International Journal of Biological Engineering and Agriculture

ISSN: 2833-5376

Volume 03 Number 03 (2024)

www.inter-publishing.com

Estimation level of blood clotting factors (F7, F8,F9) and Interleukin (IL1b,IL-37) in patient with Hemophilia through gene Micro RNA145

Abeer Awad Khaleefa[1], Qussay Noori Raddaam[2], Taghreed Khudhur Mohammed[3]

[1,2]Iraqia university, Colluge of Education

[3]Central Technical University - Al-Mansour Medical Institute

* Correspondence: abeer.A.kahleefa@aliraqia.edu.iq

Abstract: This study was conducted with the aim of knowing the correlation between blood clotting factors (F9, F8, F7), immune factors, interleukins (IL1b, IL-37) and the gene (Micro RNA145) in the blood of patients with hemophilia. Samples were taken from several hospitals in Iraq (Ramadi Hospital For women and children in Anbar Governorate, Tikrit General Hospital in Salah al-Din Governorate, Child Protection Hospital in Baghdad, Baghdad Teaching Hospital laboratories), where the study included 65 samples from patients with hereditary hemorrhage of various types (HA, HB, HC, and W.V.P). The study measured the levels of clotting factors (F9, F8, F7) using the ELISA technique, and investigated the gene expression levels of Micro RNA145 using qRT-PCR technology by converting it to cDNA. The results of the current study showed that the seventh clotting factor, F7, has a significant decrease in its percentage in patients compared to its percentage in healthy people, while the eighth blood clotting factor, F8, has no significant difference. As for the ninth blood clotting factor, F9, a significant decrease in the factor values was found. In infected patients compared to healthy people, the current study also showed that there was a significant decrease in the level of values of interleukin IL-37 in patients compared to the blood of healthy people. As for interleukin IL1b, the results of the current study showed that there was a significant increase in the values of the factor in patients with hemophilia compared to healthy people. As for the results of the genetic analysis, it was not There is a significant difference between the studied gene and the factors (8,9). The study found connections between variables and the expression of the MIR145 gene. Factor 7 was found to be positively correlated with Factors 8 and 9, suggesting potential shared biological influences. Elevated IL 37 levels coincided with increases in Factors 7 and 9, while IL 1b levels were linked to Factors 7 and 8. The links between MIR145 gene expression and Factors 7 and 9 were weaker, suggesting an association between MIR145 expression and these factors. No significant correlation was found between IL 37 and MIR145 gene expression.

Keywords: Clotting Factor, Hemophilia, IL1b, IL-37, And Mirna145.

Citation: Abeer awad khaleefa, Qussay Noori Raddaam, Taghreed Khudhur Mohammed. Estimation level of blood clotting factors (F7, F8,F9) and Interleukin (IL1b,IL-37) in patient with Hemophilia through gene Micro RNA145. International Journal of Biological Engineering and Agriculture 2024, 3(3), 212-224.

Received: 7th June 2024

Revised: 11th June 2024

Accepted: 13th June 2024

Published: 23th June 2024

Introduction

Hemophilia is a hereditary bleeding in which the blood does not clot properly, and this can lead to spontaneous bleeding as well as bleeding after injury or surgery [1]. Blood contains several proteins known as clotting factors that aid in halting bleeding. Individuals with haemophilia exhibit deficiencies in factor VIII (F8) and factor IX (F9) [2]. The degree of haemophilia a person experiences is determined by the level of factor in their blood. Reducing the amount of drug increases the risk of

bleeding, perhaps resulting in severe complications. Occasionally, an individual may get haemophilia at a later stage of life [3]. Most cases affect those who are middle-aged or older and for young women who have recently given birth or are in the later stages of pregnancy, this issue is typically treated with proper therapy [4]. Haemophilia A and B are X-linked recessive disorders caused by defective F8 and F9 genes. Haemophilia C, also known as plasma thromboplastin antecedent deficiency or Melkersson-Rosenthal Syndrome, is an autosomal recessive disorder with a prevalence of 1 in 100,000 males [5]. Acquired haemophilia can occur when autoantibodies are produced against clotting factors. Acquired haemophilia is an uncommon condition with an incidence of one in a million persons [6]. Haemophilia is characterised by internal or external bleeding that can occur spontaneously or with mild shock [7]. Complications of this condition include persistent anaemia, hemarthrosis, cerebral bleeding, and compartment syndrome, characterised by elevated pressure within a bodily region housing muscles and nerves, including the leg and arm. Timely diagnosis and monitoring are necessary to prevent the progression of these problems [8]. Clotting factors are blood proteins that collaborate with platelets to prevent or reduce bleeding. Insufficient clotting factors can lead to severe or uncontrollable bleeding [9].

