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ORIGINAL ARTICLE.

Prognostic Significance of 13q14 Deletion in Egyptian Chronic Lymphocytic Leukemia Patients

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ABSTRACT

Background: Chronic lymphocytic leukemia (CLL) is a B lymphocyte malignancy that affect mainly adults, its clinical course is variable. 13q deletion is a common cytogenetic abnormality found in CLL patients and in general, it is associated with a good prognosis and a benign clinical course. However, it was noticed that there are clinical heterogeneity among CLL patients harboring 13q deletion which may be attributed to type, size, or rate of 13q deletion. So, it was important to clarify the source of this heterogeneity.

Methods: Seventy one CLL patients were examined by conventional cytogenetic and fluorescent in situ hybridization (FISH) for 13q14 deletion.

Results: Deletion of 13q14 was detected in 45/71 CLL patients (63.4%) and those had significantly lower absolute lymphocytic count and hemoglobin concentration, 53.3% of positive patients were in Binet stage A, and 31.1% of them required chemotherapy. In 38 patients 13q14 deletion was found as an isolated abnormality and those had significantly lower WBCs count, absolute lymphocyte count and LDH than those with accompanied cytogentic abnormalities (non-isolated). The deletion was found at a rate (≥80%) in (8/ 38) patients with isolated deletion type and those had a significantly shorter time to treatment. The 13q14 deletion was biallelic in only 3 patients out of 38 with isolated type and all of them had a diffuse bone marrow infiltration pattern.

Conclusions: 13q14 deletion is a common cytogenetic abnormality in CLL patients and has a variable impact on the disease condition according to specific features of deletion such as isolated or non-isolated, deletion rate, and type of deletion being monoallelic or biallelic.

Keywords: Chronic lymphocytic leukemia; 13q14 deletion; fluorescent in situ hybridization.

INTRODUCTION

Chronic lymphocytic leukemia (CLL) is a B lymphocyte malignancy. It is represented by the autonomous accumulation of clonal B lymphocytes in bone marrow (BM), peripheral blood (PB), spleen and lymph nodes , which is usually a result of apoptosis disruption. CLL is the most commonly seen adult leukemia in Western populations and it comprises 25 to 35 percent of leukemias in United States. [1].

The clinical disease severity of CLL patients varies widely, ranging from a stable clinical condition with nearby normal life to an aggressive proliferative disease with short survival. In addition, patients show different rates of response to chemotherapy [2].

CLL severity and clinical outcome depend partially on the fundamental molecular pathogenesis. Genome-wide analysis had detected several abnormalities in the genome coding region of CLL patients that cause the

disease and determine its severity. About eighty percent of CLL patients carry at least one of four common cytogenetic abnormalities which are deletion of 13q14 del(13q), del(11q), del(17p), and trisomy 12 [3].

13q del is the most common cytogenetic abnormality that occurs in about 55% of all CLL patients. Generally, patients with an isolated del(13q14) have a benign disease course. The miRNAs (miR15 and miR15) are present in the critical region of del(13q14) and direct the expression of anti-apoptotic proteins and proteins involved in progression of cell cycle [4].

Del(13q) is considered as a favorable prognostic element when it is found as an isolated abnormality by fluorescent in situ hybridization (FISH). However, it is remarked that the course of clinical disease in CLL patients with del(13q) is totally diverse and the cause for this clinical diversity has not been settled up to now. Some researchers propose that type II deletion in which RB1 gene is lost is accompanied by more severe clinical course. Moreover, it is advocated that the deletion rate and the deletion type (being mono-allelic and/or bi-allelic) posse an impact on the prognosis [5].

