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EFFECT OF INCREASED BLOOD VISCOSITY IN HUMAN BEINGS- AN OVERVIEW

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ABSTRACT

Increased whole blood viscosity is associated with Mortality and morbidity of several diseases. There are various instruments that is used to measure blood Viscosity (shear rate 100/s). Pathogenesis and development of certain diseases like diabetes mellitus, cardiovascular diseases and haemorrhagic shock is mediated by endothelial cell dysfunction. Thus, it is important to regulate and monitor blood viscosity. Increased blood viscosity is partially owing to a greater fibrinogen content and partly due to a larger packed cell volume. Greater viscosity results in increased flow resistance. Increased blood viscosity may be one plausible biological mechanism through which increase in haematocrit and fibrinogen may promote ischaemic heart disease and stroke. Randomized control of viscosity reduction in the prevention of cardiovascular events by lowering high levels of haematocrit or plasma fibrinogen were discussed. Herbs which were used as an alternative therapy in blood thinning was discussed. The main purpose of this review is to examine the regulation of blood viscosity and its impact in illness prevention. Also, about the best therapy option (plasmapheresis) for changes in blood viscosity.

**Keywords: Alternative therapies, Blood viscosity, Hyperviscosity syndrome,
phlebotomy, Plasmapheresis, Yield shear stress**

INTRODUCTION

The blood viscosity determinants are concentration, haematocrit (HcT), and plasma viscosity, serum fibrinogen aggregation and deformation abilities of

erythrocytes, making blood a non-Newtonian fluid. Resistance of fluids against flow is known as viscosity. Viscosity is defined as the measure of resistance of a fluid to flow. If the viscosity of the fluid is low, it travels faster and easier. If the viscosity of fluid is thicker, it travels slowly. Either deformity in the shape of the RBC's or any pathological elevation the blood components. Obesity causes a rise in haematocrit, which increases blood viscosity. Every individual has a unique viscosity for which he/she becomes symptomatic, which varies from 3 to 10. The increase in whole blood viscosity caused by obesity has distinct characteristics depending on where the fat is located [1]. Plasma exchange rapidly decreases fibrinogen and viscosity without

affecting haematocrit or produces neuropathological changes [2]. Also rise of M-protein level in the blood, its effect on viscosity increases. Because of fluid movements and changes in plasma protein content, blood viscosity might rise as a result of haemoconcentration.

SYMPTOMS

Visual disturbances, fatigue, joint aches, muscle aches, paraesthesia's, epistaxis, gout, headache and poor mental retardation [3].

YIELD SHEAR STRESS(YSS) [4]

Yield shear stress estimate can be used to depict the interplay of fibrinogen and haematocrit on viscosity. The force necessary to initiate movement in a stationary column of blood is described by the formula:

$$YSS = 13.5 (10^{-6}) C_f^2 (\text{Hct}-6)^3$$

INSTRUMENTS USED TO MEASURE BLOOD VISCOSITY

Ventricular assist devices are used to calculate the levels of blood viscosity [5]. Viscometer, an instrument which is also used to measure the viscosity of the fluid.

Types of viscometers

- Ventricular Assist Device
- Ostwald Viscometer
- Brookfield Viscometer
- Couette Viscometer
- Hoespler Viscometer

- Harkness Viscometer
- Falling Body Viscometer
- Stony Brook Falling Needle Viscometer
- Cylinder Viscometer
- Cone And Plate Viscometer
- Micro-Viscometer
- Micro-fluidic Device
- Falling Needle Rheometer [6-9].

CAUSES

- Waldenstrom macroglobulinemia (WM) is the most common cause.

- A higher-than-normal range of blood viscosity is directly related to serum proteins.
- High blood viscosity is an oncologic emergency that commonly manifests as neurological impairments, vision abnormalities, and mucosal bleeding.
- Increased Hyper Viscosity Syndrome (HVS) leads to myocardial infarction, ischemia and thromboembolic events which results in multiple organ failure [10].
- Increase in blood viscosity can also cause renal diseases in Essential Hypertension (EHT).

