



ATM Gene Mutations in Iraqi Patients with Chronic Lymphocytic Leukemia Patients in Kurdistan Region -Iraq

Chra Fadhil Kudhur¹ , Kazhal Muhammad Sulaiman²

^{1,2}Department of Biology College of Education, University of Salahaddin-Erbil

Received: 19 July 2025. Received in revised form: 17 Sep. 2025. Accepted: 21 Sep. 2025.

Final Proofreading: 27 Sep. 2025. Available online: 25 Oct. 2026.

ABSTRACT

Chronic Lymphocytic Leukemia (CLL) is the most common form of leukemia in adults, often discovered incidentally in asymptomatic patients who show peripheral blood lymphocytosis during routine blood tests. Pathogenic variants in the protein kinase ataxia telangiectasia mutated (ATM) gene, situated on the long arm of chromosome 11 (11q22–23), are implicated in the development of ataxia-telangiectasia, a rare autosomal recessive neurodegenerative disorder. To meet the requirements of the study, 50 patients who were suffering from CLL at Nanakli Hospital for Blood Diseases and Cancer in Erbil City and 20 healthy individuals as a control group in both sexes of different age groups were chosen. To detect possible mutations in the ATM gene exons 19 and intron 19 and 20, which are located among these exons, the Sanger sequencing method was utilized. The results showed missense mutations in only two cases. Additionally, one case exhibited a mutation in intron 19. However, ATM gene mutations are not a suitable diagnostic or evaluative marker for CLL epidemiology in our population. Among patients aged 61–70 years diagnosed with chronic lymphocytic leukemia, 60% are male, while only 40% are female. Also, by occupation, the highest proportion of cases was among female homemakers (30%), followed by male dyers (20%).

Keywords: Chronic lymphocytic leukemia, ATM gene, Risk factors, Erbil City.

Name: Chra Fadhil Kudhur

E-mail: Chra.Khudhur@su.edu.krd



©2026 THIS IS AN OPEN ACCESS ARTICLE UNDER THE CC BY LICENSE <http://creativecommons.org/licenses/by/4.0/>

طفرات جين ATM لدى مرضى سرطان الدم الليمفاوي المزمن العراقيين في إقليم كردستان العراق

جرا فاضل خضر¹، كetzال محمد سليمان²

^{1,2} قسم علم الاحياء، كلية التربية، جامعة صلاح الدين - اربيل

الملخص

يُعد سرطان الدم الليمفاوي المزمن (CLL) أكثر أشكال سرطان الدم شيوعاً لدى البالغين، وغالباً ما يُكتشف بالصدفة لدى المرضى الذين لا تظهر عليهم أعراض والذين يُظهرون كثرة الخلايا الليمفاوية في الدم المحيطي أثناء فحوصات الدم الروتينية. تُعزى المتغيرات المُمرضة في جين بروتين كيناز ترنج توسع الشعيرات المتحور (ATM)، الواقع على الذراع الطويلة للكروموسوم 11 (q22-2311)، إلى تطور ترنج توسع الشعيرات، وهو اضطراب عصبي تنكسي نادر جسمي متخّج. ولتلبية متطلبات الدراسة، تم اختيار 50 مريضاً يعانون من سرطان الدم الليمفاوي المزمن في مستشفى ناناكلي لأُمراض الدم والسرطان في مدينة أربيل، و20 فرداً سليماً كمجموعة ضابطة من كلا الجنسين ومن مختلف الفئات العمرية. للكشف عن الطفرات المحتملة في إكسونات جين ATM 19 والإنترون 19 و20، والموجودة بين هذه الإكسونات، استُخدمت طريقة تسلسل سانجر. أظهرت النتائج حدوث الطفرات غير المتماثلة في حالتين فقط. بالإضافة إلى ذلك، أظهرت حالة واحدة طفرة في الإنترون 19. ومع ذلك، لا يمكن اعتبار طفرات جين ATM مؤشراً تشخيصياً أو تقييمياً مناسباً لانتشار سرطان الدم الليمفاوي المزمن في مجتمعنا. من بين المرضى الذين تتراوح أعمارهم بين 61 و70 عاماً والذين شُخصوا بسرطان الدم الليمفاوي المزمن، 60% منهم ذكور، بينما 40% فقط إناث. كما كانت نسبة الإصابة بالمرض مرتبطة بنوع المهنة لدى معظم النساء ربات البيوت بنسبة (30%)، يليهن رجال داير (20%).