METHODS

This retrospective cohort study was conducted in Clinical Pathology Department and Clinical Hematology Unit of Internal Medicine Department, Faculty of Medicine, Zagazig University Hospitals. Informed written consent was gained from all of the attending patients and the protocol of the current study was authorized by Zagazig University Institutional Review Board (ZU-IRB #10280). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Patients with CLL were included in this study, and the sample size was calculated by assuming the frequency of 13q14 deletion rate <80% was 80% Vs 57% in RAI stage 0-2 Vs 3-4 at 80% power and 95% CI. The estimated sample was 71 Cases open Epi. Patients who refused to give written consent were excluded. CLL diagnosis was established on existence of persistent absolute lymphocytosis of at least $5\times 10^3/\mu l$ in the peripheral blood and on doing immunophentyping , they expressed CD19, CD5, CD23 phenotype along with kappa or lambda monoclonality.

All patients were subjected to full history taking, clinical examination, ultrasonography, routine laboratory investigations including; Complete blood count (CBC) by automated cell counter Xn 2000 (Sysmex, Japan); LDH and β-microglobulin by Cobas 6000 autoanalyzer (Roche diagnostics, Germany). Immunophenotyping by flow cytometry was performed using Becton Dickinson (Franklin Lakes, New Jersey, USA) FACSCalibur device. Bone marrow trephine biopsy examination was also carried out for each patient. Specific laboratory investigations including conventional cytogenetic analysis and FISH were also achieved.

Conventional cytogenetic analysis:

Peripheral blood samples were taken from the patients on lithium heparin vacutainer, cultured on Roswell Park Memorial Institute media (RPMI 1640) supplemented by fetal calf serum, L – glutamine, penicillin-streptomycin and incubated at 37°C for 72 hours, after that the process of harvesting was done including (stopping cell division at metaphase by colcemid, allowing cells to swell and chromosomes to spread using warm hypotonic K CL, fixation using cold fixative solution; absolute methanol / glacial acetic acid (3/1)). Then cell suspension was dropped on wet cold clean glass slides and chromosomes were banded by trypsin EDTA and stained by giemsa. Finally, chromosomal examination and analysis was performed using light microscope (Olympus BX 51, Japan) supplemented by digital camera and computerized image analyzer (Imstar).

Fluorescent in-situ hybridization (FISH):

FISH was performed using D13S319 plus deletion probe (Cytocell) for 13q14.2-14.3 region labeled red, the probe mix also contain a control probe (13qter) for 13q34 region labeled green. To perform FISH technique ,cell suspension was dropped on wet cold clean slide, after it dried at room temperature it was dehydrated using ethanol at gradually increased concentrations (70%, 85%, 100%) two minutes for each then left to dry at room temperature and probe was applied on the slide, covered by cover slip, sealed with DPX. After that the process of denaturation and hybridization was performed in denaturing/hybridization system for FISH, (HyBrite™ apparatus, Dako Cytomation, California) which raise the temperature to the limit required for denaturation 74°C for 2 minutes, after that the temperature was automatically and abruptly dropped to 37°C

(hybridization temperature) for 24 hours. After that post hybridization wash was performed using 0.4 x SSC/ 0.3% NP-40 at 73°C ± 1°C for 2 minutes followed by 2X SSC/ 0.1 NP-40 at room temperature for 2 minutes. Finally counter stain DAPI II was applied and slides were examined by fluorescence microscope (Olympus, BX63) and a computerized image analysis system (cytovision Genetics workstation) using triple filter (DAPI/FITC/Texas red), for each patient 200 interphase cells were examined.

STATISCAL ANALYSIS

All data were collected, tabulated and statistically analyzed using the IBM SPSS (Statistical Package for the social sciences) statistics for windows, version 23.0 IBM Corp, Armonk, NY: USA. Quantitative data were expressed as the mean ± SD and median (range), and qualitative data were expressed as absolute frequencies (number) and relative frequencies (percentage).

The student's (t) test was carried out to compare continuous variables between two groups normally distributed. Mann-Whitney (U) test was carried out to compare continuous variables between two groups not normally distributed. Percent of categorical variables were compared using Chi-square test or fisher exact test when appropriate. Survival curves were constructed using Kaplan-Meier method and log-rank test was used for comparison. All tests were two sided. P- value < 0.05 was considered statistically significant, while P-value ≥ 0.05 was considered statistically insignificant.

