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Elevated E-Selectin Levels and Their Correlation with Blast Cells in Acute Myeloid Leukemia Patients

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A R T I C L E I N F O

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E-selectin, AML, HSCs,CD62E

A B S T R A C T:

Background: Acute myeloid leukemia (AML) is a highly aggressive blood cancer characterized by the accumulation of immature myeloid cells in the bone marrow, disrupting normal blood cell production. Unfortunately, AML carries a grim prognosis, with a substantial rate of disease, relapse, and a median overall survival of only 15 months. A vascular adhesion molecule called E-selectin is only found on activated endothelial cells. It controls the activity of hematopoietic stem cells (HSCs) in the bone marrow vascular niche and is very important for this.Evaluation The level of E-selection in AML patients as well as the correlation between E-selectin and blast cells. This study case control included a total of 50 patients with AML collected from "National center of hematology /Mustansiriyah university" from January 2022 to June 2023. twenty-five out of 50 AML patients was new diagnosis and other 25 AML patients after therapy, The age and sex matched with 50 apparently healthy individuals as control group. Blood was taken from them for an evaluation of their E-selectin level using Sandwich ELISA method. There are significant differences in the level of E-Selectin concentration in AML patients' plasma compared with the concentration of healthy group plasma. While there is no significant difference between patients before and after chemotherapy, there is a significant correlation between E-selectin level and blast cells. The level of E-selectin is elevated in AML patients, and there is an appositive correlation between E-selectin and Blast cells, which may contribute to the progression of the disease.

Introduction:

The majority of individuals diagnosed with acute myeloid leukaemia (AML) exhibit a notable elevation in the count of white blood cells, while concurrently experiencing insufficient levels of red blood cells and platelets. There is a potential for a drop in the level of white blood cells. The detection of blast cells is typically observed within the bone marrow, serving as a diagnostic marker for acute myelogenous leukaemia. Blasts expressing acute myeloid leukaemia (AML) A diverse array of sticky molecules, including as selectins, integrins, and immunoglobulin components, The taxonomic classification of superfamily is a hierarchical grouping that is used in the field of Nevertheless, the molecular formula The manifestation of symptoms differs among individuals [1].

The membrane glycoprotein known as E-selectin, which is unique to endothelial cells, is implicated in the processes of leukocyte rolling and adhesion. It is hypothesised that E-selectin may also have a potential role in facilitating angiogenesis. The administration of blocking antibodies specifically targeting E-selectin halts the formation of endothelial tubes in an experimental laboratory model of angiogenesis. The presence of elevated levels of soluble E-selectin has been associated with the development of vasculo-proliferative illnesses such as rheumatoid arthritis and various forms of malignancy [2]. The gene expression of this particular factor is increased in endothelial cells undergoing proliferation in a laboratory setting.

The shedding of E-selectin into circulation, also known as soluble E-selectin (sE-selectin), or its fast internalisation following activation, has been seen. Elevated levels of sE-selectin in the blood serve as a dependable marker for inflammation, with people experiencing chronic inflammation continuously exhibiting higher circulating sE-selectin concentration in comparison to their healthy counterparts. In a similar vein, previous studies have documented an increase in blood levels of sE-selectin, which has demonstrated a positive correlation with both the grade and the stage of breast cancer tumors, as well as the presence of metastases [3.]

The glycoprotein E-Selectin (CD62E) has a molecular weight of 115 kDa and is exclusively present on endothelial cells following activation by interleukin 1 (IL-1), tumour necrosis factor α (TNFα), or bacterial lipopolysaccharides. Upon stimulation of endothelial cells, there is a rapid presence of freshly synthesized E-selectin. Observers note that the maximal level of surface expression occurs between 3 to 6 hours, followed by a subsequent return to baseline during a 24-hour period [4]. The mechanism behind this swift decrease regulation, while not fully comprehended, has been attributed to the secretion of a solvable variant of E-selectin and the subsequent internalizations of the molecule. The control of E-selectin demonstration is potentially essential in the management of leukocyte accumulation during inflammatory responses. Multiple ligands for E-selectin have been found on white blood cells ; however, their cloning has not been accomplished thus far. Previous studies have demonstrated that monoclonal antibodies (mAbs) that target E-selectin has the ability to impede the process of leukocyte transmigration. Previous studies have proposed that the interaction between leukocytes and active endothelium, namely binding to E-selectin, leads to an upregulation of CD11b (also known as Mac-1) on the leukocytes. This upregulation subsequently generates enhanced adhesion through the interaction between ICAM-1 and Mac-1. One of the key characteristics of malignant transformation is the regulation of transcription through the interaction between E-selectin and particular receptors. The prognosis of E-selectin bindings is unfavorable [5.]

