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Detection of Chromosome 13q14 Deletion, Chromosome 11q22 Deletion and Trisomy 12 in Chronic Lymphocytic Leukemia Patients

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Abstract

Background Chronic lymphocytic leukemia (CLL) is a malignancy of mature B cells. The genetic factors have been found to play a role in the pathogenesis of the disease. Deletions of the long arm of chromosome 13, specifically involving band 13q14 (del(13q14)) constitute the single most frequently observed cytogenetic aberration in CLL, occurring in ~55% of all cases, followed by structural abnormalities of ch 12(trisomy 12), del 11q22.3-q23.1, del 6q21-q23, del 17p13.1, and 14q.

Objective To detect frequencies of chromosome 13q14 deletion, chromosome 11q22 deletion and trisomy 12 in in CLL patients using FISH technique, and to investigate the relation between those chromosomal abnormalities and clinical features and hematological parameters.

Methods This cross-sectional study was conducted on fifty newly diagnosed patients with CLL. Three ml of fresh blood were taken from each patient at admission and then transfer it to FISH unit for blood preparation. Slide preparation was done by using dual color fusion gene probe. The slides were read in the second day by fluorescent microscope.

Results Deleted chromosome 13 was found in 24 out of 50 patients, (48%). Trisomy chromosome 12 was found in 15 out of 50 patients, (30%). Deleted chromosome 11 was found in 12 out of 50 patients, (24%).

Conclusion In a sample of Iraqi adult with CLL, the most frequent chromosomal abnormality was deletion of chromosome 13 followed by trisomy of chromosome 12 and chromosome 11 deletion.

Keywords Chronic lymphocytic leukemia, FISH, deleted chromosome 13, trisomy chromosome 12

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List of abbreviations: Ab = Antibody, Ag = Antigens, ALC = Absolute lymphocyte count, BM = Bone marrow, CBC = Complete blood count, CD = Cluster of differentiation, CLL = Chronic lymphocytic leukemia, DAPI = Anti fade.4.6.diamidino2.phynlindole, DAT= Direct antiglobulin test, Del = deletion, FISH = Fluorescence in situ hybridization, Hb = Hemoglobin, IQR = Inter quartile range, IWCLL = International workshop group on CLL, LAP = Lymphadenopathy, LPD = Lymphoproliferative disorder, M CLL = Mutated chronic lymphocytic leukemia, MCL = Mantle cell lymphoma, miR-15a = MicroRNA-15a, miR-16-1 = MicroRNA-16-1, , miRNA= MicroRNA, mRNA = Messenger RNA, NHL = Non Hodgkin lymphoma, PAS = Periodic acid Schiff, PBF = Peripheral blood film, PLT = Platelet, SSC = Sodium saline citrate, TRI = Trisomy, WBC = White blood cells

Introduction

Chronic lymphocytic leukemia (CLL) is a malignancy of mature B cells characterized by blood and marrow lymphocytosis. Varying degrees of lymphadenopathy, splenomegaly, and blood cytopenia develop as the neoplasm progresses. CLL is the most prevalent adult leukemia in Western societies [1].

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It is characterized by a marked degree of clinical heterogeneity, ranging from patients that harbor a highly stable disease with a nearly normal life expectancy to patients with a rapidly progressive disease [(2)].

In Iraq, leukemia was the third most common cancer accounting for (6.48 %) of all cancers; CLL represents the 7th most common type of leukemia and constitutes (4.91%) in males, (4.29%) in females of all leukemia according to Iraqi cancer registry 2015 [(3)].

The incidence of chromosomal abnormalities has geographic variations and is variable across the world [(4)].

Genetic alterations in CLL can include chromosomal alterations, mutations, alterations in the expression of miRNAs and epigenetic modifications. Molecular cytogenetic remains an integral component of the clinical management of CLL, stratifying patients into risk groups associated with poor (11q or 17p deletion), intermediate (trisomy 12 or normal karyotype) and good prognosis (13q deletion as sole aberration), with important implications relating to commencement or escalation of therapy [(5)].

In the peripheral blood, the morphology of these cells looks like mature lymphocytes [(6)]. In CLL, lymphocytes typically show B-surface antigens, as shown by CD19, CD20dim, CD21 and CD23 [(7)].

Based on immunophenotypic characteristics and giving one point to each one of the following: CD5+, CD23+, FMC7 weak, SmIg (κ/λ staining) weak and CD79b weak. Matutes and Catovsky showed that in patients with a score of 4-5, the diagnosis is virtually always CLL, while in those cases with a score <3, the diagnosis of CLL is extremely unlikely [(8)].

Chromosome 13 deletion seems to protect against the transformation of CLL into diffuse large B-cell lymphoma, as the absence of del(13 q14) characterizes patient subgroups at high risk of developing Richter syndrome [(9-12)], whereas those with combined tri12 and NOTCH1 mutation fair worse as cells from patients with tri12 and concurrent NOTCH1 mutations may be more resistant to apoptosis leading to a less favorable course [(13,14)]. Deletion ch 11 q leads to loss ATM gene (which encodes a protein involved in DNA repair). Mechanistically, automated teller machine (ATM) is able to signal DNA damage and to mediate p53 activation which, as a major player assuring genome stability, can ultimately trigger apoptosis or oncogene-induced senescence if the damage is not repaired. Therefore, damaged cells are not adequately removed and ATM deficiency causes genomic instability [(13,15)].

The aim of current study is to detect frequencies of chromosome 13q14 deletion, chromosome 11q22 deletion and trisomy 12 in CLL patients using FISH technique, and to investigate the relation between those chromosomal abnormalities and clinical features and hematological parameters.

Methods

Selection of patients

A total of 50 (32 males and 18 females) newly diagnosed patients with CLL who were attending the Hematology Outpatient Clinic at the Medical City were included in this study during the period from February 25, 2018 until December 15, 2019.

Data collection

Full personal and demographic information was obtained, including date of birth, sex, residence, date at diagnosis, and duration of illness. Complete clinical data were obtained regarding the presenting complaint(s), including pallor, abdominal distention, any history of recurrent infections, chronic diseases. Immunophenotyping result was obtained from flowcytometry department and according to it we do scoring to the patients depending on Mutuate Scoring System. Immunophenotypic scoring system is used for the diagnosis of CLL and to differentiate CLL from other B cell malignancies [(2)]. Scores in CLL are usually >3, in other B-cell malignancies the scores are usually ≤3 [(8)].