Haemophilia A is the most prevalent kind, often known as classical haemophilia. It is caused by a deficiency in clotting factor VIII, commonly known as classical haemophilia or standard haemophilia. Haemophilia A (HA) is an inherited bleeding disorder caused by a shortage of Coagulation Factor VIII. FVIII was first characterised in 1994 by Genentech scientists [10].

Haemophilia B is a deficiency in clotting factor IX, often known as Christmas Disease. Individuals with haemophilia A or B may acquire inhibitors that hinder the effectiveness of their factor VIII or IX replacement therapy in forming blood clots to control bleeding. An alternative clotting factor known as a bypassing agent might be utilised as a substitute [11].

This study aims to estimate the levels of clotting factors (F7, F8, F9) in the blood of people suffering from the hereditary bleeding disease hemophilia. Estimating the levels of interleukin IL1b and interleukin IL_37, as well as detecting the gene (Micro RNA145) in patients' sera. By

using appropriate mechanisms and tests, we then conduct statistical operations to find the correlation between these variables.

Materials and Methods

The concentrations of both (F7, F8, F9) and (IL1b, IL-37) were measured using a microtiter plate reader device from the German company (HumaReader HS). This is done using research diagnostic kits based on the enzyme-linked immunosorbent assay (ELISA) method produced by the American company CUSABIO. Special protocols were followed to obtain the results.

Quantification of Micro RNA145 gene expression

All samples have been subjected to extraction of RNA by Direct-zol RNA Miniprep (Zymo, USA, CAT# R2062). After the extraction the samples have been immediately processed to convert from RNA to cDNA by using the kit supplied by adding 2 µl of Takara prime script mixture (2680B) and 7.5 µl of eluted RNA and 0.5 µl of stem loop primer (sequence; GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACA ACCAT) [12]. The tubes then placed into a thermal cycler machine which has been already programmed to maintain the temperature at 37C for 30 min then increase the temperature to 85C for 5 sec.

The estimation of MIR34 Gene expression has been done by real time-PCR technique. Two reaction mixture has been prepared for each sample, one for the amplification of the MIR34 and one for the amplification of the U6 gene (as a reference gene, reverse primer sequence: AAC GCT TCA CGA ATT TGC, and forward primer sequence: CTC GCT TCG GCA GCA CA GT). The mixture has included, 10 µl of Kappa sybr fast 0.5 ml of each forward and reverse primer added to the master mix (sequence of forward primer; CACCCACACCTTGTCCTC, sequence of reverse primer; GTGCAGGGTCCGAGGT), 3 µl of the prepared cDNA, and the volume completed to 20 µl by nuclease free water. The tubes then sealed and placed to a thermo cycler machine and programmed as 40 cycles of 95C for 15 seconds and 60C for 30 seconds come next, then 95C for 5 minutes.

Results and Discussion

As the results shown in figure (1), 65 samples were collected from patients suffering from hemophilia, the hereditary bleeding disease, from (Baghdad Teaching Hospital, Child Protection Hospital in Baghdad, Tikrit General Hospital in Salah al-Din, and Ramadi Women's and Children's Hospital in Anbar). Their ages ranged between (3-66) years and of both sexes. Males, females), where the percentage of females was 14% and the percentage of males was 86%, as shown in the figure (1).

