Chelonian Conservation And Biology

Vol. 19No.1 (2024) | https://www.acgpublishing.com/ | ISSN - 1071-8443

DOI:doi.org/10.18011/2024.01(1). 1079-1091

SYNDECAN-1 AND RISK FACTORS ASSOCIATED WITH ITS CONCENTRATION IN ACUTE MYELOID LEUKEMIA PATIENTS

Eman Ali Ahmed Freih[1*], Rana F. Jassim[2]

[1*, 2]Department of Chemistry /College of Education for Girls/ University of Mosul, Mosul, Iraq
***Corresponding Author**: Eman Ali Ahmed Freih

ABSTRACT:
The study included determining the syndicane-1 concentration in acute myeloid leukemia patients and comparing it with healthy cases, and studying the effects of some risk factors on its concentration in both patients and control group, complete blood count (CBC) including white blood cells, hemoglobin, platelets and blast in bone marrow has been determined, as well as, the concentration of urea, creatinine, the activity of lactic dehydrogenase, systolic and diastolic blood pressure and body temperature. The results showed a significant increase in the concentration of syndicane-1 in patients compared to healthy people, and its concentration increases significantly with age, smoking, body mass index (BMI), blood type (A), duration of disease, chemotherapy, diabetes menopause in women, WBC count, platelet count, hemoglobin and blast% in BM. Our results showed a significant increase in the concentration of creatinine, urea, lactate dehydrogenase activity, and body temperature (Tm) in patients compared to the control. The Pearson correlation coefficient (r) showed a positive correlation between syndicane-1 concentration and creatinine, urea, Tm, and LDH. We concluded that syndicane-1 concentration can be a strong biomarker for the diagnosis of acute myeloid leukemia and endothelial glycocalyx damage.

KEYWORDS: AML, Risk factors, Syndecan-1, Platelets, Hemoglobin.

Introduction:

Acute myeloid leukemia (AML) is defined as a malignant tumor of immature bone marrow-derived myeloid cells and also shows variable differentiation [1]. It occurs as a result of the change and decrease in the number of healthy cells that make up the blood, which prevents their differentiation and stimulates the proliferation or accumulation of explosions (Blasts), so the explosions replace the normal blood-forming tissues, which leads to a lack of blood cells, so the accumulation of immature cells begins in the bone marrow (BM), but in most cases, they accumulate quickly in the blood and sometimes spread to other parts of the body such as lymph nodes, spleen, liver, testicles and central nervous system [2]. It is the most common acute form of adult leukemia and is a malignant clonal disorder, characterized by poor survival with a high relapse rate and resistance to available treatments [3]. Among adults in the United States, the

incidence of AML was higher than that of the other three branches of leukemia (acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML), and chronic lymphoblastic leukemia (CLL) until 2017 [4]. Although the causes of most cases of acute myeloid leukemia are unknown, risk factors include ageing, male sex, smoking, exposure to chemicals, chemotherapy drugs, exposure to high doses of radiation, and family history of AML disease can play an important role in the incidence or development of the AML [1].

Syndicane-1 (CD138 or SDC1) is one of the members of the Syndicane family consisting of 4 members in mammals, which are Syndicane -1, 2, 3 and 4, and is located on the surface of many cells, including fibroblasts and epithelial cells, and also found in the nucleus of some cells to participate in the regulation of the process of genetic cloning, the most important one is Sindican-1 for its relationship to many diseases, which is the main on the surface of epithelial cells in adults [5].

SDC1 is a glycoprotein that contains long, negatively charged chains of heparin sulfate. In mammals, SDC1 is expressed in endothelial cells and leukocytes and consists of 310 amino acids, its molecular weight is 33 KDa and is located across the cell membrane in many cells, it is the main component of the endothelial glycolic glycocalyx, which covers the surface of endothelial cells [6,7]. The gene responsible for the cloning of SDC1 is made up of 5 exons and is located on chromosome 2 in humans [5].