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Table 1. The scoring system for diagnosis of chronic lymphocytic leukemia [16]

Marker	Points	
	1	0
CD5	Positive	Negative
CD23	Positive	Negative
FMC7	Negative	Positive
smIg	Low	Medium/High
CD22/CD79b	Low / Negative	Medium/High

SmIg= surface membrane immunoglobulin

All patients were thoroughly examined for pallor, lymphadenopathy, hepatomegaly and/or splenomegaly. A staging system is a standardized way for the cancer care team to epitomize information about how far a cancer has spread, as Rai system in the United States [17].

Table 2. Rai and Modified Rai staging system [4]

Risk Group *	Stage **	Description
Low	0	Lymphocytosis only
Intermediate	I	Lymphocytosis plus enlarged nodes
	II	Lymphocytosis plus enlarged liver or spleen with or without enlarged nodes
High	III	Lymphocytosis plus anemia (Hb less than 11) with or without enlarged nodes, liver, or spleen
	IV	Lymphocytosis plus thrombocytopenia (platelet count less than 100 x 10^9/L) with or without anemia, enlarged nodes, liver or spleen

*Modified Rai system (1987). **Rai system

A detailed explanation of the aim of the study was provided to the patients. Participation was strictly voluntary. A written consent was obtained from each patient. The study strictly obeyed the instructions of the Declaration of Helsinki for Human Rights and Institutional Review Board in College of Medicine, Al-Nahrain University.

Laboratory methods

For each patient, 3 ml of ethylenediaminetetraacetic acid blood samples was aspirated under strict aseptic techniques. The laboratory workup included the following:

1. Complete blood count: It was done using an automated (Cell-DYN, RUBY Abbott Diagnostic, USA) at Teaching Laboratories of Medical City. The diagnosis was made by flowcytometry.
2. Reticulocyte count: It was counted manually after staining with new methylene blue stain using the standard methods to exclude the presence of hemolytic anemia for the purpose of clinical staging of the disease.
3. Direct agglutination test was done by a spin tube technique to exclude autoimmune hemolytic anemia prior to clinical staging.

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4. Blood film was prepared and stained with Leishman's stain using the standard procedures.
5. Fluorescent in situ hybridization technique (FISH) include: blood preparation, slide preparation, slide reading.
6. About 750 microliters of blood added by pasture pipet to 5 ml of peripheral blood sample in centrifugate tube mixing well by pasture pipette. Then the solution stored at 4 °C in refrigerator for 1 hour, after that the solution centrifugated at room temperature for 10 min at 1000 rpm and discard the supernatant by sucking it off carefully with pasture pipet (1 ml of supernatant was left in the tube to avoid loss of material).

For hypotonic treatment, the pellet was resuspended in 5ml of KCL (37 °C) and incubated at 37 °C for 20 min. Then 1 ml of caryos (fixative material) slowly added to tube, mix carefully and leave it in refrigerator 4 °C or 30 min.

Solution centrifugated in (10 min and 1000 rpm), discard the supernatant, five ml of caryos added to solution and stored in refrigerator at (4 °C) overnight. In second day start with washing to remove all RBC so centrifugate the solution, discard the supernatant and added 5 ml of caryos. Then repeated washing three time, then five ml of caryos added to solution and stored in refrigerator (4 °C) until slide preparation start. The specimen was studied in rundown order by meta system fluorescents microscope. For purposes of this paper, orange signals are referred to as O, green signals are referred to G.

For each specimen at least 100 interphase nuclei from different areas of the same slide were scored. Results were considered clonal when the percentage of cells with any given chromosome abnormality exceeded the established cut-off value. Following internal validation of probes, the cut-off values were established at 3% for trisomy 12, 6% for chromosome 11, 8% for chromosome 13. The cut-off values for both gains and losses were determined by statistical evaluation of FISH results from control people [11].

Statistical analysis

Data were collected, summarized, analyzed and presented using statistical package for social sciences (SPSS) version 23 and Microsoft Office Excel 2010. Qualitative (categorical) variables were expressed as number and percentage, whereas, quantitative (numeric) variables were first evaluated for normality distribution using Kolmogorov-Smirnov test, and then accordingly normally distributed numeric variables were expressed as mean (an index of central tendency) and standard deviation (an index of dispersion), while those numeric variables that are not normally distributed were expressed as median (an index of central tendency) and inter-quartile range (an index of dispersion). The level of significance was considered at P-value of equal or less than 0.05.

Results

This descriptive, cross-sectional study included 50 patients with CLL (32 males and 18 females). Their ages ranged from 45-76 years, with a mean age of 62.02±8.66 years and median age of interquartile range (IQR) 64 years (14) (Table 3).

They were 34 (68%) patients with lymphadenopathy, 5 (10%) patients with hepatomegaly, 9 (18%) patients with splenomegaly, 16 (32%) with hepatosplenomegaly and 40 (80 %) patients with pallor. According to modified Rai staging they were 20 (40 %) in intermediate risk group, 30 (60 %) patients in high-risk group. According to immunological score, patients were distributed as 7 (14%) patients in score 3 and 43 (86 %) in score 4 (Table 4).

The Hb levels of the studied patients ranged from 4.4-16.3 g/dl, with a mean of 10.97±2.45, whereas the absolute lymphocyte count (ALC) ranged from 5.5-161, with a mean of 19.02±31.6, prolymphocyte% ranged from 1-8 with a mean of 1.64±1.47 (Table 5).