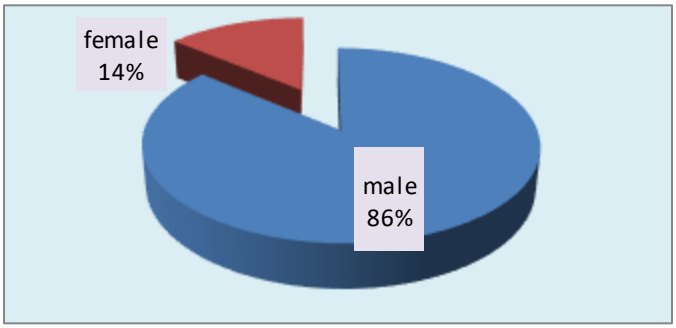

Figure 1. Distribution Of Samples According To Gender

Distribution of samples according to the age group are summarized in table (1). The ages from 1-15 years were 20 samples, i.e. 30%, from 16-30 years 28 samples, i.e. 43%, from 31-45 years 14 samples, i.e. 21%, and from 46-66 years 3 samples, i.e. 4%.

Table 1. Distribution of samples according to the age group

Age group	Frequency	Percent
1 -15	20	30.8
16-30	28	43.1
31-45	14	21.5
46-66	3	4.6
Total	65	100.0

(25) samples of healthy people were collected as a control group from the educational laboratories of Baghdad Hospital, at a rate of 38%. The comparison was between blood clotting factors (F7, F8, F9) and interleukins (IL1b, IL-37) for patients and healthy people using the standard deviation, arithmetic mean, and t-test of differences as shown in

table (2). The results of correlation among the studied parameters of the current study shown in table (3) indicated that there was a significant decrease in the values of blood clotting factor VII (F7), which reached (328.68±127.80) in patients with hemophilia compared to healthy, unaffected people, which reached (1023.24±214.03) at the level of Significant P≤0.05. Which shows that factor VII decreases with the decrease or absence of factor IX and factor VIII. This results agreed with a study [13].

The results of the current study shown in Table (2) also indicated that there was no significant difference in the values of blood clotting factor VIII (F8), which reached (12.94±97.64) in patients with hemophilia compared to healthy, unaffected people, which amounted to (2.54±0.40) because the level The significance of P = 0.531, meaning it is greater than 0.05

This means that the level of factor VIII is not affected by the decrease or increase of the rest of the factors VII and IX, but rather it is protected by the Willebrand factor V.W.P. It is not subject to proteolysis by the Willebrand factor, and its decrease is due to a genetic cause linked to the X chromosome. This result is consistent with [14]. The results of the current study shown in Table (2) also indicated a significant decrease in the values of blood clotting factor IX (F9), which reached (5.72±2.17) in patients with hemophilia.Compared to healthy, uninfected people, it reached (17.14±2.81) at a significant level of P≤0.05.This indicates that factor IX is activated by factor F11 and factor VII F7. This study is consistent with the study of [15].

The results of the current study shown in Table (2) also indicated that there was a significant decrease in the values of interleukin (IL-37), which reached (101.14±24.07) in patients with hemophilia compared to healthy unaffected people, which amounted to (238.64±92.25) at a significant level P ≤0.05. This is because this interleukin has an anti-inflammatory function, meaning it is related to autoimmunity, so it was found to be low in patients. This study was consistent with the study of [16]. The results also indicated a significant increase in the values of interleukin (IL 1b). Its value reached (341.64±69.23) for patients with hemophilia compared to healthy people without it, which amounted to (142.29±47.98) at a significant level of P≤0.05. This is because interleukin IL1b is the main mediator of cartilage damage. Blocking IL-1b can prevent

chondrocyte apoptosis and cartilage damage. These new findings suggest possibilities for preventing blood-induced joint damage in hemophilia. In addition, several IL-1b blockers, including recombinant IL-1 receptor antagonist) and this result agreed [17].

Table 2. Descriptive statistics - mean, standard deviation, and comparison between patients and healthy controls

group		N	Mean	Std. Deviation	Std. Error Mean	t	Sig. (2-tailed)
Factor7	Patients	65	328.68	127.80	15.851897	-18.905 a	0.000 S.
	Healthy	25	1023.24	214.03	42.805912		
Factor 8	Patients	65	12.94	97.64	12.110448	0.531b	0.597 N.S
	Healthy	25	2.54	0.40	.080436		
Factor 9	Patients	65	5.72	2.17	.269569	-20.534 a	0.000 S.
	Healthy	25	17.14	2.81	.561729		
IL-37	Patients	65	101.41	24.07	2.984934	-11.135 a	0.000 S.
	Healthy	25	238.64	92.25	18.450457		
IL-1b	Patients	65	341.64	69.23	8.5875023	13.206 a	0.000 S.
	Healthy	25	142.29	47.98	9.5960571		