RESULTS

A total of 71 patients diagnosed as CLL were included in the study. Age of patients ranged between 44-79 years. Out of them, 46 (64.8%) were males and 25 (35.2%) were females. Clinical and laboratory data of CLL patients are summarized in (Table1). Upon FISH analysis 45 (63.4%) were positive for 13q14 deletion and 26 (36.6%) were negative for it.

Clinical and laboratory characteristics of CLL patients positive and negative for del 13q14:

CLL patients positive for del13q14 were statistically indifferent from those with negative del 13q14 regarding age and sex distribution. On assessing Binet staging of both groups, there was a significant difference as more than half of the patients with del 13q14 (53.3%) were in stage A; while the majority of patients negative for del 13q14 were in more advanced stages as 50% of those patients were in stage B and 26.9% in stage C.

The laboratory parameters of both groups were compared and there were significantly higher absolute lymphocyte count (ALC) and hemoglobin concentration among patients negative for del13q14. Regarding other laboratory parameters there were no significant differences between the two groups.

Regarding treatment requirements the higher percent of the deletion positive group (68.9%) didn't need to be treated while the deletion negative group required chemotherapy treatment more frequently (69.2%) and this difference was statistically significant (Table 2).

Isolated and non-isolated 13q14 deletion:

In 38/71 patients (53.5%), 13q14 was found as an isolated abnormality while in 7/71 patients (9.9%), 13q14 deletion was accompanied with other cytogenetic abnormalities (non-isolated). Absolute WBCs count, ALC and serum LDH level were significantly higher in patients with non-isolated 13q14 deletion, when compared with those with isolated 13q14 deletion ($p = 0.042, 0.048$ and 0.002) respectively. While, there was non-significant difference regarding patient age, sex, other peripheral blood parameters, CD38 expression, BM infiltration pattern or disease stage between both groups (Table 3).

Association of deletion rate with clinico-laboratory characteristics and time to treatment (TTT) of CLL patients with isolated 13q14 deletion:

During FISH analysis of isolated 13q14 deletion patients, the percent of 13q14 deleted cells were assessed and hence patient were categorized into two groups; the first was 8/38 patients (21.1%) having a higher percentage of isolated del13q14 cells ($\geq 80\%$) and the other group including 30/38 (78.9%) having a lower percentage of isolated 13q14 deletion cells ($< 80\%$). There was non-significant difference between them according to age and sex distribution, laboratory findings or clinical staging (Table 4).

Upon assessing the TTT of the patients, it was clear that it was significantly shorter in patients with higher rate deletion ($p = 0.000$) (Table 4), (Figure 1)

Monoallelic or biallelic isolated 13q14 deletion:

It was observed that the majority of patients with isolated 13q14 deletion (35/38) had only one deleted copy (mono-allelic), while in the remaining patients (3/ 38) both copies were deleted (bi-allelic). On applying a comparison between the mono-allelic group and the bi-allelic group regarding the clinical and laboratory findings, there was non-significant difference between both groups regarding patients age, sex distribution, absolute WBCs, ALC, hemoglobin concentration, platelets count, β2-microglouline, LDH, CD38 expression, Binet stage , or Rai stage. However, upon doing bone marrow biopsy, the three patients with bi-allelic deletion showed diffuse infiltration pattern while only (4/35) of patients with mono-allelic deletion showed diffuse pattern of marrow infiltration and the difference was significant (p=0.004) (Table 5). It was noted also that the time needed to begin treated was statistically non-significant between the two groups (p = 0.116) (Table 5 , Figure 2).

