalities may increase morbidity and mortality of persons with DM. Various studies have proved that long before the diagnosis of type 2 diabetes mellitus in fact been going on various forms of change that will lead to increased risk. About 80% of persons with diabetes mellitus die of thrombotic complications. Traditional risk factors, such as hypertension, low levels of high density lipoprotein (HDL), are increasing in individuals with type 2 diabetes and IGT (Benjamin et al. 2006).

At the city of Samarinda in particular, there has been no research on blood viscosity profile in Diabetes Mellitus. The authors tried to describe the profile of blood viscosity in patients with Diabetes Mellitus who treated as outpatient in Internal Medicine Department, AW Sjahranie Hospital, from September 1st to October 1st, 2009.

MATERIALS AND METHODS

This research was a descriptive observational studies (non-experimental), with population comprised DM outpatients at AW Sjahranie Samarinda Hospital by taking each DM patient who came to the clinic and met the inclusion and exclusion criteria from September 1st to October 1st 2009 as samples. The inclusion criteria for this study were (1) patients with DM type 1 and 2 according to physician diagnosis based on clinical examination and laboratory results, (2) outpatient visiting Internal Clinic, AW Sjahranie Hospital in the study period, and (3) patients willing to be samples in this study.

The exclusion criteria were patients experiencing hematological disorders such as polycythemia vera and kidney disorders. As the variables in this study were diabetes mellitus, whose levels of blood viscosity measured by viscometer and hypertension with tensimeter. Data were described univariately with variables diabetes mellitus, blood viscosity and hypertension in the samples and presented in the forms of figures.

RESULTS

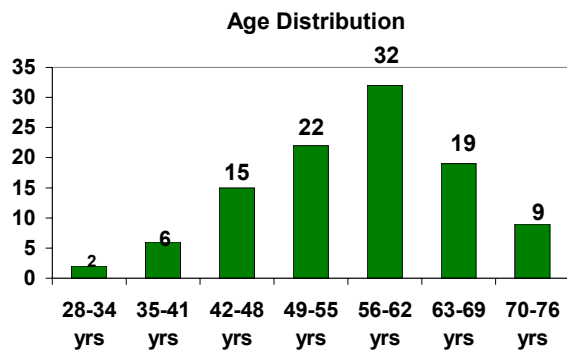


Figure 1. Age distribution of diabetic patients in Endocrine clinic, AW Sjahranie Hospital, from 1 September to 1 October 2009

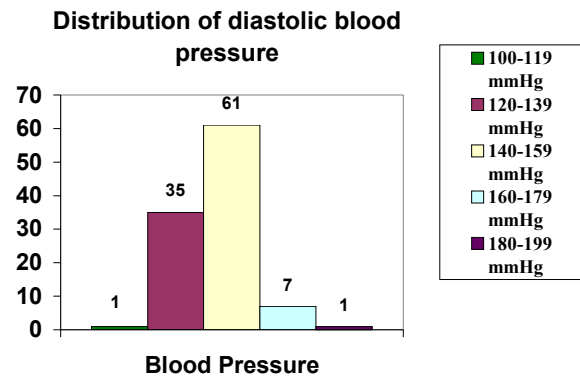


Figure 4. Diastolic blood pressure distribution of patients samples in Endocrine clinic, AW Sjahranie Hospital, from 1 September to 1 October 2009

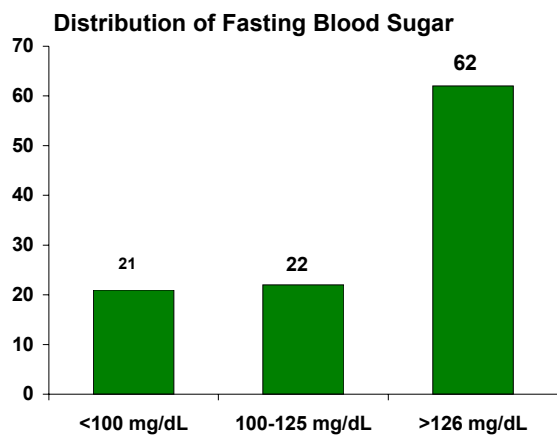


Figure 2. Fasting blood sugar distribution of diabetic patients sample in Endocrine clinic, AW Sjahranie Hospital, from 1 September to 1 October 2009