Material and Methods :

The methodology utilized in this study was carefully designed and realized to ensure the authority and consistency of

Research comprised a cohort of 50 individuals from Iraq who were diagnosed with acute myeloid leukaemia, alongside a control group of 50 people who were matched in terms of physical characteristics. The age range of the patients spanned from 20 to 70 years. The present investigation was conducted at the National Centre of Haematology, affiliated with Mustansiriyah University, spanning from January 2022 to June 2023. Every patient received a comprehensive physical examination conducted by a qualified clinical haematologist, and information pertaining to illnesses pertinent to this research was collected.

The concentration of Selectin in plasma is quantitatively evaluated through the utilisation of a sandwich enzyme immunoassay technique known as ELISA. This approach involves the utilisation of a kit provided by R&D Systems, USA.**Ethical approval**

A local ethics committee examined and approved the study protocol, subject information, and consent form in accordance with nch-erc-21-12, dated 12/3/2024

Statistical analysis: Discrete variables are analysed for the mean, standard deviation (SD), and person correlation. The categorical variables are analysed using SPSS version 28. A value of $P < 0.05$ was considered statistically significant.

Results:

This case control study includes 50 patients with AML, 25 out of 50 were new diagnosis and the other 25 were patients on treatment. Fifty healthy looking person age and sex match as control. This study was conducted from National center of hematology / Mustansiriyah university from January 2022 to June 2023.

Our research has unveiled substantial disparities in the concentration of E-Selectin in the plasma of AML patients (mean ± standard deviation: (11.12 ± 0.85 ng/ml) as opposed to the plasma of individuals in the healthy control group (mean ± standard deviation: (8.53 ± 2.8 ng/ml) ($p < 0.001$) ,Table 1; Figure 1. Conversely, we did not observe a statistically significant distinction between E-Selectin levels in patients before and after undergoing chemotherapy (p=0.9) (Table 2).

Figure 1: The compression in level of E-Selectin between Patients with AML and Controls group.

Table 1 Comparison between AML patients group and Control group:

E-selection	No.	Mean ±SD	P-value	T–test
Patients ng/ml	**50**	**11.12 ± 0.85**	**<0.001**	**7.8**
Control ng/ml	50	8.53± 1.8		

Table 2
Comparison between patients with AML before and after chemotherapy

E-selection	No.	Mean ±SD	P-value	T–test
Before therapy ng/ml	25	11.10 ± 0.95	0.9	-0.1
After therapy ng/ml	25	11.13± 0.67		

In this study the correlation between E- Selectin, Leucocytes, blast cells and platelets showed positive significant

correlation between E-selectin and Blast sells (r=0.395;p=0.031) ,while there are no significant correlation with Leucocytes and Platelets(r=0.328 ;p=0.077, r=-0.276; p=0.141) respectively ,Table (3).

Table 3:
Correlation among E- selectin, Leucocytes, Blasts and Platelets in New diagnosis patients.

Correlations

		Leucocytes	platelets
E-Selectin	Pearson Correlation	0.328	-0.276
	Sig. (2-tailed)	0.077	0.141
	N	50	50

*. Correlation is significant at the 0.05 level (2-tailed).