Table 1: Clinical and laboratory characteristics of CLL patients

	Total n(71)
Age (years)	60.6±8.93
Sex Female Male	 25 (35.2%) 46 (64.8%)
WBCs(× 10^3/ µl)	45 (15-134)
ALC (× 10^3/ µl)	39 (10-127)
Hemoglobin (gm/dl)	12.2±1.87
platelet (× 10^3/ µl)	154 (56-431)
β2-microglouline (mg/l)	3.76 (0.98-12.8)
LDH (u/l)	254 (94-987)
CD 38 Positive Negative	 19 (26.8%) 52 (73.2%)
Bone marrow pattern Diffuse Non-diffuse	 9 (12.7%) 62 (87.3%)
Binet stage A B C	 30 (42.3%) 24 (33.8%) 17 (23.9%)
Rai stage (0,1,2) (3,4)	 54 (76.1%) 17 (23.9%)
13q14 deletion Positive Negative	 45 (63.4%) 26 (36.6%)
Needed treatment Positive Negative	 36 (50.7%) 35 (49.3%)

WBCs: White blood cells , **ALC**: Absolute lymphocyte count , **LDH**: lactate dehydrogenase

Table 2: Clinical and laboratory characteristics of CLL patients positive and negative for del 13q14.

	Positive n(45)	**Negative n(26)**	**P**
Age (years)	60.7±9.1	60.23±8.8	0.82
Sex Female Male	16 (35.6%) 29 (64.4%)	9 (34.6%) 17 (65.4%)	0.936
WBCs(× 10^3/ µl)	41 (12-134)	56.5 (27-90)	0.078
ALC (× 10^3/ µl)	36 (8-127)	54.5 (25-87)	0.017 *

Hemoglobin (gm/dl)	11.77±2.0	12.98±1.33	0.002 *
platelet (× 10^3/ µl)	154 (56-412)	159 (76-431)	0.867
β2-microglouline (mg/l)	3.7 (0.98-12.8)	3.9 (0.99-12.1)	0.848
LDH (u/l)	263 (94-987)	253.5 (99-757)	0.612
CD 38 Positive Negative	 12 (26.7 %) 33 (73.3%)	 7 (26.9 %) 19 (73.1%)	0.98
Bone marrow pattern Diffuse Non-diffuse	 8 (17.8%) 37 (82.2%)	 1 (3.8%) 25 (96.2%)	0.09
Binet stage A B C	 24 (53.3%) 11 (24.4%) 10 (22.2%)	 6 (23.1%) 13 (50%) 7 (26.9%)	0.03*
Rai stage (0,1,2) (3,4)	 35 (77.8%) 10 (22.2%)	 19 (73.1%) 7 (26.9%)	0.655
Needed treatment Positive Negative	 14 (31.1%) 31 (68.9%)	 18 (69.2%) 8 (30.8%)	 0.002 *

WBCs: White blood cells , **ALC**: Absolute lymphocyte count , **LDH**: lactate dehydrogenase, ***:** significant, **t test:** mean ± SD, **Mann-Whitney test:** median (range**), Chi-square test**: number (percent)

Table 3: Clinical and laboratory characteristics of CLL patients with isolated and non-isolated del 13q14.

	Isolated n(38)	**Non-isolated n(7)**	**P**
Age (years)	60.9±9.1	59.9±9.7	0.785
Sex Female Male	 13 (34.2%) 25 (65.8%)	 3 (42.9%) 4 (57.1%)	0.686
WBCs (× 10^3/ µl)	 38.5(12-112)	 45(25-134)	0.042 *
ALC (× 10^3/ µl)	34.5(8-102)	38(19-127)	0.048 *
Hemoglobin (gm/dl)	11.8±2.07	11.5±1.73	0.662
platelet (× 10^3/ µl)	154.5(56-412)	123(85-178)	0.100
β2-microglouline (mg/l)	3.7(0.98-11.8)	6.9(1.9-12.8)	0.062
LDH (u/l)	213(94-435)	737(198-987)	0.002 *
CD 38 Positive Negative	 10 (26.3%) 28 (73.7%)	 2 (28.6%) 5 (71.4%)	0.99
Bone marrow pattern Diffuse Non-diffuse	 7 (18.4%) 31 (81.6%)	 1(14.3%) 6 (85.7%)	0.99
Binet stage A B C	 21 (%) 9 (23.7%) 8 (21.1%)	 3 (42.9%) 2 (28.6%) 2 (28.6%)	0.827
Rai stage (0,1,2) (3,4)	 30 (78.9%) 8 (21.1%)	 5 (71.4%) 2 (28.6%)	0.642