SDC1 plays an important role in stimulating cell migration and it plays an important role in stimulating cell migration and controlling inflammation. SDC1 also acts as a membrane receptor and co-receptor which can bind to several ligands via glycosaminoglycan chains to influence important cellular functions such as cellular receptor binding, inflammation regulation, cell growth, differentiation and adhesion, neuronal development, and lipid metabolism [5,8]. SDC1 may be released from the lining endothelial cells to the bloodstream when damage occurs in the endothelial glycolic glycocalyx under disease conditions such as inflammation and cancer, indicating endothelial layer damage [9]

Research Objective:

In the past few years, AML has increased in Iraq and studies on SDC1 were limited, so we proposed to study the effects of the common risk factors in AML on SDC1concentration in patients and healthy groups, and study the correlation between SDC1 concentration and some biochemical parameters.

Materials and methods

Blood samples were collected from 55 healthy people (30 males and 25 females), and 75 AML patients (40 males and 35 females) collected from the Hematology Unit at Ibn Sina Teaching Hospital in Mosul City, with ages (15-76 years) for each group, and the following variables were estimated:

SDC1 concentration was determined using a Bioassay Technology Laboratory kit (China) by enzyme-bound immunoassay technique (ELISA). The complete blood count (CBC) including white blood cells (WBC), platelets (PLT), and hemoglobin (HGB) were determined by an automatic hematology analyzer using (AC970 Swelab Hematology Reagents) also, BM smears were estimated, to determine the percentage of blast cells in BM. Creatinine, urea and LDH activity were estimated using the BIOLABO kit (France). Blood pressure (BP) was measured by mercury sphygmomanometer and body temperature (TM) by Thermometers.

Data analysis:

To analyze the data of our study, the SPSS program was used, and traditional statistical procedures were applied to obtain the standard mean value. The T-test was used to compare two variables, ANOVA was used to analyze more than two variables in one way, and the Pearson correlation factor was intended to determine the relationship between different parameters with P≤0.05 being statistically significant.

Results and discussion:

SDC1 concentration in patients with AML and control group

The results in Table (1) showed that the normal range for SDC1 is (32.21±2.49 ng/ml) in the health control group and that consists with[10], the results also showed a significant increase in SDC1 concentration in patients compared to control and that consists with [11].

SDC1 is a transmembrane glycoprotein present on the surface of endothelial cells and constitutes the backbone of the glycocalyx barrier. The degradation of endothelial glycocalyx can cause increasing proteolysis of SDC1 by several matrix metalloproteases and sheddases which increases SDC1 concentration in the blood (shed SDC1). SDC1 shedding occurs in ischemia, inflammation, sepsis, cancer and various conditions [5,10].

Table 1. SDC1 concentration in AML patients and control group

SDC1 Conc.(ng/ml) mean±S.E	
Control	Patients
32.21±2.49	61.38±7.34**

** significant at P≥0.01, S. E=stander Error

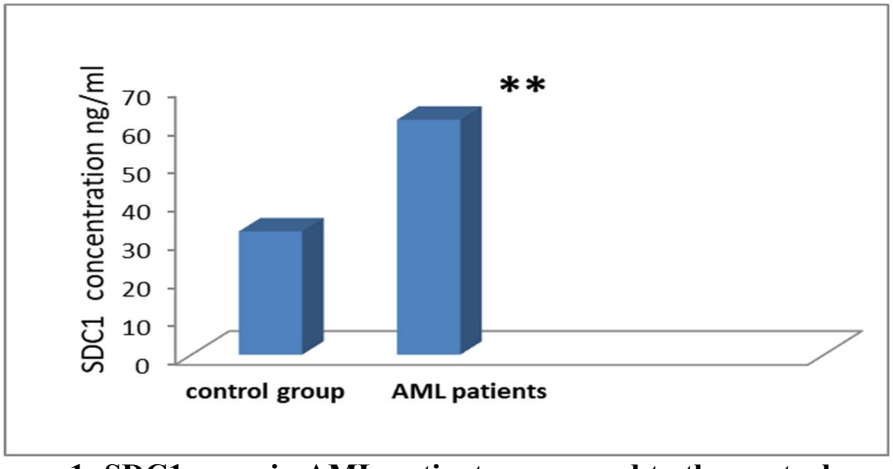

Figure 1: SDC1 conc. in AML patients compared to the control group

SDC1 concentration and effects of some risk factors in AML patients and control group:

1. The sex:

The results in Table (2) showed that there were no significant differences in SDC1 concentration between males and females in each group and that agreement with [6,11].