1. INTRODUCTION

Leukemia is defined by the unregulated proliferation of white blood cells in the bloodstream and bone marrow. Leukemia is classified into four types: Chronic Lymphocytic Leukemia, Acute Lymphoblastic Leukemia, Chronic Myeloid Leukemia, and Acute Myeloid Leukemia ⁽¹⁾. CLL is a clonal lymphoproliferative disorder characterized by peripheral B-lymphocyte counts over $5 \times 10^9/L$ that express Cluster of Differentiation 5, Cluster of Differentiation 19, and Cluster of Differentiation 23, with poor expression of Cluster of Differentiation 20, Cluster of Differentiation 79b, and surface immunoglobulin ⁽²⁾. Common chromosomal abnormalities in B-cell Chronic Lymphocytic Leukemia, such as deletions of 13q, 11q, and 17p, have been associated with therapy stratification and prognosis ⁽³⁾. Chromosomal alterations significantly contribute to carcinogenesis, and growing evidence suggests that detecting them in peripheral blood lymphocytes indicates cancer risk ⁽⁴⁾. CLL exhibits a varied

genetic mutation burden throughout its progression ⁽⁵⁾. The ATM gene belongs to the phosphatidylinositol-3 kinase (PI3K) gene family and comprises 66 exons, 62 of which are coding exons ⁽⁶⁾. The protein kinase ataxia telangiectasia mutated (ATM) acts as a tumor suppressor, is triggered by double-stranded DNA breaks, and is essential in the DNA damage response. Somatic mutations in ATM have been documented in 7–16% of CLL patients. The ATM gene, located on the q-arm of chromosome 11, is frequently lost in 10–24% of patients ⁽⁷⁾. Del(11q) has long been acknowledged as an indicator of poor prognosis in CLL, with affected patients often exhibiting lymphadenopathy, experiencing an elevated risk of progression, and typically having a worse prognosis. Conflicting data currently exist on whether ATM mutations, with or without del(11q), suggest a poor clinical outcome ⁽⁸⁾.

This research aimed to identify ATM gene mutations in exon 19 and introns 19 and 20

associated with CLL development. A multitude of elements contributing to the disease's development have also been examined. These include the patient's gender, age, occupation, residency, familial relationships between the patient's parents, and the family's medical history.

2. MATERIALS AND METHODS

2.1 Samples Collection

Approximately 4 mL of peripheral blood was collected from 50 patients with chronic lymphocytic leukemia (CLL) and 20 healthy individuals as a control group, then placed in EDTA tubes for genomic analysis. Additionally, each patient was supplied with a specialized questionnaire form to be completed, encompassing fields for personal information such as name, address, gender, age, smoking habits, blood disorders, genetic conditions, and occupation.

The questionnaire forms were completed through direct interviews with patients and their relatives, using available hospital medical records, with assistance from doctors and staff. This research was carried out from July 1, 2024, to January 7, 2025, at Nanakli Hospital for Blood Diseases and Cancer in Erbil.

2.2 Molecular assay

We extracted genetic material from blood using the Genomic DNA Extraction Kit (QIAamp Blood Mini Kit, KOREA), following the manufacturer's protocol and instructions. DNA extraction was conducted at the Immunogenic Center in Erbil, Kurdistan Region, Iraq. The concentration and purity of isolated genomic DNA were assessed using the NanoDrop (Thermo Fisher, USA) at the Salahaddin University Research Center in Erbil, Kurdistan Region, Iraq. Approximately two milliliters of extracted DNA were analyzed using the absorbance technique. This apparatus measures the optical density (absorbance) of light at specific wavelengths in diluted DNA samples. The optical density is measured at 260 and 280 nanometers. The absorbance ratio (260/280) indicates DNA quality. Absorbance ratio (R) values of 1.8 to 2.0 are considered appropriate (9), and DNA is stored at -