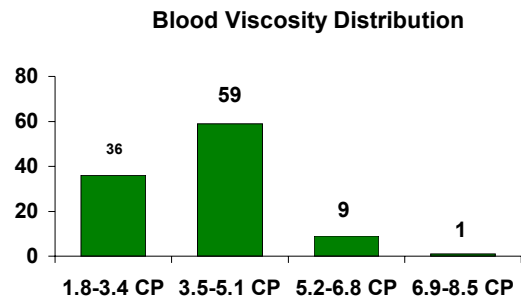


Figure 5. Blood viscosity distribution in patients sample in Endocrine clinic, AW Sjahranie Hospital, from 1 September to 1 October 2009

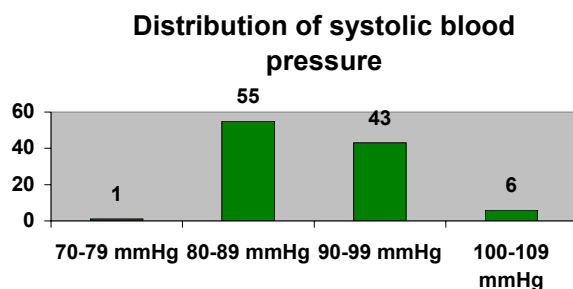


Figure 3. Systolic blood pressure distribution of samples in Endocrine clinic, AW Sjahranie Hospital, from 1 September to 1 October 2009

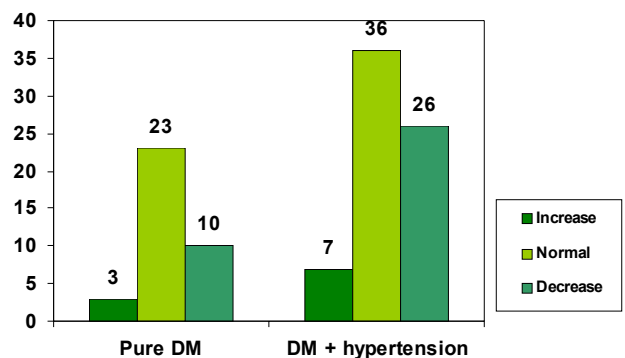


Figure 6. Blood viscosity of patients with diabetes mellitus and hypertension in Endocrine clinic, AW Sjahranie Hospital, from 1 September to 1 October 2009

DISCUSSION

Diabetes is associated with increased risk of atherosclerosis. Some studies indicate the primary and secondary changes in plasma and cellular components associated with cardiovascular hemodynamic disorders and cerebrovascular atherosclerosis (Ercan et al 2002). Blood viscosity plays a role in the process of endothelial damage and thickening of the intima during the process of atherosclerosis with increased adhesion of platelets on subendothelium, increasing protein infiltration in the artery wall and atherogenesis (Velcheva et al. 2006). The main factors affecting blood viscosity are hematocrit, plasma viscosity, decreased erythrocyte deformability and erythrocyte aggregation (Ercan et al 2002).

Of the 105 patients with DM who were investigated, the average age of the patients was 56 ± 8.02 years, consisting of 43 people (41%) men and 62 (59%) women. The youngest age was 28 years old and the oldest 76 years. This study shows the average sample age 56 ± 8 years (Figure 1). This indicates that age range above 50 tended to create a risk of degenerative diseases, such as diabetes mellitus (Aryadewi 2007). In this study female subjects was more (59%) than male subjects (41%). This research was consistent with other studies in which female subjects were in higher number than men (Aryadewi 2007, Insany & Yulia 2008, Solar 2008)

Some experts argue that with increasing age, glucose intolerance is also rising. According to Jeffrey (1991), increased blood glucose levels at the age above 50's is caused by the reduction of pancreatic cell function and insulin secretion. These changes are due to advanced age that relates with insulin resistance (lack of muscle mass and vascular changes), reduced physical activities, much eating, obesity, comorbidities, frequent stress, surgery, drug use and the presence of hereditary factors (Ikram 1996)