Table 2. SDC1 Concentration in Patients and Control Group by Sex

Sex	SDC1 conc. (ng/ml) mean± S. E	
	Control	Patients
Males	33.71±3.99	65.03±12.71
Females	30.70±3.04	57.58±7.27

2. The age:

As shown in Table (3), there was a significant increase in SDC1 concentration in ages 35-55 years and 56-76 years compared with 14-34 years but no significant differences between the last two age groups in patients and the control group and that agreement with [9]. Ageing is associated widely with oxidative stress, and endothelial glycocalyx can be exposed to oxidative stress resulting in structural modifications which can be observed with aging. Also, Age-related degradation of endothelial glycocalyx has been increased in aged humans and mice and the thickness of endothelial glycocalyx decreases in elderly people which causes the shedding of SDC1 to blood and increases its concentration in the serum[9,12].

Table 3. SDC1 Concentration in AML and Control Group Patients by Age

Age(year)	SDC1 conc.(ng/ml) mean± S. E	
	Control	Patients
14-34	23.28±1.83	45.86±3.76
35-55	33.35±2.31*	62.68±4.26*
56-76	39.44±3.85***	75.08±6.76**

* Significant variance if p≤ 0.05, and ** if P≤0.01, and *** if p≤ 0.001

3. The smoking:

Table (4) shows that the SDC1 concentration in smokers increased significantly compared to non-smokers in patients and the control group, and this may be due to the smoking which induces glycocalyx degradation and impairs the function of vascular endothelial through a decrease in NO availability by promote of oxidative stress and inflammation [13].

Table 4. SDC1 concentration in AML and Control Group Patients by smoking

Smoking	SDC1 conc. (ng/ml) mean± S. E	
	Control	Patients
non-smokers	27.07±2.07	50.43±4.60

Smokers	37.35±2.88**	72.77±9.99*

* Significant variance if p≤ 0.05, and ** if P≤0.01

4. Body mass index (BMI):

The results in Table (5) showed a significant increase in SDC1 concentration with an increase in BMI in patients and the control healthy group. Overweight and obese persons had higher SDC1 compared to healthy-weight persons, while there are no significant differences between overweight and obesity groups.

Table 5. SDC1 Concentration in AML and Control Group Patients by Body Mass Index

BMI	SDC1 conc. (ng/ml) mean± S. E	
	Control	Patients
18.5-24.9 (healthy weight)	23.62±23.62	46.84±2.11
25-29.9 (overweight)	34.86±2.47 *	62.5±5.30*
≥ 30 (obesity)	38.8±4.14 **	75.73±5.65 **

* Significant variance if p≤ 0.05, and ** if P≤0.01

Obesity is associated with metalloproteinase activation which causes the shedding of endothelial glycocalyx under pathological conditions resulting in SDC1 shedding and dysfunction of the endothelial barrier, a study showed that obese mice might have imbalanced fasting glucose and glucose tolerance, dyslipidemia, increased inflammation and SDC1 shedding [14].

5. The ABO blood types:

The results in Table (6) showed that type A in patients had significantly higher SDC1 concentration compared to types B and O also, type A in the control group had significantly higher SDC1 concentration compared to type O which consists [15].

Table 6. SDC1 concentration in AML Patients and Control Group by Blood Type

Blood Type	SDC1 conc. (ng/ml) mean± S. E	
	Control	Patients
A	38.44±4.31*	75.3±7.17 *
B	31.84±2.33	53.64±5.53*
AB	32.99±3.23	62.64±5.58
O	25.33±2.59*	52.57±4.07*

* Significant variance if p≤ 0.05

As results showed, we concluded that type A in each group had higher endothelial glycocalyx damage compared to types B and O (in patients) and type O (in control), this may be due to the molecular structure of some blood types which may cause direct damage to the endothelium, as well as endothelial cells express the antigens of blood type which cause stabilisation or destabilisation of the endothelium glycocalyx depending on blood type antigens [15,16].

6. Type of nutrition:

The results in Table (7) showed no significant differences in SDC1 concentration among those having unhealthy food compared to those having healthy food in both groups.