The data, in Table 3 reveals connections between factors studied as indicated by Pearson correlation coefficients. Notably there is a positive link between Factor 7 and Factor 8 (r =.930, p <.001) and between Factor 7 and Factor 9 (r =.882, p <.001) suggesting that these factors tend to change together. Additionally Factor 8 and Factor 9 exhibit a positive correlation (r =.967, p <.001) the most pronounced relationship observed in this analysis indicating a strong connection in their behavior or impact.

Regarding interleukin levels Factors 7 8 and 9 all exhibit associations with IL 37 with correlation coefficients of.692,.738 and.722 respectively—all with p values below.001. This implies that as the levels of these factors rise so do the levels of IL 37.

On the contrary IL 1b displays correlations, with Factor 7 (r = .604, p <.001) Factor 8 (r = .632,p <.001) and Factor 9 (r = .710,p<.001).Higher levels of these factors seem to be linked to levels of IL 1b. The genes being studied displayed a relationship, with Factor 7 (r =.342 p =.031) and Factor 8 (r =.363 p =.021) while showing a connection with Factor 9 (r =.427, p =.006). There was no correlation between the genes and IL 37 (r =.008 p =.959) indicating no association. However there was a correlation observed

between the genes and IL 1b (r = .342, p =.031) suggesting that an increase in gene expression may lead to a decrease, in IL 1b levels.

This study agreed with [18]. The results of this study shown in Table (3) indicated that there is a significant correlation between interleukin IL-37 and Factor IX with a value of (0.778) with a direct relationship, as the higher the level of Factor IX, the higher the level of interleukin. The results of this study shown in Table (3) showed that there is a significant correlation between interleukin IL1b and factor IX with a value of (-0.750). An inverse relationship. As the level of the factor increases, the level of interleukin IL1b decreases. Whenever the level of the former increases, the latter decreases. This study was consistent with [19]. The results of this study, as shown in Table (4), showed that there is no significant correlation between the gene (microRNA145) and the level Clotting Factors . This result was consistent with [20].