Table 3. Distribution of chronic lymphocytic leukemia patients according to age and gender

Characteristic		Results
Age (years)	45-49, *n* (%)	6 (12.0%)
	50-59, *n* (%)	11 (22.0%)
	60-69, *n* (%)	22 (44.0%)
	70-76, *n* (%)	11 (22.0%)
	Mean ±SD	62.02±8.66
	Median (IQR)	64 (14)
	Range	45-76
Gender	Male, *n* (%)	32(64%)
	Female, *n* (%)	18(36%)
	Male:Female	1.8:1"

n: number of cases; SD: standard deviation

Table 4. Clinical characteristics, score, staging of chronic lymphocytic leukemia patients

Characteristic	Result
LAP, *n* (%)	34 (68 %)
Organomegaly	
Hepatomegaly, *n* (%)	5 (10%)
Splenomegaly, *n* (%)	9 (18%)
Hepatosplenomegaly, *n* (%)	16 (32%)
Pallor, *n* (%)	40 (80%)
Score	
Score 3, *n* (%)	7 (14%)
Score 4, *n* (%)	43 (86%)
Stage	
II, *n* (%)	20 (40%)
III, *n* (%)	25 (50%)
IV, *n* (%)	5 (10%)

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Table 5. Hematological parameters of CLL patients

Characteristic		Result
Hb g/dL	Mean±SD	10.97 ±2.45
	Median (IQR)	10.8 (3.6)
	Range	4.4 -16.3
Platelet count 10^3/µl	Mean±SD	155.65 ±76.55
	Median (IQR)	129 (93.25)
	Range	25.3 -324
WBC count 10^3/µl	Mean ±SD	34.59 ±36.36
	Median (IQR)	24 (11.8)
	Range	7 -196
Absolute lymphocyte count	Mean ±SD	19.02 ±31.60
	Median (IQR)	7.25 (10.88)
	Range	5.5 -161
Prolymphocyte%	Mean ±SD	1.64 ±1.47
	Median (IQR)	1 (1)
	Range	1 -8

n: number of cases; SD: standard deviation; IQR: inter-quartile range

Out of the 50 studied patients, 2 (4%) had non-chromosomal aberrations and 48 (96%) had chromosomal aberrations. Chromosome 11 deletion was seen in 12/50 (24%) of patients and the percent of deleted cells has ranged from 7-19% with a mean of 15.64±4.11%. (Figures 1 and 2). Chromosome 12 trisomy was seen in 15/50 (30%) of patients and the percent of trisomy 12 cells has ranged from 15-17% with a mean of 16.21±0.58% (Figures 3 and 4). Chromosome 13 deletion was seen in 24/50 (48%) of patients and the percent of deleted cells has ranged from 8-32% with a mean 15.71±5.57 (Figures 5 and 6) (Table 6).

Three diploid cytogenetic cases are observed in three patients, two patients had chromosome 11 deletion and trisomy 12 and one patient had chromosome 11 deletion and chromosome 13 deletion and the characteristics of those diploid cases is showed in table 6.

Table 6. Chromosomal abnormalities in patients with chronic lymphocytic leukemia

Abnormality		Result
Chromosome 11 deletion	*n* (%)	12 (24%)
	Mean of deleted cells ±SD	15.64±4.11
	Range deleted cells	7-19
Chromosome 12 trisomy	*n* (%)	15 (30%)
	Mean of trisomy cells ±SD	16.21±0.58
	Rangeof trisomy cells	15-17
Chromosome 13 deletion	*n* (%)	24 (48%)
	Mean deleted cells ±SD	15.71±5.57
	Range deleted cells	8-32
Diploid cases, n (%)		3 (6%)
Ch 11 del & ch13 del n (%)		1 (2%)
% of deleted cells/% of deleted cells		7%/9%
Ch 11 del & +12 n (%)		1 (4%)
% of deleted cells/% of trisomy cells		9%/10%
Ch 11 del &+12 n (%)		1 (4%)
% of deleted cells/% of trisomy cells		7%/6%

n: number of cases; SD: standard deviation; ch: chromosome; +: trisomy; del: deletion

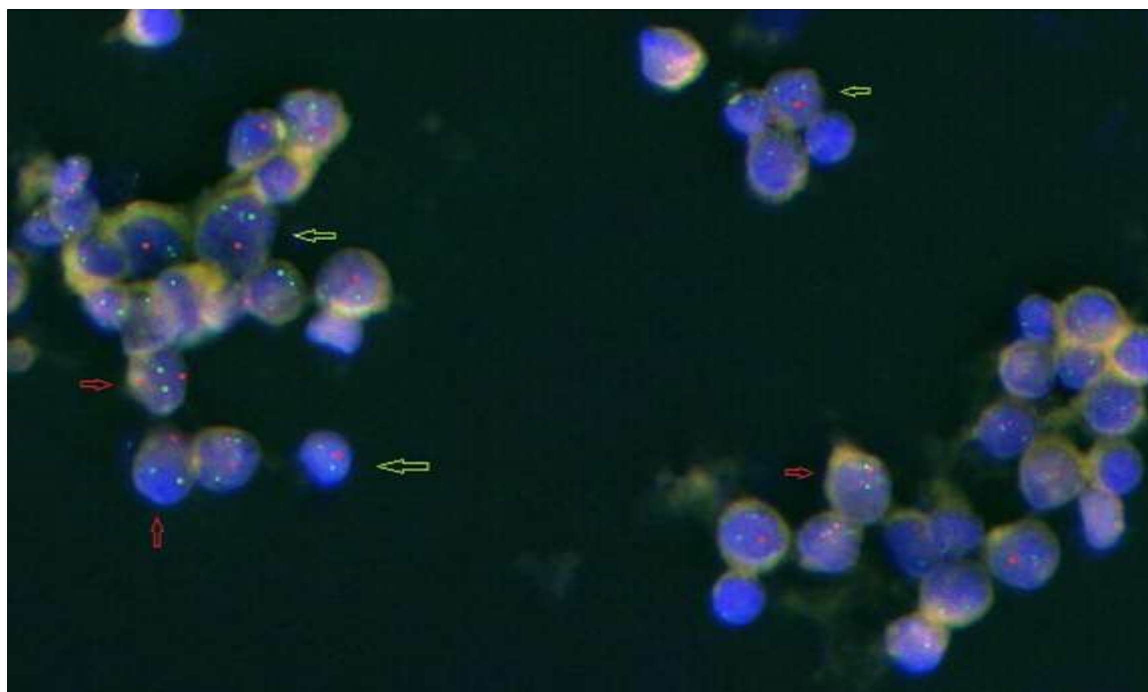

Figure 1. FISH analysis using XL ATM/11cen probe detect deletions in 11q22.3 show leukemic cells with deletions, one orange signal and two green bright fluorescence signal spots (green arrow). Red arrow represents normal FISH pattern with two orange signals and two green signals, on power 40X.