Table 7. SDC1 concentration in AML patients and control group by type of nutrition

Type of nutrition	SDC1 conc. (ng/ml) mean± S. E	
	Control	Patients
Healthy food	29.45±1.55	56.04±4.62
Unhealthy food	35.58±3.77	65.69±5.40

7. The Menopause in women:

Our study showed a significant increase in the concentration of SDC1 in Postmenopausal compared to Premenopausal women in patients and control groups as shown in Table (8), these results may be due to the sex hormones of females (estrogen and progesterone) which exert important effects on vascular endothelium such as upregulation of NO synthase, inducing vasodilation, decreasing of oxidative stress, and protect vascular endothelium from damage. It is thought that these female sex hormones affect the glycocalyx function which is essential for endothelial function, so the decrease of these hormones in postmenopausal women can promote endothelial glycocalyx damage and increase SDC1 shedding [17].

Table 8. SDC1 Concentration in AML and Control Group Patients by Menopause in Women

Menopause in women	SDC1 conc. (ng/ml) mean± S. E	
	Control	Patients
Premenopausal women	25.76±2.57	47.03±6.03
Postmenopausal women	39.33±4.54*	69.02±7.38*

* Significant variance if p≤ 0.05

8. The chemotherapy:

Table (9) showed a significant increase in SDC1 concentration in patients treated with chemotherapy compared to untreated patients and that is in agreement with [7].

Table 9. SDC1 concentration in patients by chemotherapy

	SDC1 conc. (ng/ml) mean± S. E	
Chemotherapy	Untreated patients	Treated patients
	51.47 ± 3.27	70.41 ± 4.27 **

** Significant variance if p≤ 0.01

SDC1 Shedding increases in some diseases such as microbial infections, inflammation, and cancer. chemotherapy used to treat AML has a negative side effect since it can stimulate the synthesis and shedding of SDC1 which leads to the accumulation of SDC1 in the bone marrow extracellular matrix and establishes a microenvironment that promotes the progression of tumor. There are many suggestions to combine using of matrix metalloprotease inhibitors along with chemotherapy to impede the shedding of SDC-1 which may prevent the formation of microenvironments [7,18].

9. Duration of the disease:

The results in Table (10) showed a significant increase in SDC1 concentration with the increased duration of the disease in AML patients and that consists with [5].

Table 10. SDC1 concentration in AML Patients by Disease Duration

	SDC1 conc. (ng/ml) mean± S. E	
Duration of the disease	≤ 3 years	> 3 years
	54.42±5.34	69.10±4.46*

* Significant variance if p≤ 0.05

The expression of shed SDC1 correlated with the stage of the disease and the level of shed SDC1 increased as the tumour stage progressed, which is a poor prognostic indicator in multiple myeloma [5].

10. Other diseases:

A significant increase in SDC1 concentration had been found in patients with AML and diabetes compared with heart diseases and hepatomegaly while no significant differences had been observed between hepatomegaly and heart diseases as the results shown in Table (11) and this is in agreement with [19].

Table 11. SDC1 Concentration in Patients of AML and Other Diseases

Other diseases	SDC1 conc. (ng/ml) mean± S. E
Hepatomegaly	46.67±5.037
Heart diseases	52.41±5.209

Diabetes	72.50±5.680*

* Significant variance if p≤ 0.05

Endothelial dysfunction and inflammation are two factors preceding the progress of diabetes, it was suggested that chronic inflammation in diabetes increases the SDC1 shedding, this may be due to many proinflammatory agents such as tumour necrosis factor and interleukin-6 which accelerate the shedding of SDC1 ectodomains from the surface of the leukocyte, endothelial and vascular smooth muscle cells to the serum[19,20].

11. Family history:

As shown in Table (12) there was a non-significant difference in SDC1 concentration in AML patients according to family history.

Table 12. SDC1 concentration in AML Patients by family history

family history	SDC1 conc. (ng/ml) mean± S. E
Yes	60.35 ± 3.716
No	62.94 ± 7.53

The correlation between SDC1 and hematological parameters in patients:

1. The white blood cell (WBC) count

The results in Table (13) showed a significant increase in SDC1 concentration in AML patients who had a WBC count (≥50x1000 cell/mm^3) compared to (<50x1000 cell/mm^3) and that consists with [9].