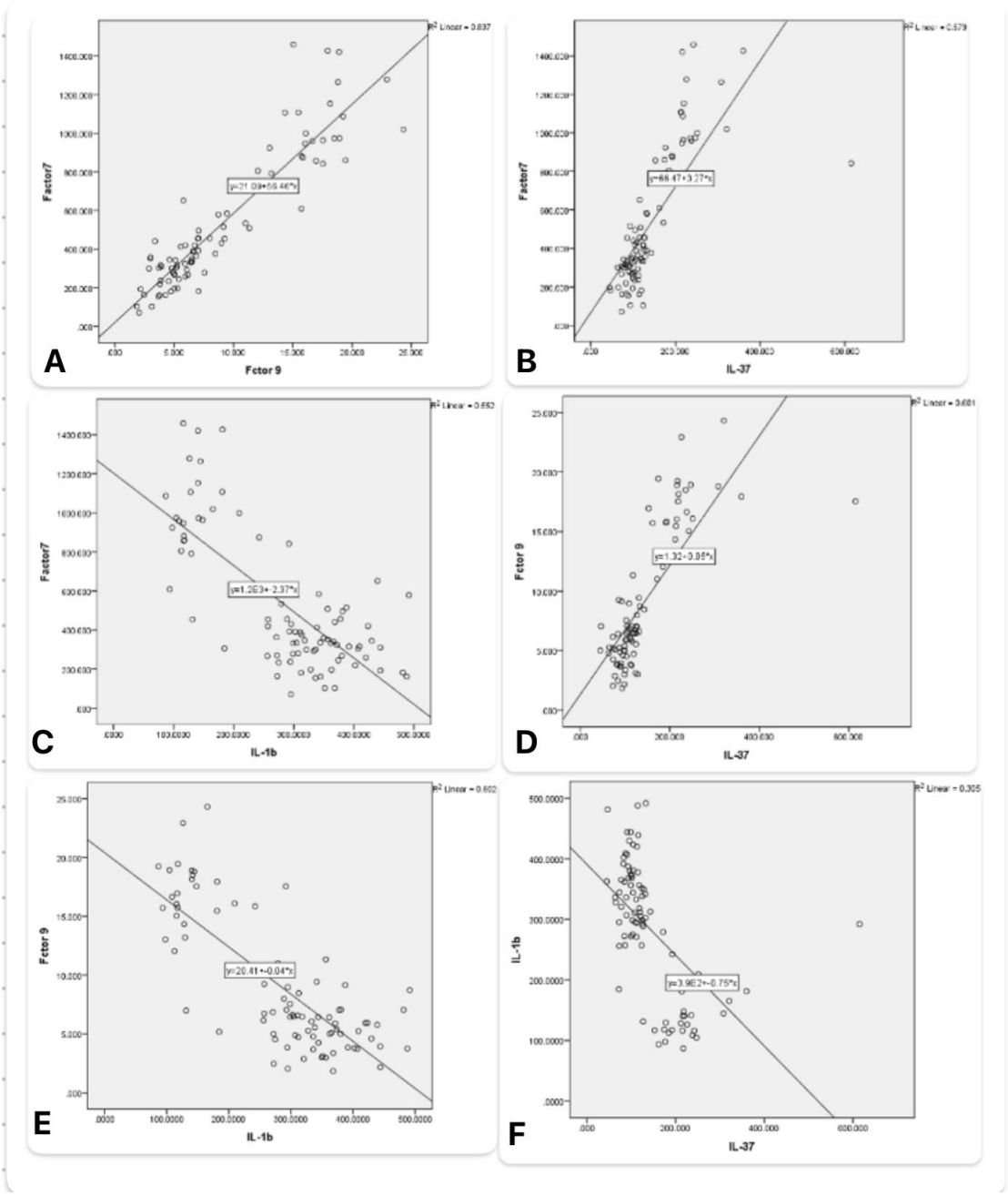

Figure 2. correlations among the studied parameters; A) correlation between factor 7 and factor 9. B) correlation between factor 7 and IL-37. C) correlation between factor 7 and IL-1b. D) correlation between factor 9 and IL-37. E) correlation between factor 9 and IL-1b. F) correlation between IL-1b and IL-37.

The data presented in Table (3) reveals connections, between the variables under study and the expression of the MIR145 gene. Factor 7 exhibits a relationship with both Factor 8 (r =.930, p <.001) and Factor 9 (r =.882 p <.001) indicating that an increase in Factor 7 corresponds to higher levels of Factors 8 and 9. Furthermore Factors 8 and 9 demonstrate a correlation with each other (r =.967, p <.001) implying potential shared biological influences.

A moderate positive correlation was observed between Factor 7 and IL 37 (r =.692, p <.001) while Factors 8 and 9 also displayed associations with IL 37 (r =.738 and r =.722 respectively; p <.001 for both). This suggests that elevations in IL 37 levels coincide with increases, in Factors 7 8 and 9.

Interestingly IL 1b shows a connection, with Factor 7 (r = .604, p <.001) Factor 8 (r = .632, p <.001). Factor 9 (r = .710, p <.001) indicating that elevated levels of these factors are linked to decreased levels of IL 1b.

Regarding MIR145 gene expression, the links with Factor 7 (r =.342 p =.031) Factor 8 (r =.363, p =.021) and Factor 9 (r =.427, p =.006) are positive and statistically significant but relatively weaker. This implies an association between MIR145 expression and these factors though not as strong as the connections among the factors themselves. No notable correlation is observed between IL 37 and MIR145 gene expression (r =.008 p =.959) indicating no link in this dataset. Conversely there is an inverse relationship, between IL 1b and MIR145 gene expression (r = .342, p =.031) suggesting that higher IL 1b levels correspond to lower MIR145 expression.

The study showed that Factor 7 Factor 8 and Factor 9 are positively correlated with the MIR145 gene expression indicating a synergistic effect, on gene expression. This study can be considered as one of the pioneers to seek into the correlation among those factors and interleukins with the gene expression of MIR145. However, many previous studies showed the role of numerous MIRs in Hemophilia [21][22]. And one study focused on the relation between MIR145 [23].