20° for subsequent applications. Forward primer for ATM exon 19: 5'GCCAGGCTGTTCTCAAAC'3; reverse primer: 5'CAAGCGACTGAGGGAAACAC'3. The PCR mixture was prepared according to the kit protocol (QIAamp Blood Mini Kit (QIAGEN), KOREA). The PCR reaction was conducted for 35 cycles in a programmable thermocycler (AB Applied Biosystems), comprising denaturation at 95°C, annealing at 60°C, and extension at 72°C, each for 30 seconds. The PCR reactions were conducted in a 30 µL volume. The components of the PCR reaction and their respective amounts in a total volume of 30 µL. After ensuring that the lid was properly placed on the tank and that the wires were precisely positioned, a voltage of 100-120 volts was applied to the power source for ten minutes, allowing the DNA to exit the wells and migrate towards the positive electrode. This was executed to guarantee optimal outcomes and maximum resolution. Ultraviolet light at 240 and 366 nm during UV transillumination enabled visualization of the DNA band ⁽¹⁰⁾.

2.3 Sanger Sequencing

The exon 19 PCR products of the ATM gene were purified and sequenced using the Sanger technique with a 3130 Genetic Analyzer (Applied Biosystems, Hitachi High Technologies, Tokyo, Japan) in Iran, with support from the Immunogene Center in Erbil, Kurdistan area, Iraq. The sequence results were examined using software such as FinchTV and BioEdit to identify both known and new mutations. We used the GenBank reference sequence [NM 000051.4] for mutation nomenclature. The sequence variations were designated and referenced in the literature in accordance with the nomenclature established by the Human Genome Variation Society (HGVS; <http://www.hgvs.org>).

2.4 Statistical Analysis

Statistical analysis and graphical representations were conducted utilizing GraphPad Prism software (version 9.0). Chi-square tests and descriptive statistics were utilized to examine chronic lymphocytic leukemia (CLL) in connection with

many factors. We used a chi-square test of independence to analyze relationships among certain categorical variables. A chi-square test evaluates the relationship between two variables in a contingency table. The gathered data were systematically categorized and processed with Microsoft Office Excel 365.

3. RESULTS AND DISCUSSION

3.1 Demographic Study

First, here is the study of demographic characteristics, basic information, abundance and frequency of the subjects:

Table 1: Demographic characteristics, basic information, abundance and frequency of the subjects.

		Patient		control	
variable		Abundance	Frequency	Abundance	Frequency
Gender	Male	31	62	13	65
	Female	19	38	7	35
Occupation	housewife	15	30	6	30
	Employee	6	12	2	10
	Dyer	10	20		
	Teacher	2	4	4	20
	Industrial	3	6		
	Mechanics	4	8	0	0
	Carpenter	3	6	0	0
	Traffic police	1	2	1	5
	Police	1	2	0	0
	Petrol station attendant	1	2	0	0
	Farmer	1	2	0	0
	Jobless	3	6	0	0
	Worker	0	0	7	35
Residence	Erbil	28	56	20	100
	Outside of Erbil	22	44	0	0
Age groups	41-50	7	14	6	30
	51-60	12	24	6	30
	61-70	20	40	6	30
	71-80	10	20	1	5
	>80	1	2	1	5
Consanguinity	Yes	18	36	11	55
	No	32	64	9	45

3.1.1 The distribution of patients with chronic lymphocytic leukemia according to their ages and sex

Figure (1) indicates that the majority of patients with CLL are male, comprising 62%, attributed to

their occupations and several other reasons, while females account for 38%, as shown in Table 1 ⁽¹¹⁾. CLL occurs at 30 cases per 100,000 annually among individuals over 80 years of age, with a notable male predominance. CLL prevalence increases with age, with the median age of onset in the United States ranging from 67 to 72 years ⁽¹²⁾.

Sex chromosomes, sex hormones, and genetic determinants significantly influence the genesis and course of hematological malignancies. Loss of sex chromosomes, particularly tumor suppressor genes in the pseudo-autosomal region of the X chromosome, is commonly reported in several illnesses. This may be attributed to sex hormones, as shown in studies on androgen-induced immunosuppression (13), which found that androgens influence the rate of immunological response and may help explain disparities in disease occurrence between males and females, particularly in malignancies.

Figure 1 indicates that the majority of patients with CLL fall within the age range of 61 to 70 years, including 60% of the male population. Only 40% of individuals aged 61 to 70 years are female. Comparable results were observed in (14). The male-to-female ratio in many lymphoid neoplasms, including CLL, at diagnosis is 2:1. It is preceded by a comparable incidence in monoclonal B-cell lymphocytosis, the precursor disease to CLL, where men have a higher risk of developing the malignancy.