Table 13. SDC1 Concentration in AML Patients by Leukocyte Ratio

WBC count	SDC1 conc. (ng/ml) mean± S. E
< 50 x1000 cell/mm^3	52.83±4.04
≥ 50 x1000 cell/mm^3	68.28±5.40*

* Significant variance if p≤ 0.05

Leukocytosis is an increase in the number of WBC in blood, which is caused by overproduction of immature WBC (blasts) in BM, because of abnormal pathways of hematopoietic stem proliferation and differentiation [21]. The expression of SDC1 is associated with leukocytosis and endothelial damage. The activated leukocytes may cause glycocalyx degradation by releasing proteases or adhesion to the endothelium which leads to increases in SDC1 concentration. The association between endothelial damage and leucocytosis increases the risk of hemorrhage and early death in AML [9,10].

2. platelet (PLT) counts

Our results in Table (14) showed a significant increase in SDC1 concentration in patients with low platelet compared to high platelet count and this is in agreement with [10].

Table 14. SDC1 Concentration in AML Patients by Platelet Count

PLT count	SDC1 conc. (ng/ml) mean± S. E
≥ 50×1000/mm³	52.49±3.17
< 50×1000/mm³	71.24±5.53 **

** Significant variance if p≤ 0.01

platelets and hemoglobin decrease in the blood, and this is due to the replacement of normal cells of bone marrow with cancer cells or due to substances produced by the cancer cells that inhibit platelets and hemoglobin production which leads to thrombocytopenia and bleeding, SDC1 expression increases with thrombocytopenia, bleeding and damage of endothelial cell [10,21].

3. Hemoglobin concentration

The results in Table (15) showed a significant increase in SDC1 concentration in AML patients with hemoglobin level (< 10 g/dL) than (> 10 g/dL) and that in agreement with [10,11].

Table 15. SDC1 Concentration in AML Patients by Hemoglobin Percentage

Hemoglobin concentration	SDC1 conc. (ng/ml) mean± S. E
≥10 g/dL	54.60±3.84
< 10 g/dL	68.63±5.61*

* Significant variance if p≤ 0.05

Hemoglobin concentration decreases in AML due to a decrease of red blood cell production in the BM because of the overcrowding of the BM with blasts, which leads to anemia, the most common abnormal hematological symptom of AML, followed by leucocytosis and thrombocytopenia [21]. SDC1 expression increases with thrombocytopenia, bleeding and damage of endothelial cells [10,21].

4. percentage of Blasts Cells in BM

The results in Table (16) showed a significant increase in SDC1 concentration with blast cells (≥60%) compared to (< 60 %) in AML patients. Blast cells percentage in the BM are immature blood cells and non-functional cells that accumulate in the BM and compete with precursors of normal hematopoietic and replace it, leading to cytopenia, leukocytosis and thrombocytopenia which increases the expression and shedding of SDC1[21,22].

Table 16. SDC1 concentration in AML Patients by Bone Marrow blast Cells

Blasts in B.M	SDC1 conc. (ng/ml) mean± S. E
< 60 %	48.36±2.53
≥60 %	69.86±4.65**

** Significant variance if p≤ 0.01

The concentration of some clinical variables in AML patients compared to the control group:

The results in Table (17) showed a significant increase in the concentration of urea and creatinine in patients compared to the control group and that consists with [23], these two parameters reflect the impairment in renal function, acute renal failure is a possible complication of AML due to the releases of lysozyme from leukemia cells which may cause tubular injury and increase urea and creatinine in the bloodstream [23,24]**.** Also, there was a significant increase in the activity of LDH in patients compared to the control group and that consisted with [24], LDH activity is elevated in blood in several disease states including inflammations, infections and malignancies, and its concentration can be elevated due to cellular necrosis in AML patients [25].

Body temperature in patients showed a significant increase in patients compared to the control group and this may be due to infection which is very common in AML patients, while there were no significant differences in systolic and diastolic blood pressure (BP) between patients and the control group.