Lastly our research revealed a correlation between IL 1b and MIR145 gene expression suggesting a feedback loop mechanism as proposed by Feng et al. (2022) [24]. According to their hypothesis elevated levels of inflammatory cytokines could lead to the suppression of MIR145 expression.

Table 3. Correlation Among The Studied Parameters And MIR145 Gene Expression

stat		Factor7	Factor 8	Fctor 9	IL-37	IL-1b	Genes
Factor7	Pearson Correlation	1	.930**	.882**	.692**	-.604**	.342*

	Sig. (2-tailed)		0	0	0	0	0.031
	N	40	40	40	40	40	40
Factor 8	Pearson Correlation	.930**	1	.967**	.738**	-.632**	.363*
	Sig. (2-tailed)	0		0	0	0	0.021
	N	40	40	40	40	40	40
Fctor 9	Pearson Correlation	.882**	.967**	1	.722**	-.710**	.427**
	Sig. (2-tailed)	0	0		0	0	0.006
	N	40	40	40	40	40	40
IL-37	Pearson Correlation	.692**	.738**	.722**	1	-.349*	0.008
	Sig. (2-tailed)	0	0	0		0.027	0.959
	N	40	40	40	40	40	40
IL-1b	Pearson Correlation	-.604**	-.632**	-.710**	-.349*	1	-.342*
	Sig. (2-tailed)	0	0	0	0.027		0.031
	N	40	40	40	40	40	40
genes	Pearson Correlation	.342*	.363*	.427**	0.008	-.342*	1
	Sig. (2-tailed)	0.031	0.021	0.006	0.959	0.031	
	N	40	40	40	40	40	40