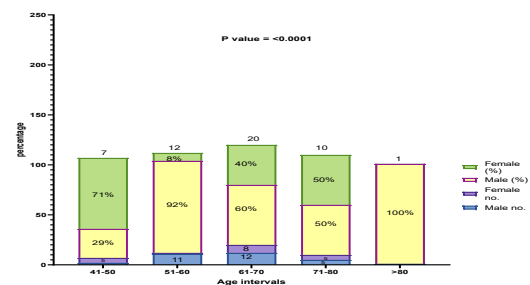


Fig. 1: Distribution of patients with Chronic Lymphocytic Leukemia by age and sex.

3.1.2 The distribution of patients with Chronic Lymphocytic Leukemia according to their occupations

Figure (2) indicates that CLL was more prevalent among homemakers at 30%, followed by dyers at 20%. Occupational exposure studies provide the strongest evidence for a potential role of chemicals in CLL development. Reports indicate an elevated risk associated with specific sectors, occupations, and workplace exposures. The use of dishwashing detergents and personal care products, such as cosmetics, may contribute to CLL development, as (15) determined in the research (Exposure to Chemicals and Radiation During Childhood and Risk for Cancer Later in Life).

The heightened hazards of CLL noted in farm laborers are postulated to be associated with exposure to various chemicals, including pesticides, and/or biological agents. Potential carcinogenic processes associated with pesticide exposure include oxidative stress, disruption of methyltransferase activity, endocrine disruption, DNA methylation and other epigenetic modifications, and reduced S-adenosylmethionine, among others (16).

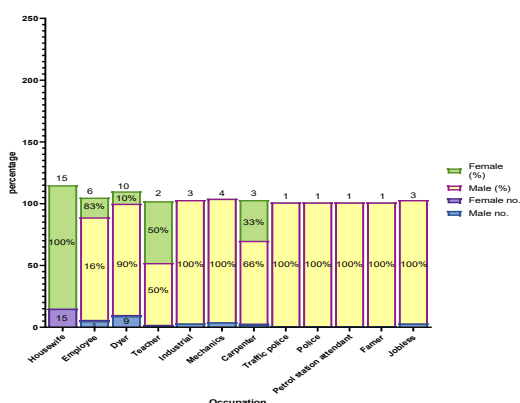


Fig. 2: Distribution of patients with Chronic Lymphocytic Leukemia by occupation.

3.1.3 The Distribution of patients with Chronic Lymphocytic Leukemia according to their location

Figure (3) illustrates that the majority of patients with CLL resided in Erbil city, accounting for 56%. Conversely, Table 1 shows that 44% of CLL patients lived outside Erbil city. This 14% disparity

between patients residing outside the city and those within can be attributed to health culture and economic status.

Urban areas, characterized by large populations and significant environmental contaminants, significantly affect public health. The elevated incidence of disease diagnoses among males in the metropolis may be attributed to the aggregation of environmental pollutants, as indicated in the published research (17). Urban populations may face higher exposure to industrial pollutants, traffic-related air pollution, and other carcinogens. Urban residents often have different dietary habits, reduced sunlight exposure (affecting vitamin D levels), and lower physical activity compared to rural populations.

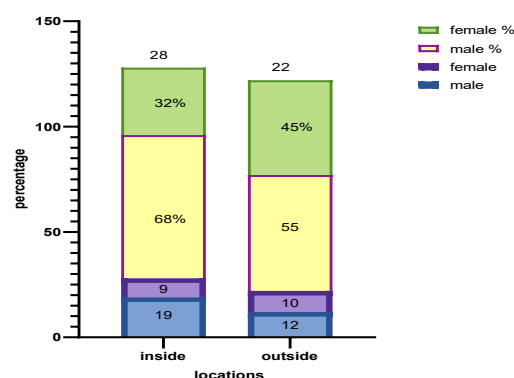


Fig. 3: Distribution of patients with Chronic Lymphocytic Leukemia by location.