Table 17. The concentration of some clinical parameters in AML patients compared to control

Clinical variables	Control group mean± S. E	Patients mean± S. E
Urea mmol/l	6.92 ± 1.66	11.45 ± 1.25 *
Creatinine mmol/l	89.86 ± 5.65	141.2 ± 13.89 **
LDH U/l	192.6 ± 13.32	406.9 ± 57.62 **
Systolic BP mm Hg	128.7±2.8	126.6±5.9
Diastolic BP mm Hg	89.28±2.3	83.44±4.5
Tm ºC	37.10±0.10	38.01±0.24**

* Significant variance at P≤0.05, **at P≤0.01

correlation between SDC1 and some clinical variables in AML patients and control group:

Our results in Table (18) showed a significant positive correlation between SDC1 concentration and urea, creatinine, LDH, and body temperature, and this may be due to the glycocalyx damage

under inflammatory and infection conditions which contributes to the impairment of renal function and increases body temperature, while a non-significant negative correlation was observed between SDC1 concentration and systolic and diastolic pressure.

Table 18. correlation between SDC1 and some variables in the control group and AML patients

Clinical Variables	Control group		Patients	
	r- value	p-value	r- value	p-value
Urea mmol/l	0.834	0.0197 *	0.7646	0.01 *
Creatine mmol/l	0.7093	0.0743	0.6589	0.0383 *
LDH U/l	0.8783	0.0093 **	0.7065	0.0224 *
Systolic BP mm Hg	-0.5424	0.0684	-0.1548	0.5669
Diastolic BP mm Hg	-0.4446	0.1476	-0.1203	0.6571
Tm ºC	0.424	0.1017	0.518	0.016 *

* Significant variance at P≤0.05, **at P≤0.01

Conclusion:
SDC1 could be a marker of AML, and its concentration is affected by age, smoking, BMI, ABO blood type, Menopause in women, chemotherapy, duration of disease, diabetes, WBC count, platelet count, hemoglobin and blast in BM. Also, SDC1 correlated positively with urea, creatinine, LDH and blood temperature.

Acknowledgement
We would like to extend our grateful and gratitude to the University of Mosul, College of Education for Girls for all the facilitation that it provided us to complete the research.

Conflict of interests
There is no conflict of interest.

Reference:
1. Narayanan, D. and Weinberg, O. K. How I investigate acute myeloid leukemia. *Int. J. Lab. Hematol*. **2020**, 42(1): 3-15.
2. Prada-Arismendy, J.; Arroyave, J.C.; Röthlisberger, S. Molecular biomarkers in acute myeloid leukemia. *Blood Rev*. **2017**, **31**(1): 63-76.
3. Murphy, T. and Yee, K.W. Cytarabine and daunorubicin for the treatment of acute myeloid leukemia. *Expert Opin. Pharmacother*. **2017**, 18(16): 1765-1780.
4. Shallis, R.M.; Wang, R.; Davidoff, A.; Ma, X.; Zeidan, A.M. Epidemiology of acute myeloid leukemia: Recent progress and enduring challenges. *Blood Rev*. **2019,** 36: 70-87.