Discussion:
AML is a highly hostile blood cancer characterized by the accumulation in the bone marrow the immature myeloid cells, disrupting normal blood cell production. Unfortunately, AML has a poor prognosis, with a high rate of not response to treatment and a median total survival of only 15 ms. Alarmingly, standard AML therapy has remained stagnant for over 30 years, highlighting the considerable challenges in improving treatment strategies using current research approaches [6]. In the vascular niche of the bone marrow, activated endothelial cells specifically express E-selectin, a vascular adhesion molecule, which critically regulates the activity of hematopoietic stem cells (HSCs)., as demonstrated by research conducted by Winkler and colleagues in 2012 [7].
This study showed that there were significant differences in level of E- selectin between AML patients and controls group while there were no significant differences between new diagnosis AML patients and tread AML patients, Selectins constitute a family of cell adhesion molecules with a well-established role in facilitating the rolling and homing of leukocytes to target tissues. Among the selectins, E-selectin (CD62E), found exclusively on activated or inflamed endothelial cells, and P-selectin (CD62P), present on both platelets and endothelial cells, often work in conjunction with integrin ligands [8]. Previous research has revealed the distinctive role of E-selectin in regulating the transition between dormancy and proliferation of hematopoietic stem cells (HSCs). When HSCs come into contact with E-selectin on the bone marrow endothelial niche, it directly triggers HSC activation and proliferation, leading to their commitment to specific lineages. Conversely, the absence of E-selectin or its therapeutic blockade promotes HSC quiescence, enhancing their self-renewal capacity and resistance to chemotherapy [9]. However, in the context of malignancies, our current findings indicate a different role for E-selectin interactions, where they actively contribute to the survival of malignant cells [10].

E-selectin has also been associated in conferring resistance to malignancy management, as proven by various studies [11, 12, 13]. Research in multiple myeloma (MM) and leukemia has demonstrated that cancer cells receive protection from cytotoxic drugs when they interact with the vascular network within the bone marrow (BM), thereby triggering pro-survival signaling pathways that facilitate cancer progression [14] .Notably, in an acute myeloid leukemia (AML) mouse model, it was observed that leukemic cells with an enhanced capacity to bind E-selectin exhibited a remarkable 12-fold increase in resistance to chemotherapy [12]. Furthermore, cancer cells in suspension, induced by exposure to cytotoxic drugs, acquired heightened adhesion properties. This change resulted in the upregulation of specific ligands and/or receptors, ultimately contributing to the development of drug resistance [15,16].

In conclusion, our findings indicate that the levels of E-selectin exhibit a significant elevation in AML patients both before and after treatment. Notably, we observed a correlation between E-selectin levels and the presence of blast cells, suggesting that as the number of blast cells increases, the level of E-selectin also rises. This association may play a pivotal role in disease progression and contribute to resistance against therapeutic interventions.

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Institutional Review Board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Zarqa
University (Zu-2022/11/4916/16).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data availability statement

Data is available upon request from the corresponding author.

Declaration of competing interest

The authors declare no conflict of interest.

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References:

1- Aref S, Salama O, Al-Tonbary Y, Fouda M, Menessy A, El-Sherbiny M. L and E selectins in acute myeloid leukemia: expression, clinical relevance and relation to patient outcome. Hematology. 2002;7(2):83-87. https://doi.org/10.1080/10245330290012329.

2- Gerritsen ME. In: Microcirculation. 2008.

3- Toyokawa T, Kubo N, Tamura T, Sakurai K, Amano R, Tanaka H, Muguruma K, Yashiro M, Hirakawa K, Ohira M. The pretreatment Controlling Nutritional Status (CONUT) score is an independent prognostic factor in patients with resectable thoracic esophageal squamous cell carcinoma: results from a retrospective study. BMC Cancer. 2016;16:722. https://doi.org/10.1186/s12885-016-2743-2.

4- Hakomori S, Cummings RD. Glycosylation effects on cancer development. Glycoconj J. 2012;29:565-566. https://doi.org/10.1007/s10719-012-9421-0.