3.1.4 The Distribution of patients with Chronic Lymphocytic Leukemia according to the presence of consanguinity between parents

Figure 4 depicts the distribution of patients with CLL based on parental consanguinity. Consanguineous marriage is defined as a relationship between biologically related persons. This relationship comprises a series of parameters that, when combined, can indicate a specific percentage of either detrimental or advantageous outcomes affecting filial health. The high prevalence of consanguinity in our populations contributes to the persistence of recessive inheritance patterns, increasing the risk of homozygous or doubly heterozygous clinically affected progeny, which imposes considerable psychological and financial strains on families and

substantial burdens on the economic resources of numerous countries in the region. The "premarital screening program" addresses a preventable disease (18).

The chart clearly indicates that patients without parental consanguinity make up a significant percentage (64%), whereas patients with consanguineous parents represent a smaller proportion (36%). This finding aligns with results from (19), which concluded from the study (Age-standardized Incidence Rates for Leukemia Associated with Consanguineous Marriages in 68 Countries) that leukemia rates are lower in countries with a high prevalence of consanguineous marriages.

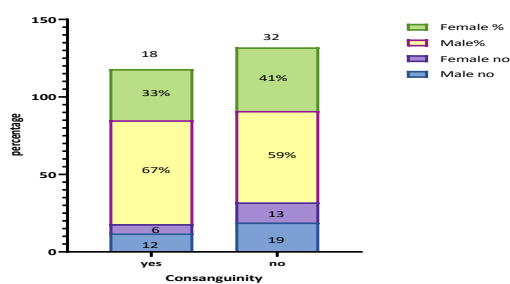


Fig. 4: Distribution of patients with Chronic Lymphocytic Leukemia according to the presence of consanguinity between parents.

3.2 Molecular Genetic Study

The study's findings indicated that ATM mutation should not be regarded as an appropriate assessment criterion for the evaluation and diagnosis of CLL. The results show a strong correlation between age and increased CLL risk, as the likelihood of infection rises with advancing age.

3.2.1 Gel Electrophoresis of PCR Product

As detailed in the preceding section, PCR was performed on seventy samples using primers to amplify specific regions of the ATM gene, including exon 19 and introns 19 and 20 between these exons. The evaluation of PCR product amplification was performed using gel electrophoresis prior to dispatching the amplified samples for sequencing. To optimize primers, we determined the annealing temperature that produced the most distinct band. The PCR product bands on

the gel corresponded to specific molecular weights on the DNA ladder, as shown in Figures 5 and 6.

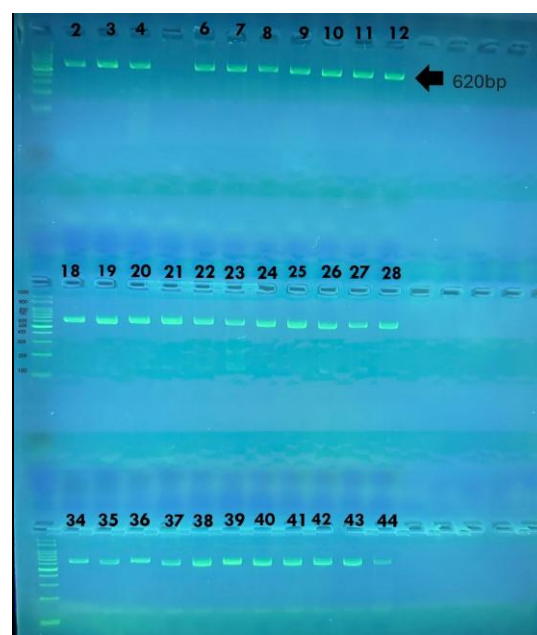


Fig. 5: Agarose gel electrophoresis of the amplified PCR product of the ATM gene (Exon 19 and Introns 19 and 20). The band was separated by electrophoresis and visualized under ultraviolet light after staining with a safe dye (L 100bp M: ladder); Lanes 2-50: 2-50 subjects (Experimental Group) in the current study. All patient samples had a band at 620 bp.