5. Czarnowski, D. Syndecans in cancer: A review of function, expression, prognostic value, and therapeutic significance. *Cancer Treat. Res. Commun.* **2021**, 27: 100312.
6. Niedworok, C.; Kempkensteffen, C.; Eisenhardt, A.; Tschirdewahn, S.; Rehme, C.; Panic, A.; Szarvas, T. Serum and tissue syndecan-1 levels in renal cell carcinoma. *Transl. Androl. Urol*. **2020,** 9(3): 1167.
7. Ramani, V.C. and Sanderson R.D. Chemotherapy stimulates syndecan-1 shedding: a potentially negative effect of treatment that may promote tumor relapse. *Matrix Biol.* **2014**, 35: 215-222.
8. Szatmári, T.; Ötvös, R.; Hjerpe, A.; Dobra, K. Syndecan-1 in cancer: implications for cell signaling, differentiation, and prognostication. Dis. Markers, **2015**, 2015:796052.
9. Larsen, A.M.; Leinøe, E.B.; Johansson, P.I.; Birgens, H.; Ostrowski, S.R. High syndecan-1 levels in acute myeloid leukemia are associated with bleeding, thrombocytopathy, endothelial cell damage, and leukocytosis. *Leuk. Res*. **2013,** 37(7): 777-783.
10. Alghandour, R.; Ebrahim, M.A.; Ghazy, H.; Shamaa, S.; Emarah, Z.; Al-Gayyar, M.M. Evaluation of the diagnostic and prognostic value of syndecan-1 in acute leukemia patients. *Cureus*, **2020**, 12(9).
11. Shaker, R.I. and Al-Bayaa, I.M. Assessment of soluble syndecan-1 level in adult patients with de novo acute myeloid leukemia and its correlation with hematological parameters and treatment response. *Iraqi J. Hematol*. **2023**, 12(2): 123-127.
12. Sun, L.; Wang, L.; Ye, K.X.; Wang, S.; Zhang, R.; Juan, Z.; Min, S. Endothelial glycocalyx in aging and age-related diseases. *Aging dis*. **2023**, 14(5): 1606.
13. Higashi, Y. Smoking cessation and vascular endothelial function. *Hypertens Res***. 2023**, 46(12): 2670-2678.
14. Wu, F.; Dorman, B.; Zeineddin, A.; Kozar, R.A. Fibrinogen inhibits metalloproteinase-9 activation and syndecan-1 cleavage to protect lung function in ApoE null mice after hemorrhagic shock. *J. Surg. Res*, **2023**, 288, 208-214.
15. Itenov, T.S.; Sessler, D.I.; Khanna, A.K.; Ostrowski, S.R.; Johansson, P.I.; Erikstrup, C.; Jensen, J.U. ABO blood types and sepsis mortality. *Ann. Intensive Care*, **2021**, 11, 1-9.
16. Jeong, I.H.; Seo, J.Y.; Choi, S.; Kim, H.Y.; Cho, D. ABO Blood Group Antigen Changes in Acute Myeloid Leukemia and No Significant Association with RUNX1 and GATA2 Somatic Variants. *Ann. Lab. Med*., **2023**, 43(6), 635.
17. Potje, S.R.; Martins, N.S.; Benatti, M.N.; Rodrigues, D.; Bonato, V.L.; Tostes, R.C. The effects of female sexual hormones on the endothelial glycocalyx. *Curr. Top. Membr*. **2023**, 91: 89-137.
18. Guo, S.; Wu, X.; Lei, T.; Zhong, R.; Wang, Y.; Zhang, L.; Wu, L. The role and therapeutic value of syndecan-1 in cancer metastasis and drug resistance. *Front. cell dev. biol.* **2022**, 9, 784983.
19. Wang, J.B.; Guan, J.; Shen, J.; Zhou, L.; Zhang, Y.J.; Si, Y.F.; Sheng, Y. Insulin increases shedding of syndecan-1 in the serum of patients with type 2 diabetes mellitus. *Diabetes Res. Clin. Pract.* **2009,** 86(2): 83-88.
20. Kaur, G.; Rogers, J.; Rashdan, N.A.; Cruz-Topete, D.; Pattillo, C.B.; Hartson, S.D.; Harris, N.R. Hyperglycemia-induced effects on glycocalyx components in the retina. *Exp. Eye Res*., **2021**, 213, 108846.
21. Al-Dulaim S.M. Study of the hematological parameter changes of Iraqi Acute Myeloid Leukemia patients before and after Chemotherapy. *J. Popul. Ther. Clin. Pharmacol*. **2023**, 30(12): e210–e217.

22. Pimenta, D.B.; Varela, V.A.; Datoguia, T.S.; Caraciolo, V.B.; Lopes, G.H.; Pereira, W.O. The bone marrow microenvironment mechanisms in acute myeloid leukemia. *Front. cell dev. biol.* **2021**, 9: 764698.
23. Mohammed, H.Q. Study of some biochemical parameters in patients of acute myeloid leukemia. *Al Mustansiriyah J. Pharm. Sci*. **2007**, 4(1): 39-46.
24. Taalab, M.M. and Shaaban Y.E. prognostic Impact of Pretreatment Serum Lactate Dehydrogenase Levels in Adult Patients with Acute Myeloid Leukemia: Single Center Experience. *Benha Med. J.* **2023**, 40(3): 684-692.
25. Farhana, A. and Lappin, S.L. Biochemistry, lactate dehydrogenase StatPearls [Internet]: Publishing; **2022**.