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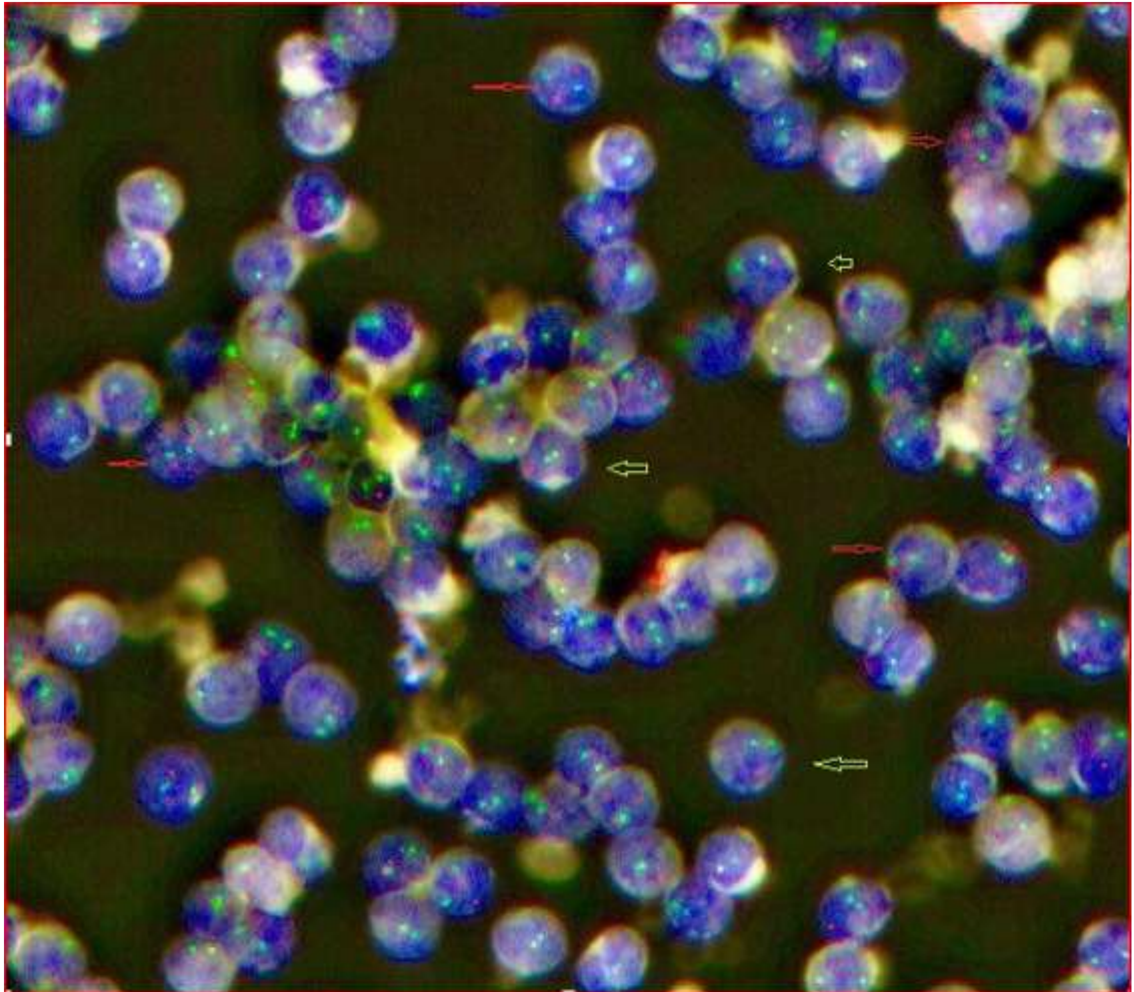

Figure 2. FISH analysis using XL ATM/11cen probe detect deletions in 11q22.3 show leukemic cells with deletions, one orange signal and two green bright fluorescence signal spots (green arrow|). Red arrow represents normal FISH pattern with two orange signal spots and two green signal spots, on power 40X.