RISK FACTORS

1. Shear rate: Blood cells agglomerate at low shear rates, increasing blood viscosity. At high shear rates, blood cells get separated and thus decreases blood viscosity.
2. Changes in fibrinogen levels.
3. Iron deficiency: Iron deficiency increases blood viscosity.
4. Both plasma viscosity and haematocrit influences blood viscosity [11-13].

TREATMENT

The therapeutic options to decrease blood viscosity are therapeutic phlebotomy (300-400 cc) or Plasmapheresis to reduce acute-phase proteins levels.

When the blood temperature reduces from 36.5°C to 22°C, viscosity of blood raises to

about 26.13% and if the temperature raises from 36.5°C to 39.5°C, viscosity of blood declines to 10.38% [12]. Food diets can decrease the levels of blood viscosity depending on the health status [13]. A major factor in cardiovascular diseases, Grounding RBCs raises their surface charge, which reduces blood viscosity and clumping [14].

The most widely and successfully used treatment for hyper viscosity is TPE. A possible lowering effect of viscosity is obtained when the IgM from plasma is removed. Thus, to relieve the symptoms of hyper viscosity, TPE is simultaneously rapid and efficient.

Therapeutic Plasma Exchange (TPE) removes paraproteins, thereby decreasing viscosity. Replacement fluid with albumin daily 1-1.5 Total Plasma Volume (TPV), a total of 1 – 3. The duration of TPV is determined by considering paraproteins, patient serum viscosity and patient status. TPE is given as prophylaxis to lower IgM to <5000mg/dl may be performed.

METHODS

Divided into 2 types:

1. **Direct Methods:** This takes place while phlebotomy, rheopheresis during the plasma exchange.
2. **Indirect Methods:** Decreases the blood viscosity by balancing the factors that impact basically platelets, erythrocytes and endothelial cell [15].

Warfarin contributes a greater decrease in blood viscosity levels than aspirin in patients with acute cardioembolic stroke [16].

Warfarin, heparin and aspirin, blood thinners also known as anti-platelets, anti-coagulants are mostly used in the treating the levels of blood viscosity.

ALTERNATIVE THERAPIES

Herbs Used:

Gingko biloba, *Huperzia serrata*, *Panax ginseng*, *Crocus sativus*, *Bacopa monnieri*, *Panax notoginseng*, *Camellia sinensis* and *Curcuma longa* are used in treating HVS [17].

Blood thinning can be achieved by adding turmeric, ginger, almonds, vitamin E, grape seed extract, sunflower oil, safflower oil, cayenne peppers, garlic, whole grains, cassia cinnamon to regular food habits [18].

COMPLICATIONS

Diabetes Mellitus

Obesity and sedentary lifestyle can also cause diabetes. Diabetes mellitus is a heterogeneous disorder. It increases the glucose level in the blood [19].

Diabetic ulcers are difficult to be cured as a result of abnormal patterns of vascular endothelial growth factor receptors (VEGFR'S) [20].

TYPES: [21, 22]

1. Type 1 diabetes: Insulin Dependent Diabetes Mellitus

The loss of insulin-producing pancreatic beta cells is assumed to be triggered by immune-related. Type 1 diabetes is commonly thought of as a condition that affects children and adolescents [23].

2. Type 2 diabetes: Non-Insulin Dependent Diabetes Mellitus

It's marked by insulin insufficiency produced by pancreatic beta cell malfunction and resistance of insulin in target tissues [24].

3. Pre-diabetes:

It's a type of hyperglycaemia in which glycaemic parameters are greater than usual but lower than the diabetes threshold [25].

4. Gestational Diabetes:

GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [26].

RISK FACTORS

Weight gain and obesity [27].

Genetic markers, diet, prenatal metabolic environment, degree of glucose intolerance, degree of insulin resistance serum insulin concentrations [28]. Genetic, lifestyles (obesity, overweight, abdominal obesity, habitual physical inactivity), insulin resistance (hyperinsulinemia, impaired glucose tolerance (IGT), atherogenic dyslipidaemia, triglycerides, hypertension, prothrombic state, hyperuricemia, PCOS [29].

