

BLOOD VISCOSITY IN PATIENTS WITH DIFFUSE LARGE B CELL NON-HODGKIN'S LYMPHOMA

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The aim of the study was to evaluate blood viscosity as possible marker of disease progression in patients with newly diagnosed non-Hodgkin's lymphoma (NHL). **Methods:** The viscosity of blood samples from 20 patients with newly diagnosed aggressive NHL (stage I, n = 7; stage II, n = 4; stage III, n = 7; stage IV, n = 2) was analyzed using Brookfield DV-II + (USA) machine. **Results:** Blood viscosity in NHL patients (median: 5.5 ± 1.46 miliPascal) inversely correlated with lactatdehydrogenase (LDH) level, international prognostic index (IPI) score, and stage ($p = 0.02$, $r = -0.51$; $p = 0.03$, $r = -0.63$; and $p = 0.04$, $r = -0.45$, respectively) and positively correlated with hemoglobin level ($p = 0.02$, $r = 0.65$). **Conclusion:** According to our data, blood viscosity may be considered as a follow up marker in NHL patients along with LDH level or sedimentation rate.

Key Words: blood viscosity, non-Hodgkin's lymphoma.

Blood viscosity composed of vascular and rheologic components is considered as important parameter in a wide variety of clinical disorders, including cancer. The normal range for blood viscosity is 3.2 ± 0.4 miliPascal (mPas) [1]. Elevated plasma viscosity was reported in patients with breast and ovarian cancer [2–5]. Increased plasma viscosity impairs blood flow properties and may induce hypoxia in the microcirculation that favors thrombosis, settlement of tumor cells and thus metastasis. The viscosity of the blood is primarily related to hematocrit but also to the amount of albumin, fibrinogen and other macromolecules present in the blood [6].

Non-Hodgkin's lymphoma (NHL) is a malignant disorder which curability is highly possible [7]. Important prognostic factors of NHL are the stage of the disease and international prognostic index (IPI) value as well as hemoglobin level [8, 9]. Hemoglobin levels < 11 g/dL were shown to be a poor prognostic criteria for survival of NHL patients [9]. The aim of our study was to analyze the changes in blood viscosity in newly diagnosed NHL patients on the background of alterations in fibrinogen, albumin and hemoglobin levels.

Twenty newly diagnosed patients with histologically documented diffuse large B cell NHL were enrolled in the study. Written inform consent was taken from all patients. Patients possessing diabetes mellitus, chronic renal failure, hypertension, coronary vascular disease, infectious disease, collagen vascular disease or coagulopathy were excluded from the study. The median age of the patients was 52 years (range: 26–79), the male/female ratio was 14/6. Patient's characteristics are presented in the Table (stage I, n = 7; stage II, n = 4; stage III, n = 7, stage IV, n = 2; by IPI score, IPI 0, n = 1; IPI 1, n = 3; IPI 2, n = 6; IPI 3, n = 6; IPI 4, n = 4).

Table. Patient's characteristics and blood viscosity

No of patient	Sex	Age	Stage	LDH	ENIN	IPI	Hb (g/dL)	Fbr	Blood Viscosity (miliPascal)
1	M	39	3E	445	1	3	9.3	243	4.5 ± 0.2
2	F	59	1E	167	1	0	12.9	226	7.8 ± 0.3
3	M	66	1E	186	1	2	16.6	194	7.9 ± 0.2
4	F	38	2E	736	1	2	8.8	228	4.6 ± 0.2
5	M	72	1E	156	1	2	13.3	216	7.7 ± 0.2
6	M	29	3E	296	1	3	11.1	243	4.8 ± 0.1
7	M	77	4	318	0	4	11.6	256	5.7 ± 0.1
8	M	52	2E	259	2	4	11.8	251	4.7 ± 0.2
9	F	30	2E	235	1	2	12.3	223	7.2 ± 0.3
10	F	65	3E	373	1	3	9.7	236	3.7 ± 0.1
11	M	64	1	129	0	2	7.9	241	5.3 ± 0.2
12	M	41	3	328	0	3	12.8	264	4.7 ± 0.2
13	M	26	4	510	0	4	15.1	236	5.8 ± 0.2
14	M	42	1	123	0	1	8.8	214	7.6 ± 0.2
15	M	79	1E	141	1	3	11.2	181	4.7 ± 0.2
16	M	65	3	263	0	4	10.8	177	4.0 ± 0.1
17	M	29	3s	164	0	1	12.1	215	5.7 ± 0.2
18	M	53	1E	136	1	1	13.4	251	8.2 ± 0.3
19	F	63	2E	233	1	3	10.8	190	4.4 ± 0.2
20	F	51	3	290	0	2	12.6	244	5.9 ± 0.1

Notes: ENIN – extranodal involvement number; M – male; F – female; Hb – hemoglobin; LDH – lactate dehydrogenase (normal:100–200 U/L), Fbr – fibrinogen (normal:170–400 mg/dL).

Blood samples in a volume of 5 cc were taken prior to chemotherapy using tubes with anticoagulant and immediately frozen at -40 °C. On the day of measurement, all samples were melted and their viscosity was measured at 37 °C in a Brookfield DV-II + (USA) machine which was calibrated with distilled water. Each sample was measured four times and the average of the measurements was taken (mean \pm levels, see the Table).