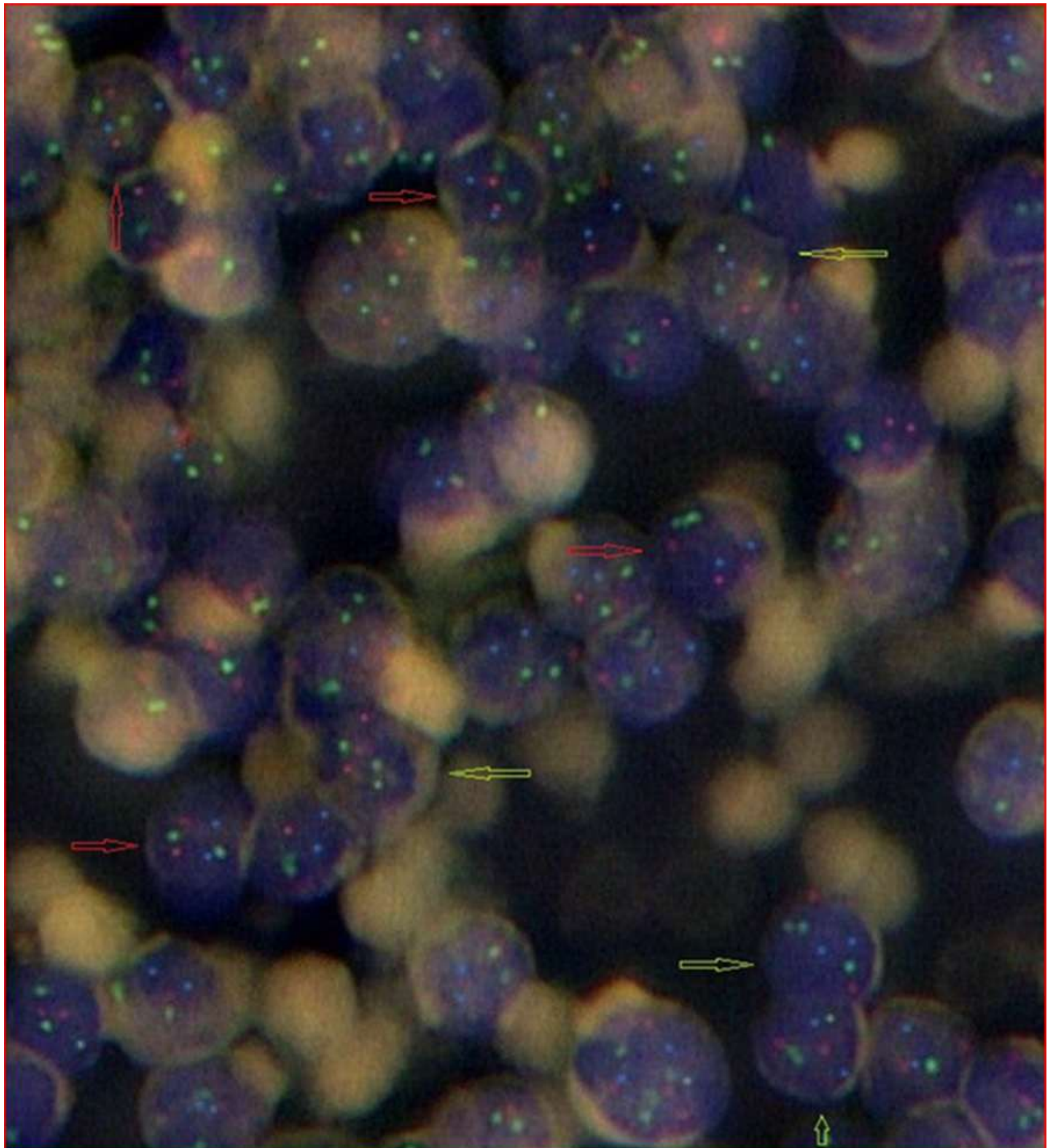

Figure 3. FISH analysis using XL DLEU/LAMP/12cen LSI probe show leukemic cells with trisomy 12, yellow arrows 3 green signals for chromosome 12 and two orange signal, two blue signals for chromosome 13 on power 60 x. Normal FISH pattern with red arrows for chromosome 12

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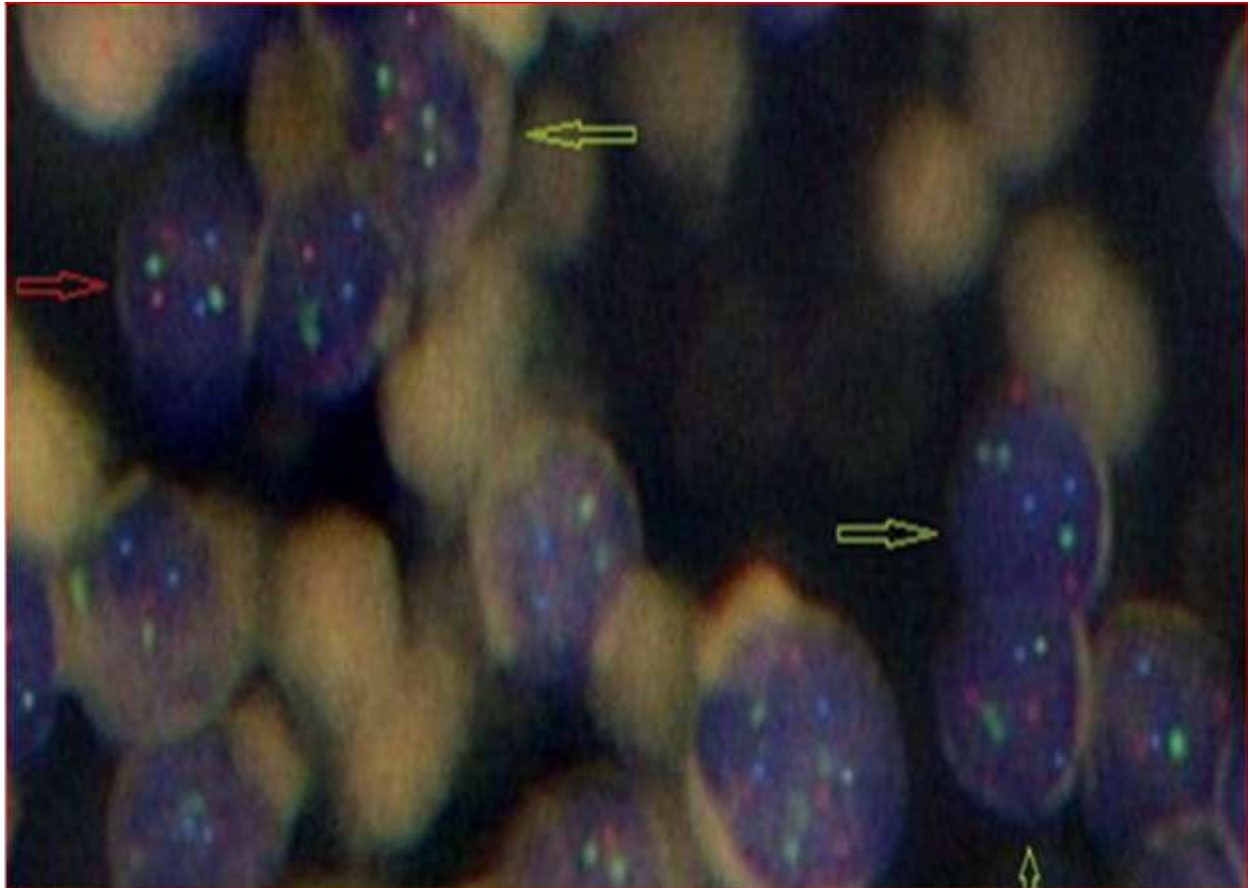

Figure 4. FISH analysis using XL DLEU/LAMP/12cen LSI probe show leukemic cells with trisomy 12, green arrows 3 green signals for chromosome 12 and two orange signal, two blue signals for chromosome 13 on power 60 x. Normal FISH pattern with 2 green signals, two orange signals, two blue signals red arrows