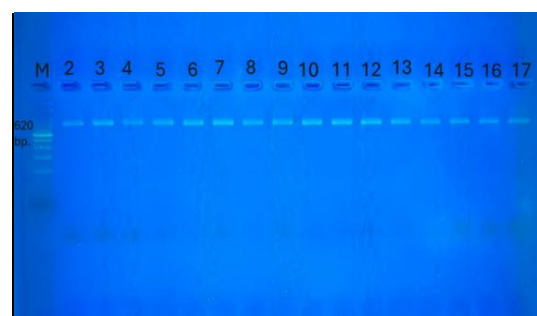


Fig. 6: Agarose gel electrophoresis of the amplified PCR product for the ATM gene, namely Exon 19 and Introns 19 and 20. We separated the bands by electrophoresis and visualized them under ultraviolet light after staining with a safe dye (L 100bp M: ladder); Lanes 2-17 represent normal healthy persons (Control Group) in the current investigation. All control samples had a band at 620 bp.

We directly sequenced the examined regions in both cases and controls. Missense mutations were detected. Of the 70 participants investigated, 50 were patients with CLL and 20 were controls. This study indicated that the incidence of positive

(mutant) results is minimal; Table 2 shows that most patient test outcomes are negative.

Table 2: The number and ratio of mutations.

Test Result	frequency	percentage
Negative (normal)	68	97.14
Positive (mutant)	2	2.85
Total	70	100

Mutations in the ATM gene were identified in 2 out of 50 patients, including a missense mutation where the original codon was AAG (Lysine) and the mutation changed it to AGG (Arginine) at position 53249, and the original codon was GAG (Glutamic acid) and the mutation changed it to GAC (Aspartic acid) at position 53253; both mutations are in sample 49 in Figure 7.

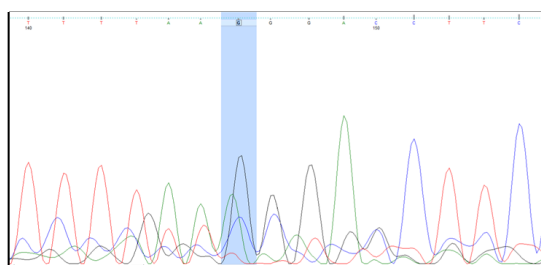


Fig. 7: The nucleotide sequence (Forward) shows a missense mutation (A>G) identified in the ATM gene Exon 19 in patient number 49.

In sample 50, the original codon was GAG (Glutamic acid), and the mutation changed it to AAG (Lysine) in Figure 8. It identified a mutation in the ATM gene characterized as compound heterozygous: a missense mutation in exon 19, resulting in an amino acid substitution from glutamic acid to lysine. The normal nucleotide sequence of the ATM gene (Exon 19) in the control sample is shown in Figure 9.

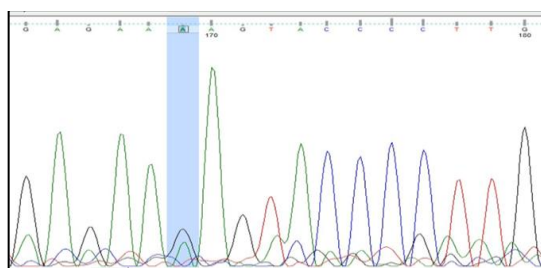


Fig. 8: The nucleotide sequence (Forward) shows a missense mutation (G>A) identified in the ATM gene (Exon 19) in patient number 50.

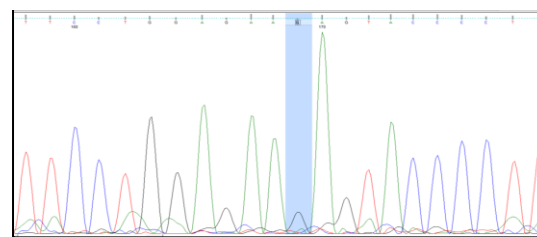


Fig. 9: The normal nucleotide sequence (Forward) of the ATM gene (Exon 19) in control sample 1.

A mutation was identified in intron 19 of the ATM gene in case number 49. The variation is potentially intronic and may influence normal RNA splicing, as depicted in Figure 10.

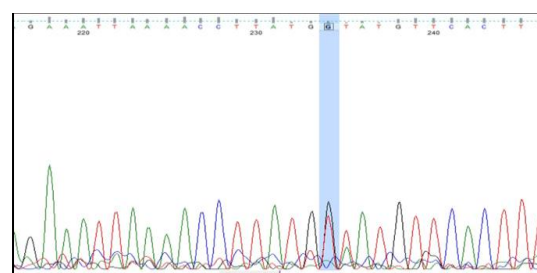


Fig. 10: The nucleotide sequence shows a splicing mutation (T>G) identified in intron 19 of the ATM gene in patient 49.