WBCs: White blood cells , **ALC**: Absolute lymphocyte count , **LDH**: lactate dehydrogenase, ***:** significant, **t test:** mean ± SD, **Mann-Whitney test:** median (range**), Chi-square test**: number (percent)

Table 4: Association of deletion rate with clinical and laboratory characteristics of CLL patients with isolated del13q14.

	≥80% n (8)	<80% n (30)	P
Age (years)	55.75±8.83	62.3±8.8	0.071
Sex Female Male	2 (25%) 6 (75%)	11 (36.7%) 19 (63.3%)	0.689
WBCs (× 10^3/ µl)	47.0(23-100)	37.5(15-88)	0.059
ALC (× 10^3/ µl)	40.5(19-90)	32.5(10-92)	0.084
Hemoglobin (gm/dl)	11.9±2.8	11.8±1.9	0.968
platelet (× 10^3/ µl)	149.5(75-231)	159.5(56-412)	0.333
β2-microglouline (mg/l)	4.34(1.69-11.8)	3.6(0.98-10.8)	0.390
LDH (u/l)	260(100-435)	213(94-432)	0.774
CD 38 Negative Positive	6 (75%) 2 (25%)	22 (73.3%) 8 (26.7%)	0.99
Bone marrow pattern Diffuse Non-diffuse	3 (37.5%) 2 (62.5%)	4 (13.3%) 26 (86.7%)	0.146
Binet stage A B C	3 (37.5%) 2 (25%) 3 (37.5%)	18 (60%) 7 (23.3%) 5 (16.7%)	0.39
Type of deletion Biallelic Monoallelic	1 (12.5%) 7 (87.5%)	2 (6.7%) 28 (93.3%)	0.519
Time to treatment (TTT) (Month)	13±4.95	93.8±15.5	0.000 *

WBCs: White blood cells , **ALC**: Absolute lymphocyte count , **LDH**: lactate dehydrogenase, ***:** significant, **t test:** mean ± SD, **Mann-Whitney test:** median (range**), Chi-square test**: number (percent)

Table 5: Clinical and laboratory features of CLL patients with monoallelic and biallelic isolated 13q14 deletion.

	Monoallelic n(35)	Biallelic n (3)	P
Age (years)	60.9±9.2	60.7±9.7	0.96
Sex Female Male	13 (37.1%) 22 (62.9%)	0 (0%) 3 (100%)	0.538
WBCs(× 10^3/ µl)	36(12-112)	56.3(25-67)	0.357
ALC (× 10^3/ µl)	33(8-102)	48.2(19-62)	0.516
Hemoglobin (gm/dl)	11.83±2.02	11.8±3.09	0.961
platelet (× 10^3/ µl)	155(56-412)	154(87-180)	0.533
β2-microglouline (mg/l)	3.7(0.98-11.8)	3.12(2.98-4.8)	0.935
LDH (u/l)	257(94-432)	226(196- 244)	0.743
CD 38 Positive Negative	9 (25.7%) 26 (74.3%)	1 (33.3%) 2 (66.7%)	0.99
Bone marrow pattern Diffuse Non-diffuse	4 (11.4 %) 31 (88.6%)	3 (100%) 0 (%)	0.004 *
Binet stage	20 (57.1%)	1 (33.3%	0.72

A B C	8 (22.9%) 7 (20%)	1(33.3%) 1 (33.3%)	
13q14 deletion rate <80% ≥80%	28 (80%) 7 (20%)	2 (66.7%) 1 (33.3%)	0.519
Time to treatment (TTT) (Month)	89.5(11-118)	69(6-80)	0.116