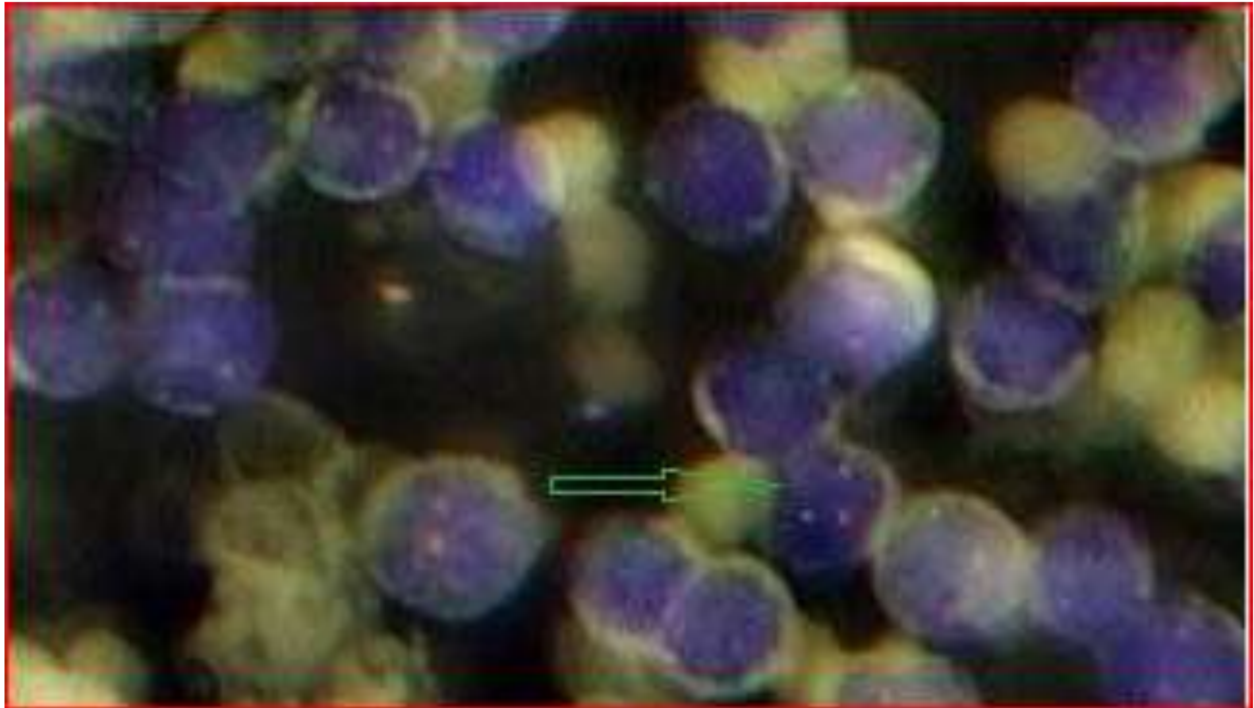

Figure 5. FISH analysis using XL DLEU/LAMP probe detect deletions on chromosome 13q show leukemic cell with monoallelic deletion of chromosome 13 as detected by FISH, the orange (spectrum: orange)-labeled probe detects the minimal deleted region, the green (spectrum: green)-labeled probe detects a terminal DNA segment of the long arm of chromosome 13 to facilitate its identification. Chromosomes are counterstained by DAPI, on power 60x

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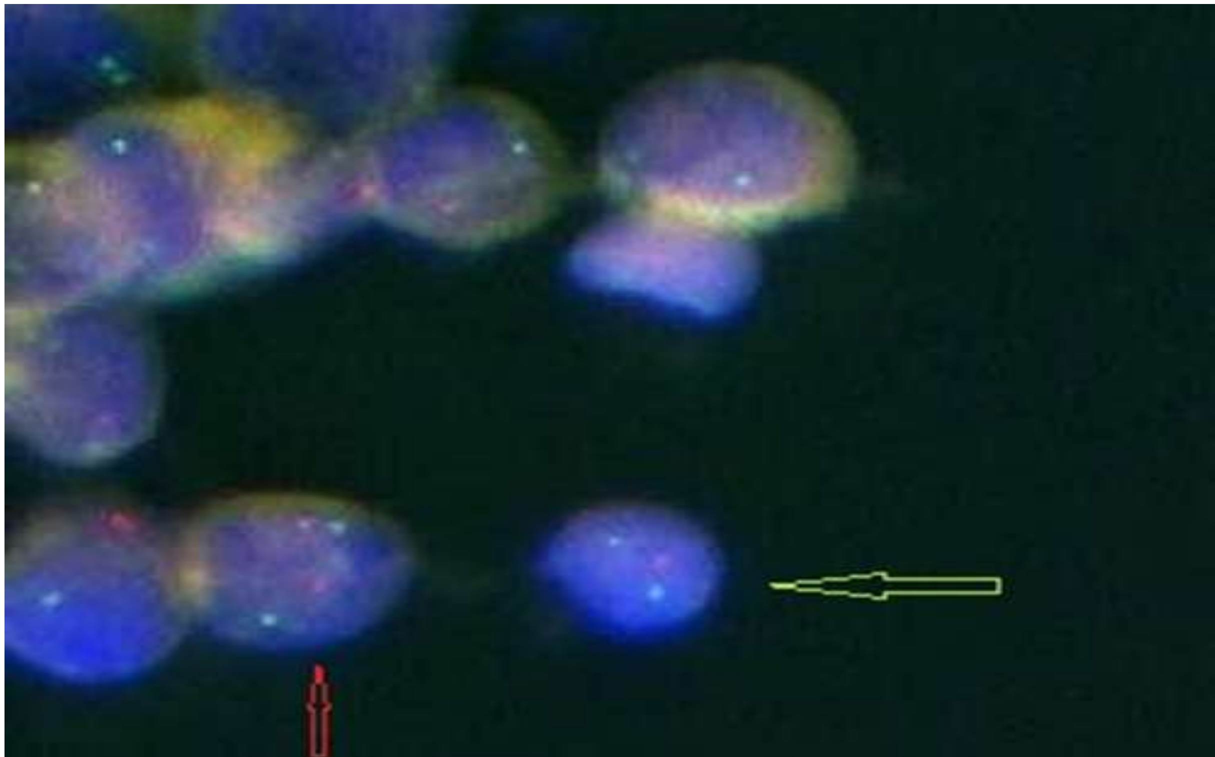