The ATM mutation frequency among CLL patients in the Kurdistan area of Iraq is 4%. This result is analogous to the findings of (20) in their study (Incidence and Clinical Implications of ATM Aberrations in Chronic Lymphocytic Leukemia). Both ATM mutations were missense mutations; no nonsense or frameshift variants were observed. Missense mutations accounted for an ATM mutation frequency of 8%; nonsense and frameshift mutations were not detected. Given the low ATM mutation frequency in this cohort, we evaluated nonmutational ATM abnormalities in CLL by analyzing ATM activation in response to external irradiation.

Estimates of A-T incidence indicate that the carrier frequency of pathogenic ATM mutations is approximately 1% in the population. The biochemical and genetic characteristics of leukemic cells, including the mutational status of immunoglobulin heavy chain variable genes (IGHV) and chromosomal aberrations, Expression of CD38 and ZAP-70, and p53 malfunction, have significant predictive value and have facilitated

stratification of patients into risk categories ⁽⁶⁾. Numerous epidemiological studies indicate that the prevalence of A-T heterozygous carriers varies from 0.5% to 1% across different nations; these individuals exhibit a markedly elevated risk of developing breast cancer and CLL. One-third of CLL patients had an inactive ATM, demonstrating deficiencies in the p53 damage response and in apoptosis triggered by ionizing radiation ⁽²¹⁾.

Significantly, almost 60% of leukemias in our group lacked an ATM mutation. Consequently, these subclones are expected to proliferate through distinct survival strategies. The minimal region of 11q deletion encompasses several genes, and while no mutations have been detected in alternate candidates, epigenetic gene silencing and haploinsufficiency at specific loci may contribute to the aggressive phenotype of 11q-deleted CLL with wild-type ATM ⁽²²⁾.

This study has some drawbacks. The sample size was limited. Furthermore, patient survival was measured only because of time and data constraints, which may further underscore the significance of the research.

4. CONCLUSION

From the results of the present study: -

The investigation of ATM gene exons 19 and introns 19 and 20 in patients with CLL revealed missense mutations in exon 19 in two cases. Additionally, one case showed a mutation in intron 19 that could potentially affect RNA splicing.

Conflict of interests: The authors declared no conflicts of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

REFERENCES

1. Mohsen AM, Ali ZA. Ceruloplasmin and some biochemical parameters as a marker for acute myeloid leukemic patients. *Tikrit Journal of Pure Science*. 2023;28(4):13-25. <https://doi.org/10.25130/tjps.v28i4.1526>

2. Kwok M, Agathangelou A, Davies N, Stankovic T. Targeting the p53 pathway in CLL: State of the art and future perspectives. *Cancers*. 2021;13(18):4681. <https://doi.org/10.3390/cancers13184681>
3. Ruggero A, Tirado CA. Hypodiploidy: A Poor Prognostic Cytogenetic Marker in B-CLL. *DNA*. 2025;5(3):32. <https://doi.org/10.3390/dna5030032>
4. Kazhal MS. Chromosomal aberrations in the peripheral blood lymphocytes of Dental Radiographers who exposed to diagnostic X-ray in Erbil city / Iraqi Kurdistan region. *Tikrit Journal of Pure Science*. 2023;22(9):40-6. <https://doi.org/10.25130/tjps.v22i9.873>
5. Alatawi SM. Epigenetic characterisation of chronic lymphocytic leukaemia with frequently altered DNA damage response genes [PhD thesis]: University of Birmingham; 2022.
6. Guarini A, Marinelli M, Tavolaro S, Bellacchio E, Magliozzi M, Chiaretti S, et al. ATM gene alterations in chronic lymphocytic leukemia patients induce a distinct gene expression profile and predict disease progression. *Haematologica*. 2012;97(1):47. <https://doi.org/10.3324/haematol.2011.049270>
7. Robbe P, Ridout KE, Vavoulis DV, Dréau H, Kinnersley B, Denny N, et al. Whole-genome sequencing of chronic lymphocytic leukemia identifies subgroups with distinct biological and clinical features. *Nat Genet*. 2022;54(11):1675-89. <https://doi.org/10.1038/s41588-022-01211-y>
8. Thorvaldsdottir B, Mansouri L, Sutton L-A, Nadeu F, Meggendorfer M, Parker H, et al. ATM aberrations in chronic lymphocytic leukemia: del (11q) rather than ATM mutations is an adverse-prognostic biomarker. *Leukemia*. 2025;1-11. <https://doi.org/10.1038/s41375-025-02615-5>
9. Ghatak S, Muthukumaran RB, Nachimuthu SK. A simple method of genomic DNA extraction from human samples for PCR-RFLP analysis. *Journal of biomolecular techniques: JBT*. 2013;24(4):224. <https://doi.org/10.7171/jbt.13-2404-001>