WBCs: White blood cells , **ALC**: Absolute lymphocyte count , **LDH**: lactate dehydrogenase, ***:** significant, **t test:** mean ± SD, **Mann-Whitney test:** median (range**), Chi-square test**: number (percent)

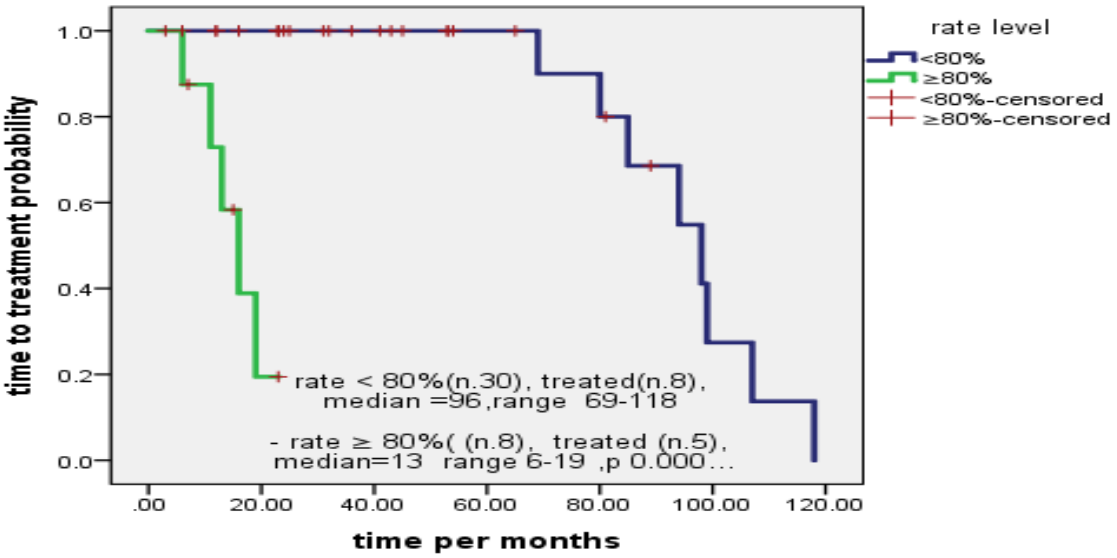

Figure 1: Relationship between isolated 13q14 deletion rate and TTT in CLL patients.