Figure 6. FISH analysis using XL DLEU/LAMP probe detect deletions on chromosome 13q, show leukemic cells with monoallelic deletion of chromosome 13, the orange (spectrum: orange)-labeled probe detects the minimal deleted region, the green (spectrum: green)-labeled probe detects a terminal DNA segment of the long arm of chromosome 13. To facilitate its identification Chromosomes are counterstained by DAPI. one orange signal and two green signals (green arrow) on power 60x. red arrow represent normal FISH pattern with two orange signals and two green signals

Significant negative correlation between percent of trisomy cells and Hb level. No other significant correlation was found (P> 0.05) (Table 7), (Figure 7).

Table 7. Correlation between percent of deleted cells for chromosome 11 and chromosome13 and trisomy cells for chromosome 12 to hematological parameters

Characteristic	Percentage of del Ch 11		Percentage of tri Ch 12		Percentage of del Ch 13	
	r	p	r	p	r	p
Hemoglobin (Hb) g/dL	-0.080	0.815	-0.553	0.040*	-0.060	0.780
Platelet count 10^3/µl	-0.360	0.277	0.126	0.667	-0.400	0.053
WBC count10^3/µl	0.385	0.242	0.362	0.204	0.144	0.501
Atypical lymphocyte/ 100 Ly	0.480	0.135	0.229	0.431	-0.240	0.259
Lymphocyte count	0.409	0.212	0.367	0.197	0.194	0.363
Prolymphocyte %	-0.267	0.428	-0.267	0.356	-0.377	0.070

Del: deletion, Ch: chromosome, tri: trisomy

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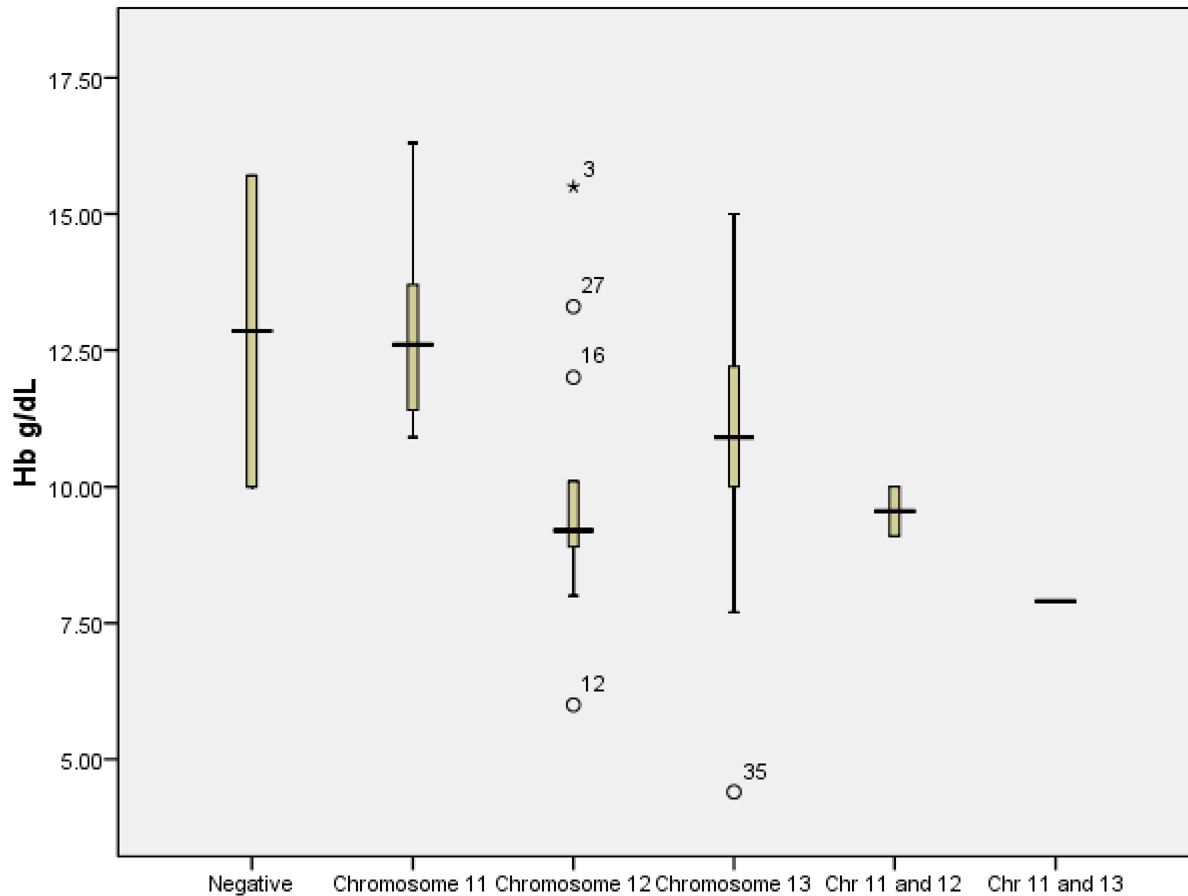

Figure 7. Comparison of hemoglobin level to chromosomal abnormalities

Discussion

CLL is the accumulation of monoclonal B cells in the bone marrow and peripheral blood [(1)]. Identification of specific chromosomal aberrations is an important tool for diagnosis and risk stratification in CLL patients [(15-18)].

In this study, the median age of the patients was 64 years and the range was 45-76 years. It is well known that this disorder is a disease of elderly. This age was close to the results obtained by other Iraqi studies in 2013, 2014 and 2016, 2019 [(19-22)] and a study in Pakistan in 2015 [(23)]. Whereas the median age at presentation, in western countries was higher; it was reported to be 70 years [(24,25)]. This difference can be attributed to the difference in population structure, environmental variations, genetic predisposition between Iraq and western countries, and difference in life expectancy.