Lifestyle risk factors of interest includes physical activity level, dietary habits, smoking habits, alcohol use and adiposity [30]. Diabetes mellitus mostly occurs after neonatal period and results from complex interactions between both environmental

and incompletely penetrate genetic factors. Single gene disorders causing type 2 diabetes mellitus in younger aging groups (MODY) [31, 32]. Risk factors are illustrated in **Figure 1**.

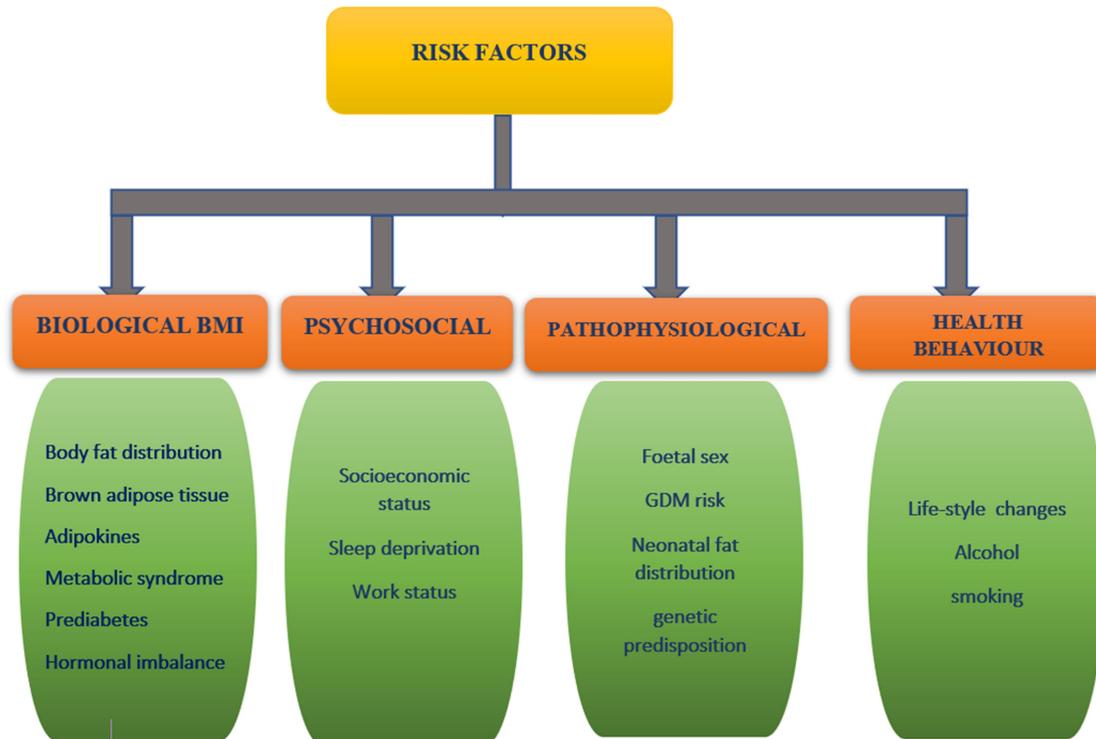


Figure 1: Risk factors of diabetes mellitus

CHRONIC KIDNEY DISEASE

Especially in Essential Hypertension (EHT), increase blood viscosity levels can cause renal disease. Both haematocrit and plasma viscosity affect blood viscosity. The hypothesis that increased blood viscosity was a cause of proteinuria [33-36].

CANCER

An increase in blood viscosity was observed in cancer patients. A decrease in

blood viscosity was seen during cancer treatment [37].

MENSTRUAL CYCLE

During the menstrual phase and the premenstrual phase on the menstrual cycle, blood viscosity and its determinants show significant changes [38, 39].

STROKE [40, 41]

Blood viscosity increases in small artery occlusion (SAO) group which indicates

contribution of dehydration to the onset of ischemic stroke. Mechanism of stroke is

illustrated in **Figure 2**.