From the data obtained more DM with hypertension have increased blood viscosity compared with pure DM. This is consistent with the theory that hyperglycemia and hypertension are all factors that affect blood flow blockage, causing increased blood viscosity. According Poiseuille's law, which is corrected by Haganbach, pressure changes in blood flow is proportional to the length of blood vessel, peripheral resistance and viscosity and inversely proportional to the diameter of blood vessels (Iffa 2007). The number increased blood viscosity, normal or decreased more in DM with hypertension compared to pure DM. This was due to the amount of DM with hypertension (66%) more than pure DM (34%). Increased blood pressure causes an increase

in intraplaque hemorrhage, which would aggravate the stenosis of the blood vessel atherosclerosis, increased platelet aggregation and blood viscosity, and the decrease of TPA activity (endogenous tissue plasminogen activator). This will change the balance between fibrinolysis and thromboses, so thromboses become more dominant (Hariyono 2009).

Research by Surya also gets a sample with hypertension at 63.4% (Solar 2008). DM is generally followed by hypertension, which increase blood pressure more than 10-25% compared to normal people (Komunitas ABG 2007). Hypertension in patients with diabetes is caused by insulin resistance. Several relationship mechanisms that could explain the occurrence of high blood pressure in a patient with insulin resistance is the disturbance in renal salt regulation, increased activity of the sympathetic nervous system, changes in the cellular level and composition of electrolyte transport and increased activity of growth factors (Waspadji 1996).

Higher yields was obtained in the study of Komatsu et al. (1997) with an average of 5.75 ± 0.20 CP. Stephanus Lembar (2006) reported that DM is an endocrine metabolic disorders in human body as a result of increased blood sugar levels in the bloodstream, causing a slowing of blood flow due to increased blood concentration and viscosity (Stephen 2006). Glucose in DM is not regulated by either a negative effect on red blood cells and causes a significant increase in blood viscosity (Komunitas ABG 2007). It is reported that the blood plasma of patients with uncontrolled diabetes have high thickness (viscosity) (Tjokroprawiro 1996). The difference is likely because the majority of diabetic patients have received blood-thinning therapy with aspirin.

Increased plasma proteins, such as fibrinogen or plasma alpha2-macroglobulin major factor, increased blood viscosity in patients with DM. Fibrinogen particle has non-symmetrical molecular weight and construction so that the viscosity is very high (Komatsu 1997). Abnormality of blood and RBC aggregation is the most striking in patients with poor glucose control (Martinez et al. 2003). Abnormalities that occur can be observed in diabetic micro- and macroangiopathy diabetes and plays a role in reducing tissue oxygenation and lead to vascular complications of diabetes. The more severe hemoreologic abnormalities in type 2 diabetic patients may be based on the effect of hemoreologi with other metabolic abnormalities associated with insulin resistance than the quality of glucose control (Schwartz et al. 2007).

Hyperglycemia increases the formation of plasma proteins that contain sugar, such as fibrinogen,

haptoglobin, macroglobulin alpha, coagulation factor V-VII (Guyton 1997). Fibrinogen is a major component of blood viscosity so that the levels of fibrinogen can be known through examination of blood viscosity. High fibrinogen level is a cardiovascular risk factor in diabetic patients and the general public (Fujisawa et al. 1999). Blood clotting and viscosity tended to increase, so there will be susceptibility to thrombosis becomes. If the mass is attached to the blood vessels, it will cause an embolism and lead to atherosclerosis, blood vessels thicken and leak. As a result of this thickening, blood flow is reduced, especially those toward the skin and nerves. An uncontrolled blood glucose level is also likely to cause increasing levels of fatty substances in the blood, thus accelerating the occurrence of atherosclerosis (Community ABG 2007).

The lesions can cause fatty plaque on the surface of the arterial wall. Plaque begins with a small accumulation of cholesterol crystals in the intima and smooth muscle that lies beneath. Crystals grow larger and form crystals woven together like a big mattress. In addition, smooth muscle tissue and fibrous tissue surrounding the plaques will proliferate to form increasingly larger plaque. Cholesterol accumulation plus cellular proliferation can be very large so that the plaque protruding far into the lumen and greatly reduce blood flow, even covers the entire blood vessel. Plaque eventually accumulate dense connective tissue that is very excessive, so sclerosis (fibrosis) become very large and arteries become stiff and hard. Calcium salts often precipitate together with cholesterol and other lipids from plaque, causing calcification of the bones that make arteries hard sometimes like a rigid channel. Both the advanced stage of the disease is called the hardening of the arteries (Guyton 1997).