10. Sambrook J, Russell D. Molecular cloning: A laboratory manual. Mol. Cloning A Lab Man. 2001.
11. Eichhorst B, Robak T, Montserrat E, Ghia P, Niemann CU, Kater AP, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(1):23-33. <https://doi.org/10.1016/j.annonc.2020.09.019>
12. Yang S, Varghese AM, Sood N, Chiatton C, Akinola NO, Huang X, et al. Ethnic and geographic diversity of chronic lymphocytic leukaemia. Leukemia. 2021;35(2):433-9. <https://doi.org/10.1038/s41375-020-01057-5>
13. Gubbels Bupp MR, Jorgensen TN. Androgen-induced immunosuppression. Frontiers in immunology. 2018;9:370132. <https://doi.org/10.3389/fimmu.2018.00794>
14. Vanura K. Sex as decisive variable in lymphoid neoplasms-an update. ESMO Open. 2021;6(1):100001. <https://doi.org/10.1016/j.esmoop.2020.100001>
15. Carpenter DO, Bushkin-Bedient S. Exposure to chemicals and radiation during childhood and risk for cancer later in life. Journal of Adolescent Health. 2013;52(5):S21-S9. <https://doi.org/10.1016/j.jadohealth.2013.01.027>
16. Benavente Y, Costas L, Rodríguez-Suarez MM, Alguacil J, Santibáñez M, Vila J, et al. Occupational Exposure to Pesticides and Chronic Lymphocytic Leukaemia in the MCC-Spain Study. Int J Environ Res Public Health. 2020;17(14). <https://doi.org/10.3390/ijerph17145174>
17. Lien S-YA, Young L, Gau B-S, Shiao SPK. Meta-prediction of MTHFR gene polymorphism-mutations, air pollution, and risks of leukemia among world populations. Oncotarget. 2016;8(3):4387. <https://doi.org/10.18632/oncotarget.13876>
18. Dunia Z. Study of Prevalence of Thalassemia trait among couples undergoing premarital examination in Al-Hamdaniya. Tikrit Journal of Pure Science. 2022;26(2):22-5. <https://doi.org/10.25130/tjps.v26i2.203>
19. Saadat M. Age-standardized incidence rates for leukemia associated with consanguineous marriages in 68 countries, an ecological study. Mediterranean Journal of Hematology and Infectious Diseases. 2015;7(1):e2015027. <https://doi.org/10.4084/MJHID.2015.027>
20. Ouillette P, Li J, Shakhovich R, Li Y, Melnick A, Shedden K, et al. Incidence and clinical implications of ATM aberrations in chronic lymphocytic leukemia. Genes, Chromosomes and Cancer. 2012;51(12):1125-32. <https://doi.org/10.1002/gcc.21997>
21. Stankovic T, Stewart GS, Fegan C, Biggs P, Last J, Byrd PJ, et al. Ataxia telangiectasia mutated-deficient B-cell chronic lymphocytic leukemia occurs in pregerminal center cells and results in defective damage response and unrepaired chromosome damage. Blood, The Journal of the American Society of Hematology. 2002;99(1):300-9. <https://doi.org/10.1182/blood.V99.1.300>
22. Kalla C, Scheuermann MO, Kube I, Schlotter M, Mertens D, Döhner H, et al. Analysis of 11q22-q23 deletion target genes in B-cell chronic lymphocytic leukaemia: evidence for a pathogenic role of NPAT, CUL5, and PPP2R1B. Eur J Cancer. 2007;43(8):1328-35. <https://doi.org/10.1016/j.ejca.2007.02.005>