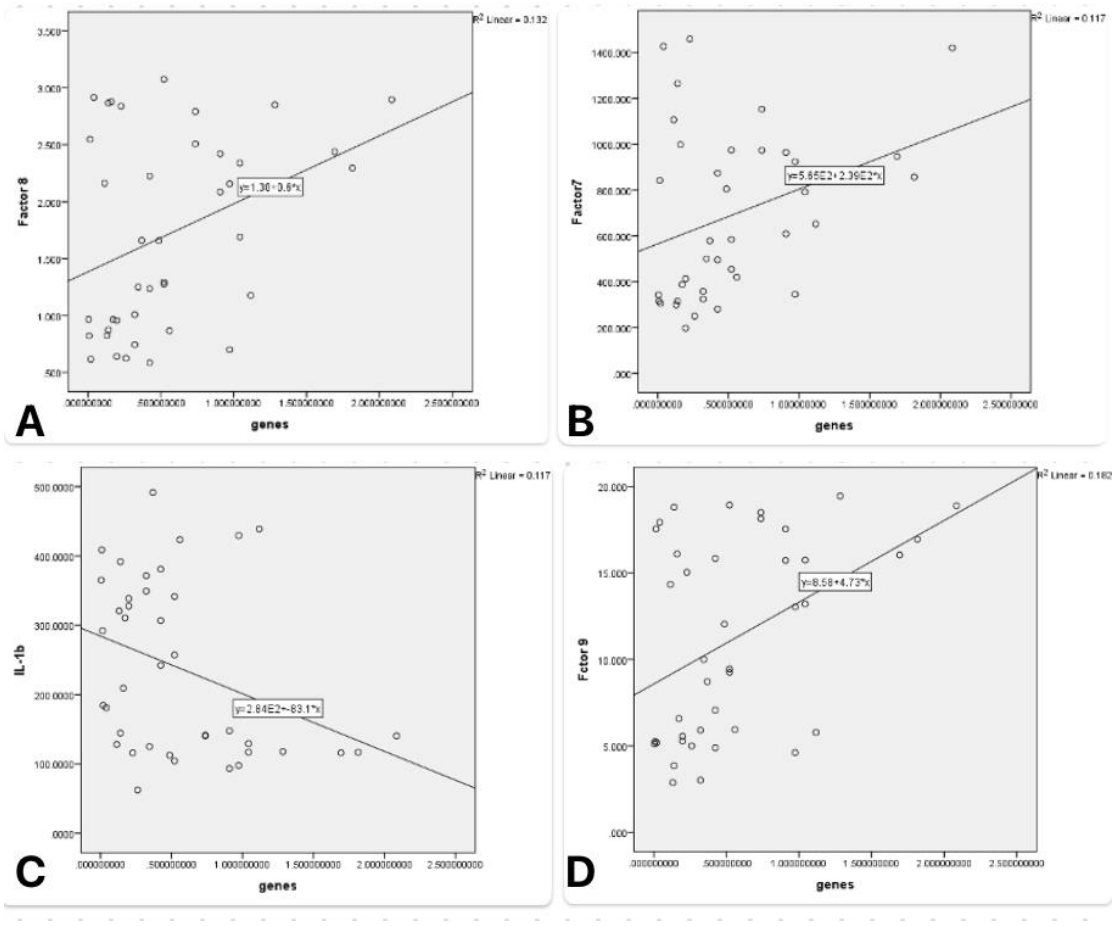

Figure 3. correlations among the studied parameters; A) correlation between factor 8 and MIR145 gene expression. B) correlation between factor 7 and MIR145 gene expression. C) correlation between factor IL-1b and MIR145 gene expression. D) correlation between factor 9 and and MIR145 gene expression.

Conclusion

1. Factor VII (F7) showed a significant decrease in patients compared to healthy individuals.
2. Factor VIII (F8) did not exhibit a significant difference, indicating that its levels are not affected by the variations in other factors (F7 and F9).
3. Factor IX (F9) demonstrated a significant decrease in patients compared to healthy individuals, suggesting that Factor IX is activated by Factor XI and Factor VII.
4. Interleukin IL-37 showed a significant decrease in patients compared to healthy individuals.
5. Interleukin IL-1b exhibited a significant increase in patients with hemophilia compared to healthy individuals.
6. The study reveals connections between elements and MIR145 gene expression, but discrepancies need further exploration. Future studies should consider population variations, research methods, and environmental factors, and conduct longitudinal investigations.

References

1. Mitchell WB, Walsh C. Hemophilia. Atlas of Diagnostic Hematology [Internet] 2023 [cited 2024 Apr 1];360–7. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551607/
2. Al Allaf FA, M Taher M. Mutation Screening of the Factor VIII Gene in Hemophilia A in Saudi Arabia: Two Novel Mutations and Genotype-Phenotype Correlation. Journal of Molecular and Genetic Medicine 2016;10.
3. Al-Allaf FA, Taher MM, Abduljaleel Z, Bouazzaoui A, Athar M, Bogari NM, et al. Molecular Analysis of Factor VIII and Factor IX Genes in Hemophilia Patients: Identification of Novel Mutations and Molecular Dynamics Studies. J Clin Med Res [Internet] 2017 [cited 2024 Apr 1];9:317. Available from: /pmc/articles/PMC5330775/
4. Benson G, Auerswald G, Dolan G, Duffy A, Hermans C, Ljung R, et al. Diagnosis and care of patients with mild haemophilia: practical recommendations for clinical management. Blood Transfusion [Internet] 2018 [cited 2024 Apr 1];16:535. Available from: /pmc/articles/PMC6214819/
5. Wheeler AP, Gailani D. Why factor XI deficiency is a clinical concern. Expert Rev Hematol 2016;9:629–37.
6. Jayakrishnan T, Shah D, Mewawalla P. Hemophilia C: A Case Report With Updates on Diagnosis and Management of a Rare Bleeding Disorder. J Hematol [Internet] 2019 [cited 2024 Apr 1];8:144. Available from: /pmc/articles/PMC7153668/
7. McCarthy ML, Ordway SM, Jones RM, Perkins JG. Successful perioperative management in a patient with factor XI deficiency. BMJ Case Rep 2018;2018.
8. Purcell D, Terry BA, Sharp BR. Acute Compartment Syndrome. Emergency Orthopedics Handbook [Internet] 2023 [cited 2024 Apr 1];79–85. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448124/
9. Doherty TM, Kelley A. Bleeding Disorders. Gynakol Endokrinol [Internet] 2023 [cited 2024 Apr 1];17:25–38. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541050/
10. Mansouritorghabeh H. Clinical and Laboratory Approaches to Hemophilia A. Iran J Med Sci [Internet] 2015 [cited 2024 Apr 1];40:194. Available from: /pmc/articles/PMC4430880/
11. Konkle BA, Fletcher SN. Hemophilia B. GeneReviews® [Internet] 2023 [cited 2024 Apr 1];Available from: https://www.ncbi.nlm.nih.gov/books/NBK1495/
12. Kramer MF. STEM-LOOP RT-qPCR for miRNAS. Current protocols in molecular biology / edited by Frederick M. Ausubel ... [et al.] [Internet] 2011 [cited 2023 Mar 3];CHAPTER:Unit15.10. Available from: /pmc/articles/PMC3152947/
13. Misenheimer TM, Kumfer KT, Bates BE, Nettesheim ER, Schwartz BS. A candidate activation pathway for coagulation factor VII. Biochemical Journal [Internet] 2019 [cited 2024 Apr 2];476:2909. Available from: /pmc/articles/PMC6792035/
14. Sorrells MG. Development of microfluidic devices to measure and model hemostasis. 2022 [cited 2024 Apr 2];Available from: https://repository.mines.edu/handle/11124/15381
15. Alshaikhli A, Killeen RB, Rokkam VR. Hemophilia B. Transfusion Medicine and Hemostasis: Clinical and Laboratory Aspects [Internet] 2023 [cited 2024 Apr 2];533–6. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560792/