Regarding the physical characteristic of CLL patients included in this study, it was noticed that the most frequent presenting signs were pallor, lymphadenopathy and hepatosplenomegaly, hepatomegaly, splenomegaly respectively. Those results were comparable to other Iraqi studies [(26,27)], also, western study reported that lymphadenopathy was more common than splenomegaly and hepatomegaly [(28)].

In the current study, about 43 out of 50 patients (86%) were in score 4 and 7 out of 50 patients (14%) were in score 3 and the diagnosis was confirmed by immunohistochemistry. It is in acceptance with Rodrigues et al. study [(29)].

Regarding the modified Rai clinical stages of CLL patients in this study, 40% of patients were in intermediate risk, 60% of patients were within high-risk group as well as three diploid cytogentic patients were in high-risk group.

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This fact reveals that more than halve of patients enrolled in the current study had advanced stage of the disease. An Iraqi study reported higher percentage of patients within high-risk group [26], similar to this study, whereas a western study showed lower percentage of patients fell within high-risk group and higher percentage of patients fell within intermediate risk group, probably due to better awareness of patients seeking early medical services so the patients will be diagnosed earlier [29].

Regarding hemoglobin level; the median Hb level was 10.8 g/dl with IQR of 3.6 and the range was from 4.4-16.3 g/dl, which is close to many Iraqi and non-Iraqi studies [30,31]. In general, anemia may reflect progression of bone marrow failure. In the present study, 56% of patients had Hb less than 11 g/dl whereas 44% had Higher Hb; and this goes with the high frequency of patients in the high-risk group.

Regarding platelet count, the current study revealed that the median of platelet count was 129 $\times 10^9$/L IQR (93.25) and the range was 25.3 -324 $\times 10^9$/L. Similar results were reported by many Iraqi studies [26,32]. Moreover 31 out of 50 (62%) patients had thrombocytopenia. Those results were comparable to another study [33]. Thrombocytopenia was usually attributed to bone marrow failure and reflecting the degree to which bone marrow has been replaced with leukemic cells, thus the high percent of thrombocytopenic patients in the present study reflect high percent of CLL patients in high-risk group.

Leukocyte count is a well-known continuous prognostic variable, where by increasing counts confer a poorer outcome [33-35]. The present study showed that WBC count was more than the upper limit of normal in 95 % of our cases, the leukocyte count was in the range of 7-196 X10^9/L and the median WBC count was 24 $\times 10^9$ with IQR (11.8). Those results match Korejo et al in 2020 study [36].

In the current study the median level of ALC was 7.25 $\times 10^9$/L with IQR of (10.88) and the range was 5.5-161 X10^9/L, which was comparable with an Iraqi study [37]. ALC has been used as a prognostic factor and high lymphocyte count of more than 50,000/L has been linked to poor prognosis [38].

Regarding prolymphocyte percent, the median of prolymphocyte was (1%) and the range was (1-8%), as we did not include cases with increased circulating prolymphocytes >10% meeting criteria for CLL/PLL (prolymphocytic leukemia). It agrees with the findings of Frater et al study who stated that high percent of prolymphocyte associated with poor prognosis [39].

Identification of specific chromosomal aberrations is an important tool for diagnosis and risk stratification in CLL patients [40]. In the current study, 48 out of 50 CLL patients (96%) present with chromosomal aberrations and two patients were negative for three FISH probes which is in acceptance with Skowronska et al. who found 92% of CLL cases had genomic abnormalities [14].

The median of Hb level and median platelet count in those two patients who were negative for the three chromosomal abnormalities were higher than patients with chromosomal abnormalities and this was similar to other studies [41,40]. Moreover, negative chromosomal aberrations cases showed higher median of WBC counts compared to positive cytogentic abnormalities cases.

The current study did not find any significant correlation between the percent of the studied chromosomal aberration in CLL cells and hematological parameters. Only the percent of trisomy 12 in the cells showed a significant negative correlation with Hb concentration. This was similarly observed by Tabernero et al. study [42]; this presumably due to that trisomy clone had proliferation advantage with respect to non-trisomy cells, thus those leukemic cells will grow rapidly in the bone marrow and result in impaired hematopoiesis. This impairment had resulted in low Hb concentration, low platelet count, high WBC count and ALC in trisomy 12 cases compared to those in patients with del 11 and deletion 13. This clarifies the adverse effect of trisomy 12 in CLL patients.

Lastly the current study showed no relation between percent of deleted or trisomy cells and CD38 or light chain restriction expression. However, it was noted that the highest percent

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of cases with positive CD38 were in patient carrying trisomy 12 where 73.3% of them carry CD38 compared to those with deletion 13 and deletion 11 where 56.5% and 41.6% of the patients were expressing CD38 respectively. Also, the three patients with diploid abnormalities were expressing CD38. The expression of this bad prognostic marker in those patients could explain the adverse prognosis of trisomy 12 and diploid aberration in CLL patients [43].

The lack of surface light chain in CLL is rare fact but in this study, it was observed in 35 out of 50 CLL patients. In contrast, 32 of 396 cases (8.1%) of CLL were reported by Matutes et al. to have no surface light chain [9]. This variability may be related to different factors including patient selection, inclusion criteria, and geographical differences.

The absence of immunoglobulin expression on malignant B cells can result from defects at any level from gene transcription to translocation of fully assembled proteins to the cell surface; that mean there is marked derangement of surface immunoglobulin synthesis which denote more aggressive disease [44].

From this study, it can be concluded that the frequency of deletion chromosome 13 in a sample of Iraqi adult CLL patient was the most common cytogenetic aberrations, followed by trisomy chromosome 12 and chromosome 11 deletion and deletion chromosome 13 was associated with better hematological parameters than trisomy chromosome 12. Thus, we may propose that del ch. 13 may ameliorate the hematological parameters, whereas trisomy chromosome 12 was associated with poor prognostic parameters.

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Author contribution

Dr. Hashim conducted the study, collected the data and performed the statistical analysis and drafting the manuscript. Dr. Abdulateef contributed in the designing, organization and finalization of manuscript.

Conflict of interest

There are no conflicts of interest.

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