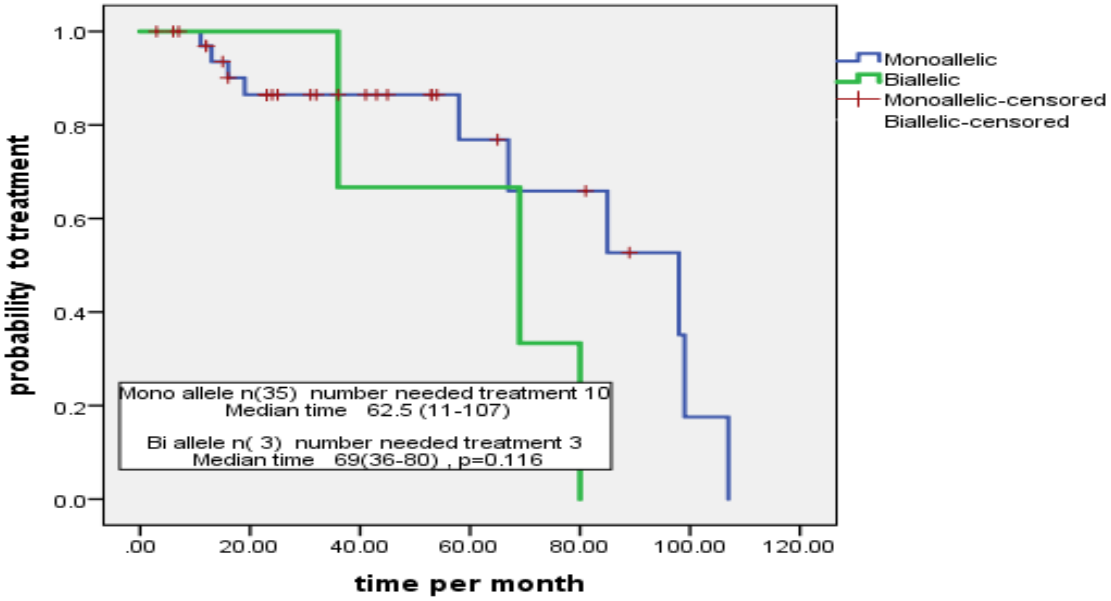

Figure 2: Relationship between type of del13q14 (monoallelic or biallelic) and TTT in CLL patients.

DISCUSSION

CLL is a mature B cell neoplasm represented by monoclonal expansion of B lymphocytes in the PB , BM and lymphoid tissues [6]. Cytogenetic aberrations are highly implicated to the outcome of CLL cases and cytogenetic anomalies like loss of ATM or TP53 genes harbored an inferior outcome, while isolated 13q deletion and normal karyotype have a favorable outcome [7]. The course of CLL cases having isolated 13q deletion was known to be diverse; some patients with the isolated form of the deletion do not need therapy for years, while others acquire threatening disease with shorter time to treatment [8-12].

In the current work, 13q14 deletion was detected in (63.4%) of the studied CLL patients, In the work conducted by Rowntree et al.[13], 13q14 deletion was encountered in 51.5% of their cases, nearby results were encountered in previous studies in which 13q14 deletion was detected in more than fifty percent of CLL patients [7, 11, 12]. While, a lower percent of 37.5 % of the studied CLL patients had that deletion in the work conducted by Ahmed et al. [14]

According to presence or absence of 13q14 deletion, we divided our study patients into positive and negative groups in a trial to evaluate the impact of 13q14 deletion on CLL clinical behavior. In the current work, we did not find significant difference between both groups as regards age. Other researches have announced that 13q14 deletion is mainly related to older age [15,16]. In our study, males were more frequently affected with CLL which was in concordance with other studies of CLL [17,18], but we got the result that patient gender was not a statistically significant factor between positive and negative groups. We held a comparison between the deletion positive and the negative groups as regard some laboratory parameters. On one hand, we found statistically significant difference between both groups regarding both hemoglobin level and ALC that came concordant to the work of Ahmed et al. [14]. On the other hand, we did not find a statistically significant difference as regard any of total WBC count, platelet count, serum LDH level, β2-microglobulin, BM pattern of infiltration or CD38 positivity between the positive and the negative groups. Several studies attempted to evaluate the prognostic significance of 13q14 deletion in CLL cases. In our research, we found that the majority of the cases with 13q14 deletion didn't need chemotherapeutic medication at the diagnosis or at the time of follow up in contrast with other cases who were negative for 13q14 deletion and this came in the same line with other studies that propose that deletion 13q14 is associated with better prognosis[14,16,19]. In our contest to assess for Binet staging, we reached that there was a statistically significant association with deletion 13q14 which came in agreement with Ahmed et al. [14]. While as regards Rai staging, we found that there was not a statistically significant association with deletion 13q14 that met the results of Durak Aras et al.[5].

The matter of course of CLL cases with isolated 13q14 deletion was messy; some cases with isolated 13q14 don't need therapy for long periods while others proceed into aggressive course [8-12]. In present work, 13q14 deletion was found as an isolated abnormality in (53.5%) of CLL patients, while in only (9.9%) of patients additional cytogenetic abnormalities were detected that came in the same line with preceding studies [11,12,20,21]. We were interested to investigate the relation between effect of the studied clinical and laboratory parameter and the state of 13q14 deletion isolation. In the present work, there was a statistically significant association between the non-isolated deletion and each of higher total leucocytic count, ALC and serum LDH level that came in concordance with the results obtained by Miao et al.[21]. On the other hand, we didn't find statistically significant association between the state of 13q14 deletion isolation and any of patient age, sex, hemoglobin concentration, platelet count, β2micoglobin, CD38 positivity, BM infiltration pattern, Rai and Binet staging.