Profiles of the kidneys disorders with hypoalbuminemia causes high blood viscosity by increasing lysophosphatidylcholine (LPC). Hypoalbuminemia will be accompanied by a reduced ability of cell deformability. Hypoalbuminemia increases plasma fibrinogen and triglyceride levels and can alter the lipid composition of red blood cell membrane. All these conditions will contribute to the deformability of red blood cells to result in hyperviscosity (Joles 1997).

Prevention of complications required a good control of DM which is a therapeutic target. Diabetes is well controlled when blood glucose levels reach the expected level (80-100 mg/ dL) and lipid and A1C levels (<6.5%) also achieve the expected levels, as do the nutritional status and blood pressure ($\leq$ 130/80 mm Hg). To obtain the optimal result of diabetes management, needed behavior change is needed for healthy lifestyles and

education needs to be given for individuals with diabetes (Perkeni 2007).

Because blood viscosity is associated with cardiovascular disease and diabetes, monitoring the viscosity plays an important role in the prevention of complications, plasma protein components such as fibrinogen, haptoglobin and macroglobulin can be known through examination of blood viscosity. Examination of blood viscosity is the most optimal examination as the examination protocol in the hospital because of the way the checks easier, faster and cheaper than the expensive fibrinogen inspection and testing facilities other plasma protein components that does not exist in most hospitals, including AW Sjahranie Hospital, Samarinda.

CONCLUSION

Factors that affect blood viscosity are hematocrit, plasma proteins, temperature, level of blood flow, blood vessel size, blood pressure, erythrocyte, and chemical components of blood. These viscosity disorders over time will cause damage to several vital organs such as kidneys, heart, brain and retina of the eye.

REFERENCES

1. Arsana GP et al. (2007). Korelasi antara brachial-ankle pulse wave velocity dan profil lipid pada karyawan Rumah Sakit Sanglah Denpasar. *Penyakit Dalam* 8
2. Aryadewi N (2007). Analisa Faktor Resiko Terjadinya Kaki Diabetik pada Pasien Diabetes Mellitus di Bagian Penyakit Dalam RSUD Abdul Wahab Sjahranie Samarinda. Samarinda, Program Studi Kedokteran Umum Universitas Mulawarman, 2007.
3. Benyamin, Andi F, Gustaviani R (2006). Gangguan hemostasis pada diabetes melitus. In: Setiyohadi B, Alwi I, Sudoyo AW (eds). *Buku Ajar Ilmu Penyakit Dalam*. 4th ed., Jakarta, Pusat Penerbitan Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Indonesia, vol. 2, p 788
4. Davis (2009). What is the viscosity of blood?. Available from <http://www.madsci.org/posts/archives/1999-03/.Me.q.html>. Accessed April 18, 2009.
5. Departemen Kesehatan Republik Indonesia (2005). *Diabetes Mellitus Masalah Kesehatan Masyarakat yang Serius*. Available from <http://www.depkes.go.id/index/php>. Accessed April 18, 2009.