Staging procedures in all patients were done using complete blood count, blood chemistry, lactatdehydrogenase (LDH) level and erythrocyte sedimentation rate, computed tomography and bone marrow biopsy. IPI scores were calculated according to stage and clinical signs. The parameters which may have an effect on viscosity such as fibrinogen (Beckman Coulter ACL® 10000) and albumin (Beckman Coulter Synchron LX® 20 Autoanalyser) were measured in blood analyses before treatment.

To assess the trends, we used the median values of intake in each category. 95% confidence intervals for all relative risks were calculated. *P* values < 0.05 were

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Abbreviations used: IPI – international prognostic index; LDH – lactatdehydrogenase; NHL – non-Hodgkin's lymphoma.

considered significant. For independent prognostic parameters, Spearman's Rho correlation was used.

Median blood viscosity was found to be 5.5 ± 1.46 milliPascal (range: 3.7–8.2, normal: 3.2 ± 0.4) [1]. Blood viscosity inversely correlated with LDH, IPI score, and stage ($p = 0.02$, $r = -0.51$; $p = 0.03$, $r = -0.63$; and $p = 0.04$, $r = -0.45$, respectively) and positively correlated with hemoglobin level ($p = 0.02$, $r = 0.65$) (Fig. 1, 2). Sex, age, fibrinogen level, and extranodal involvement were not associated with blood viscosity ($p = 0.57$, $p = 0.95$, $p = 0.57$ and $p = 0.84$ respectively). Albumin levels were shown to have a significant inverse correlation with the stage ($p = 0.02$, $r = -0.516$) and positive correlation with blood viscosity ($p = 0.05$, $r = 0.442$).

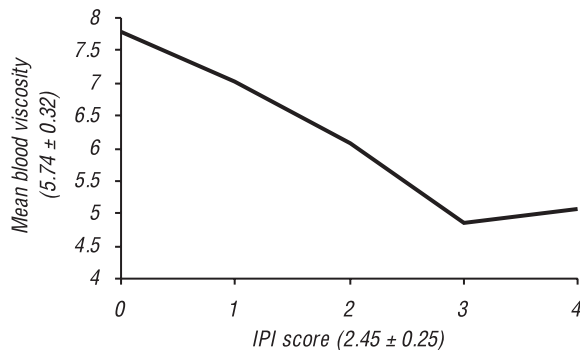


Fig. 1. Correlation of mean blood viscosity with IPI score

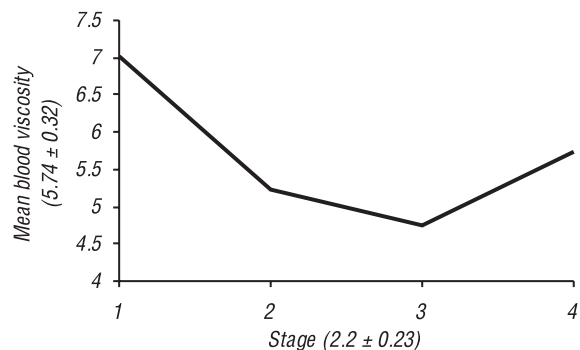


Fig. 2. Correlation of mean blood viscosity with the stage of the disease

This is the first report on the blood viscosity in NHL patients showing its inverse correlation with the stage of the disease and IPI score. Elevated levels of acute phase substances such as fibrinogen, C-reactive protein in NHL patients may contribute to these results.

In conclusion, we believe that evaluation of blood viscosity may be used as an easy and useful marker of the disease progression. Further trials may demonstrate the impact of blood viscosity on prognosis in NHL patients.

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ВЯЗКОСТЬ КРОВИ У БОЛЬНЫХ ДИФFUЗНОЙ В-КЛЕТОЧНОЙ НЕХОДЖКИНСКОЙ ЛИМФОМОЙ

Цель: анализ вязкости крови в качестве маркера возможного маркера прогрессии заболевания у больных неходжкинской лимфомой (НХЛ). **Методы:** вязкость крови 20 пациентов НХЛ (стадия I, n = 7; стадия II, n = 4; стадия III, n = 7; стадия IV, n = 4) измеряли на приборе Brookfield DV-II + (США). **Результаты:** вязкость крови больных НХЛ (средняя величина: 5.5 ± 1.46 миллиПаскаль) находилась в обратной корреляции с уровнем лактатдегидрогеназы (ЛДГ), величиной международного прогностического индекса (IPI) и стадией заболевания ($p = 0.02$, $r = -0.51$; $p = 0.03$, $r = -0.63$; $p = 0.04$, $r = -0.45$ соответственно) и в прямой зависимости от уровня гемоглобина ($p = 0.02$, $r = 0.65$). **Выводы:** согласно полученным данным, вязкость крови можно рассматривать в качестве маркера течения заболевания у больных НХЛ наряду с уровнем ЛДГ и показателем скорости оседания эритроцитов.

Ключевые слова: вязкость крови, неходжкинская лимфома.