Different studies examined 13q deletion at different rates in CLL patients. A statistically significant difference was discovered in CLL patients between patients having deletion rate more than 65% and less than 65% as regards TTT, however no difference was checked as regards of overall survival (OS) [11]. It was suggested that patients with deletion 13q14 more than 70% had a worse prognosis [10,22,23]. Different studies announced that isolated deletion of 13q in CLL patients having a rate of deletion of more than 80% had a statistically significantly shorter TTT and overall survival than those with a deletion of lower than 80% [8,9]. It was noted that isolated deletion 13q in a rate more than 90% is accompanied with poor outcome and was

considered as an independent prognostic factor [8]. In our study, we did our work at a cut off value of 80% deletion rate to find out the prognostic implement of the percentage of cells harboring 13q14 deletion on the disease outcome. We divided the patients with isolated 13q14 deletion into two groups; the first was at ≥ 80% deletion rate and the other was at < 80% deletion rate. Clinical and laboratory data were collected and comparison was held between cases with ≥ 80% and cases with < 80% deletion rate. We noted that there were no significant differences between the two groups as regards of any of the studied clinical or laboratory factors that came in union with Miao et al. [21]. We were interested to test if there is a difference between the two groups as regards the period of TTT and disease stage. We reached that the time to first treatment of the patients with deletion rate for 13q14 deletion 80% or more was significantly shorter. So, cytogenetic analysis of CLL patients with 13q14 deletion should be accompanied with evaluation of the deletion rate in order to assess its issue as a prognostic marker and to highlight its prognostic significance.

The mechanism by which 13q deletion could affect the outcome of CLL cases is still indefinite. But it may be attributed to variation in gene expression such as down-expression of genes involved in the apoptotic process and overexpression of genes involved in cellular proliferation [9].

It was noted that monoallelic deletion is more usual in comparison with either biallelic or combined deletions [24]. In our work, there were 3 cases displaying the biallelic form of the deletion out of the 38 patients carrying the isolated 13q14 deletion (8%) that came in a meeting point with other studies [19, 20, 24,25]. Available data about the impact of deletion type either monoallelic or biallelic on the outcome diversity of cases with isolated 13q deletion are antagonistic. Durak Aras et al. [5], a previous work claimed that biallelic 13q deletions were accompanied by additional threating presentation which could be attributed to higher proliferation rate in lymphocyte growth [25]. Another study reported that biallelic deletions were noted to be accompanied with shorter time to first treatment and an advanced Binet stage but the authors could not consider the biallelic deletion as an independent prognostic factor [23]. Clashing results were reported in other studies as it was reached that the deletion type had no impact on TTT and OS [11, 24]. Through our research, we were in interest to evaluate the potential clinical variations in cases carrying monoallelic or biallelic deletion of 13q. In our results, it was remarked that the biallelic deletion form did not have a consequent on disease stage, time to first treatment or any of the studied clinical or laboratory parameters except for the BM infiltration pattern.

Limitation of the study:

Limited number of cases found with biallelic deletion, also the size of deletion and status of RB1 gene could not be clarified by the used FISH probe. So, we hope in the future to conduct further studies on larger number of patients and use another FISH probe to detect RB1 gene deletion and study its effect on clinical course of the disease.

Conclusions:

The 13q deletion is a common cytogenetic abnormality in CLL patients and has a variable impact on the disease condition according to specific features of deletion; isolated deletion is better than non-isolated one, the higher rate of deletion is associated with shorter TTT, biallelic is associated with diffuse pattern of bone marrow infiltration. So, it is recommended to study CLL patients for 13q14 deletion by FISH to clarify its nature and hence manage patients properly.

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