5- Barbier V, Erbani J, Fiveash C, Davies JM, Tay J, Tallack MR, Lowe J, Magnani JL, Pattabiraman DR, Perkins AC, Lisle J. Endothelial E-selectin inhibition improves acute myeloid leukaemia therapy by disrupting vascular niche-mediated chemoresistance. Nat Commun. 2020; 11(1): 2042. https://doi.org/10.1038/s41467-020-15988-4.

6- Erbani J, Tay J, Barbier V, Levesque JP, Winkler IG. Acute myeloid leukemia chemo-resistance is mediated by E-selectin receptor CD162 in bone marrow niches. Front Cell Dev Biol. 2020;8:668. https://doi.org/10.3389/fcell.2020.00668.

7- Winkler IG, Barbier V, Nowlan B, Jacobsen RN, Forristal CE, Patton JT, Magnani JL, Lévesque JP. Vascular niche E-selectin regulates hematopoietic stem cell dormancy, self-renewal and chemoresistance. Nat Med. 2012;18(11):1651-1657. https://doi.org/10.1038/nm.2969.

8- Kansas GS. Selectins and their ligands: current concepts and controversies. Glycoconj J. 1996;13:469-497. https://doi.org/10.1007/BF00731248.

9- Barbier V, Erbani J, Fiveash C, Davies JM, Tay J, Tallack MR, Lowe J, Magnani JL, Pattabiraman DR, Perkins AC, Lisle J. Endothelial E-selectin inhibition improves acute myeloid leukaemia therapy by disrupting vascular niche-mediated chemoresistance. Nat Commun. 2020;11(1):2042. https://doi.org/10.1038/s41467-020-15988-4.

10- Barbier V, Erbani J, Fiveash C, Davies JM, Tay J, Tallack MR, Lowe J, Magnani JL, Pattabiraman DR, Perkins AC, Lisle J. Endothelial E-selectin inhibition improves acute myeloid leukaemia therapy by disrupting vascular niche-mediated chemoresistance. Nat Commun. 2020;11(1):2042. https://doi.org/10.1038/s41467-020-15988-4.

11- Azab AK, Quang P, Azab F, Pitsillides C, Thompson B, Chonghaile T, Patton JT, Maiso P, Monrose V, Sacco A, Ngo HT. P-selectin glycoprotein ligand regulates the interaction of multiple myeloma cells with the bone marrow microenvironment. Blood. 2012;119(6):1468-1478. https://doi.org/10.1182/blood-2011-05-355420.

12- Barbier V, Erbani J, Fiveash C, Davies JM, Tay J, Tallack MR, Lowe J, Magnani JL, Pattabiraman DR, Perkins AC, Lisle J. Endothelial E-selectin inhibition improves acute myeloid leukaemia therapy by disrupting vascular niche-mediated chemoresistance. Nat Commun. 2020;11(1):2042. https://doi.org/10.1038/s41467-020-15988-4.

13- Manier S, Sacco A, Leleu X, Ghobrial IM, Roccaro AM. Bone marrow microenvironment in multiple myeloma progression. Biomed Res Int. 2012;2012:157503. https://doi.org/10.1155/2012/157503.

14- Martinez-Moreno M, Leiva M, Aguilera-Montilla N, Sevilla-Movilla S, Isern de Val S, Arellano-Sanchez N, Gutiérrez NC, Maldonado R, Martínez-López J, Buño I, García-Marco JA. In vivo adhesion of malignant B cells to bone marrow microvasculature is regulated by α4β1 cytoplasmic-binding proteins. Leukemia. 2016;30(4):861-872. https://doi.org/10.1038/leu.2015.331.

15- Damiano JS, Cress AE, Hazlehurst LA, Shtil AA, Dalton WS. Cell adhesion mediated drug resistance (CAM-DR): role of integrins and resistance to apoptosis in human myeloma cell lines. Blood. 1999;93(5):1658-1667. https://doi.org/10.1182/blood.V93.5.1658.

16- Al-Hashemi HS, Rahman SAHA, Shabeeb ZA. Expression of immune checkpoint molecules in Iraqi acute myeloid leukemia patients. Iraqi J Hematol. 2021;10(1):1-16. https://doi.org/10.4103/ijh.ijh_46_20.