6. Ercan, et al. (2002). The Effects of cholesterol levels on hemorheological parameters in diabetic patients. *Clinical Hemorrheology and Microcirculation* 26, 257-263
7. Fujisawa, et al. (1999). Association of plasma fibrinogen level and blood pressure with diabetic retinopathy, and renal complications associated with proliferative diabetic retinopathy in type 2 diabetes mellitus. *Diabetic Medicine* 16, 522-526
8. Gustaviani R (2006). Diagnosis dan klasifikasi diabetes melitus. In Setiyohadi B, Alwi I, Sudoyo AW et al. (eds). *Buku Ajar Ilmu Penyakit Dalam*, 4th ed., Jakarta, Pusat Penerbitan Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Indonesia, Vol. 3, p 1879-1881
9. Guyton AC and Hall JE (1997). Metabolisme lemak. In: Setiawan I (ed). *Buku Ajar Fisiologi Kedokteran*, 9th ed., Jakarta, EGC, p 1077-1091
10. Guyton AC and Hall JE (1997). Tinjauan sirkulasi, fisik medis dari tekanan, aliran dan tahanan. In: Setiawan I (ed). *Buku Ajar Fisiologi Kedokteran*, 9th ed., Jakarta, EGC, p 205-215
11. Hariyono T (2009). Tingkat resiko stroke pada penderita hipertensi. Available from <http://stroke.muslim-Indonesia.com>. Accessed August 20, 2009.
12. Iffa (2007). Penyakit arteri perifer oklusif: Ketika nadi tersumbat karena radang dan penuaan. *Gerai 6*
13. Ikram, HA (1996). Diabetes melitus pada usia lanjut. In: Noer S, Waspadji S, Rahman AM et al. *Buku Ajar Ilmu Penyakit Dalam*. 3hd ed., Jakarta, Balai Penerbit FKUI, vol. 1, p 692-696
14. Insany, VY (2008). Gambaran Penderita Sindrom Metabolik berdasarkan Jenis Kelamin, Usia dan Pekerjaan pada Pasien Diabetes Mellitus Tipe II di Klinik Endokrin Penyakit Dalam RSUD AW Sjahranie Periode 14 Agustus – 11 September 2008. Samarinda, Fakultas Kedokteran Universitas Mulawarman.
15. Joles (1997). Hypoalbuminemia causes high blood viscosity by increasing red cell lysophosphatidylcholine. *Kidney International* 52, 761-770
16. Klabunde V (2007). Available from <http://cvpharmacology.com/index.html>. Accessed April 18, 2009.
17. Komatsu et al. (1997). Effects of glucagon administration on microcirculation and blood rheology. *Clinical Hemorrheology and Microcirculation* 17, 271-277
18. Komunitas ABG (2007). Penyakit yang Menyebabkan Pembuluh Darah Tersumbat. Available from <http://abgnet.blogspot.com>. Accessed from April 18, 2009.
19. Martinez et al. (2003). Decreased red blood cell aggregation subsequent to improved glycaemic control in type 2 diabetes mellitus. *Diabetic Medicine*, 301-306
20. Perkeni (2007). *Konsensus Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 di Indonesia 2006*. Jakarta, PB Perkeni
21. Roche (2008). Anemia. Available from <http://www.roche.co.id>. Accessed October 15, 2009.
22. Schwartz, et al. (2007). haemorheological disturbance in hypertensive type 2 diabetic patients. Influence of antihypertensive therapy. *Fundamental and Clinical Pharmacology* 21, 387-396
23. Stephanus, 2006. HbA1c sebagai kontrol penderita Diabetes Mellitus. Available from <http://www.tanya.dokteranda.com>. Accessed April 18, 2009.
24. Supandiman, I et al. (2003). *Pedoman Diagnosis dan Terapi Hematologi Onkologi Medik*. Bandung, Q-Communication, p 202-211
25. Surya and Guntur, M (2008). Analisa Faktor Resiko Terjadinya Penyakit Jantung Koroner pada Pasien Diabetes Mellitus Tipe II di Klinik Endokrin, Bagian Penyakit Dalam, RSUD Abdul Wahab Sjahranie Samarinda. Samarinda, Fakultas Kedokteran Universitas Mulawarman
26. Tjokroprawiro, A (1996) Angiopati diabetik (Mikro- dan makroangiopati diabetik. In: Noer S, Waspadji S, Rahman AM et al. *Buku Ajar Ilmu Penyakit Dalam*. 3hd ed. Jakarta, Balai Penerbit FKUI, vol. 1, p 601-615
27. Velcheva et al. (2006). Hemorheological parameters in correlation with the risk factors for carotid atherosclerosis. *Clinical Hemorrheology and Microcirculation* 35, p 195-198
28. Waspadji, S (1996). Resistensi insulin sebagai faktor risiko aterosklerosis. In: Noer S, Waspadji S, Rahman AM et al. *Buku Ajar Ilmu Penyakit Dalam*. 3hd ed., Jakarta, Balai Penerbit FKUI, vol. 1, p 697-705