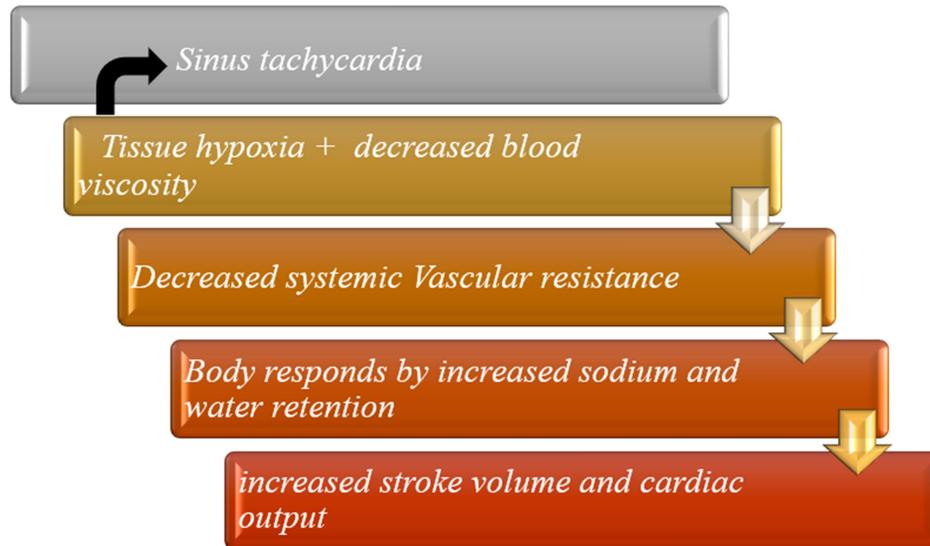


Figure 2: Mechanism of stroke

THYROID [3]

Alteration in plasma protein pattern is due to increase in plasma viscosity in the hypothyroid region, increased haematocrit in a consequence of increased whole blood viscosity.

HYPERTENSION [33]

Because a quick rise in haematocrit is more likely to cause hypertension, a low dose of erythropoietin should be used to attain a haematocrit of over 35 percent after 3-4 months of treatment.

THROMBO-EMBOLIC EVENTS

Hyper viscosity is a risk factor for thrombosis which eventually damages endothelium [42].

ORGAN FAILURE

There is a strong correlation between the sequential organ failure and the patient's plasma viscosity, which ensures a prognosis of mortality based on the severity of organ dysfunction [43].

RHEUMATOID ARTHRITIS

Autoantibodies to citrullinated peptide are generated in RA, and they are a specific and sensitive diagnostic tool. Synovial fluids in humans contain citrullinated human fibrinogen and citrullinated fibrins. In acute rheumatoid arthritis, this pro-inflammatory cytokine is overexpressed [44].

DISCUSSION

The blood viscosity determinants are plasma viscosity, haematocrit (HcT), and aggregation and deformation abilities of

erythrocytes, making blood a non-Newtonian fluid. Frank and Ryan presumed that the changes in blood viscosity is related to the pathogenic mechanism especially in patients with history of polycythaemia or Waldenström macroglobulinemia [45].

Although the medium for this pronounced influence of tube density isn't yet understood, it may give a fresh medium along which the circulating red cells mass could on the influence on the renal product of erythropoietin. Since it's established that the packed red cell volume is the major determinant for whole blood density in-vivo, it's feasible that a fall of blood density during anaemia contributes to the improvement of erythropoietin product, while an increase of density during polycythaemia would support inhibition of erythropoietin product. A very high white blood cell count may result in hyperviscosity state which leads to poor absorption of cerebrospinal fluid, that creates a clinical representation similar to benign intracranial hypertension along with bilateral disc swelling.

For every drop in the core temperature of 1^o C blood viscosity increases 2%, which results in increased haematocrit and haematologic concentration [46].

CONCLUSION

HVS is a medical emergency, and prompt treatment is required to avoid life-threatening consequences such as thromboembolic events, myocardial infarction, and catastrophic ischemia, which can lead to multiple organ failure. To avoid difficulties, the patient must stay hydrated all time. Plasmapheresis is the final therapy option. It can reverse the clinical manifestations associated with HVS and is well-tolerated and safe. If plasmapheresis can't be performed, Phlebotomy may be an option. It is important to regulate blood viscosity to prevent diseases in future.

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