16. Lin PC, Chiou SS, Hsu WY, Liao YM, Tsai SP, Su HL, et al. Plasma levels of IL-1β and IL-37 in patients with severe haemophilia. J Int Med Res [Internet] 2020 [cited 2024 Apr 2];48. Available from: /pmc/articles/PMC7375719/
17. Lin PC, Chiou SS, Hsu WY, Liao YM, Tsai SP, Su HL, et al. Plasma levels of IL-1β and IL-37 in patients with severe haemophilia. J Int Med Res [Internet] 2020 [cited 2024 Apr 2];48. Available from: https://pubmed.ncbi.nlm.nih.gov/32691667/
18. Petrillo T, Ayombil F, Veer CV, Camire RM. Regulation of factor V and factor V-short by TFPIα: Relationship between B-domain proteolysis and binding. Journal of Biological Chemistry 2021;296:100234.
19. Lin PC, Chiou SS, Hsu WY, Liao YM, Tsai SP, Su HL, et al. Plasma levels of IL-1β and IL-37 in patients with severe haemophilia. Journal of International Medical Research [Internet] 2020 [cited 2024 Apr 2];48. Available from: https://journals.sagepub.com/doi/full/10.1177/0300060520940512
20. Jankowska KI, Sauna ZE, Atreya CD. Role of microRNAs in Hemophilia and Thrombosis in Humans. International Journal of Molecular Sciences 2020, Vol. 21, Page 3598 [Internet] 2020 [cited 2024 Apr 2];21:3598. Available from: https://www.mdpi.com/1422-0067/21/10/3598/htm
21. Sennblad B, Basu S, Mazur J, Suchon P, Martinez-Perez A, Vlieg A van H, et al. Genome-wide association study with additional genetic and post-transcriptional analyses reveals novel regulators of plasma factor XI levels. Hum Mol Genet [Internet] 2017 [cited 2024 Apr 5];26:637. Available from: /pmc/articles/PMC5703348/
22. Jankowska KI, Sauna ZE, Atreya CD. Role of microRNAs in Hemophilia and Thrombosis in Humans. Int J Mol Sci [Internet] 2020 [cited 2024 Apr 5];21. Available from: /pmc/articles/PMC7279366/
23. Sennblad B, Basu S, Mazur J, Suchon P, Martinez-Perez A, Vlieg A van H, et al. Genome-wide association study with additional genetic and post-transcriptional analyses reveals novel regulators of plasma factor XI levels. Hum Mol Genet [Internet] 2017 [cited 2024 Apr 5];26:637. Available from: /pmc/articles/PMC5703348/
24. Feng X, Yao F, Lang Y, Cao Z. Downregulation of miR-145 alleviates ox-LDL-induced inflammation by targeting QKI in macrophages. Am J Transl Res [Internet] 2022 [cited 2024 Apr 5];14:4251. Available from: /pmc/articles/PMC9274569/