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Original Article

Frequency of 17p Deletion in Chronic Lymphocytic Leukemia Patients Presenting to Combined Military Hospital Rawalpindi

Atiq-ur-Rehman, Riaz Ahmad, Muhammad Nadeem, Umair Tufail, Amjad Khan, Fayyaz Hussain*

Department of Oncology, Combined Military Hospital /National University of Medical Sciences (NUMS) Rawalpindi Pakistan,
*Department of Medicine, Ayub Teaching Hospital Abbottabad Pakistan

ABSTRACT

Objective: To assess the frequency and factors related to the presence of 17p deletion among patients diagnosed with chronic lymphocytic leukaemia at the Oncology Department of Combined Military Hospital Rawalpindi

Study Design: Cross-sectional study.

***Setting And Duration Of Study*:** Oncology Department, Combined Military Hospital, Rawalpindi Pakistan, Feb 2020 to Mar 2021.

***Methodology*:** Patients with Chronic lymphocytic leukaemia were recruited for the study. The fluorescence in situ hybridization method was used to look for the presence of 17p deletion, using 10% cells as a cut-off value. Demographics, treatment status, and β2-microglobulin levels were correlated with 17p deletion in our study population.

***Results*:** A total of 102 patients diagnosed with Chronic Lymphocytic leukaemia were included in the analysis. The mean age of the patients was 55.82±7.17 years.74(72.5%) were male, while 28(27.5%) patients diagnosed with this condition were female. 17p deletion was present in 16(15.7%) patients, while 86(84.3%) patients were not detected with 17p deletion. Elevatedβ2-microglobulin levels were strongly related to 17p deletion in our target population (*p*-value-0.005).

***Conclusion*:** 17p deletion was a fairly common finding among patients of chronic lymphocytic leukaemia presenting to our department. Patients with elevated β2-microglobulin levels were more at risk of having this genetic mutation than those with normal β2-microglobulin levels.

Keywords: 17p deletion; Chronic lymphocytic leukemia; Diagnosis; Mutations.

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INTRODUCTION

The incidence of haematological malignancies has increased in recent years because of advancements in diagnostic and management procedures.[1] Blood cancers are a diverse group of disorders with a wide range of symptoms, management plans, and prognostic factors.[2] One of the biggest achievements of medical science in this field has been the studying of genetic linkage and mutations causing these disorders, making this more complex to treat. Understanding of the genetics of leukaemia is the first step in deciding further management and predicting the prognosis.[3]

Molecular genetics is an evolving field and creating an impact on the diagnosis and management of a lot of disorders.4 Mutational landscape involves multiple mutations, with each mutation having its influence on the nature and prognosis of the disease.[5] Around 80% of patients of chronic lymphocytic leukaemia have either 1 out of 4 common chromosomal mutations, namely deletion 13q14, deletion 11q22-23, deletion 17p12, and trisomy 12.[6]

Clinicians and researchers have been studying various mutations linked with CLL, including 17p deletion, in various oncology centres around the globe. Yuan *et al*. studied at Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China, in 2019 on 305 patients suffering from CLL. Their study concluded that the percentage of cells with 17p deletion and the size of a subclone of 17p should be considered in addition to clinical factors to predict the prognosis of patients of CLL with TP53 disruption.[7] Begacean *et al*. in the same year came up with another perspective and evaluated role of 17p deletion in treatment response among patients with CLL. They concluded that 17p deletion protects the tumour cells from DNA-damaging agents such as fludarabine and bendamustine, and the presence of this deletion also alters the pharmacokinetic properties of rituximab making it less effective for these patients.[8] Hafelach *et al*. revealed that the most frequent abnormality found in their patients on FISH analysis was loss of 17p,

Correspondence: Dr Atiq-ur-Rehman, Department of Oncology, Combined Military Hospital Rawalpindi Pakistan
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which was present in 14 out of 63(22%) patients included in their study.[9]

A recent study published by Mahmood *et al*. concluded that deletion was common among patients of CLL in Pakistan, and patients harbouring this deletion had poor treatment response and survival outcomes.10 Haematological malignancies have been commonly encountered malignancies in our part of the world and pose a great burden on our healthcare budget. If the management and prognosis of a particular leukaemia get sorted at the start, this may limit the misery of the patient as well as the financial impact. This study was planned to assess the frequency and factors related to 17p deletion among patients diagnosed with chronic lymphocytic leukaemia at the oncology department of a combined military hospital in Rawalpindi.

METHODOLOGY

The cross-sectional study was conducted at the Oncology Department, Combined Military Hospital Rawalpindi, Pakistan from February 2020 to March 2021 after IERB approval (123/11). The sample size was calculated by the WHO sample size calculator using population prevalence of 17p deletion in CLL as 7%.[11]

Inclusion Criteria: Patients of either gender, aged 18 and 70 years diagnosed with CLL presenting to Oncology Department who may or may not be under active treatment, were included.

Exclusion Criteria: Patients with malignancies other than CLL, autoimmune disorders, chronic liver disease, pregnant women, patients with unclear diagnoses or suspicion of other causes leading to deranged haematological profiles were excluded.

All patients of CLL diagnosed by consultant oncologist/haematologist based on the International Workshop on Chronic Lymphocytic Leukemia IWCLL criteria, based on persistent lymphocytosis, lymphocyte morphology on peripheral blood smears, and immunophenotyping results.[12] were included using non-probability consecutive sampling technique and after written informed consent. The Fluorescence In Situ Hybridization method was used to look for the presence of 17p deletion by using 10% cells as the off value β2-microglobulinlevels>4.0mg/dl were taken as cut off for high β2-microglobulin levels.[13,14]

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The p-value lower than or up to 0.05 was considered as significant.

RESULTS

A total of 102 patients diagnosed with chronic lymphocytic leukaemia at Oncology Department during the study period were included in the analysis. The mean age of the patients was 55.82±7.17 years. 74(72.5%) were male, while 28(27.5%) patients diagnosed with this condition were female. 17p deletion was present in 16(15.7%) patients, while 86(84.3%) patients were not detected with 17p deletion.Table-I

Table-I: Characteristics of Study Participants Included in the Analysis (n=102)

Characteristics	n(%)
Age (years)	
Mean±SD	48.51±8.127
Range (min-max)	19 years-59 years
Gender	
Male	74(72.5%)
Female	28(27.5%)
17p Deletion	
Absent	86(84.3%)
Present	16(15.7%)
Deranged Beta 2	
Microglobulin	59(57.8%)
No	43(42.2%)
Yes	
On Treatment	
No	47(46.1%)
Yes	55(53.9%)

shows the general characteristics of study participants.Table-II

Table-II: Relationship of 17p Deletion in the Patients of Chronic Lymphocytic Leukemia (n=102)

Factors	No 17p deletion	Presence of 17p deletion	*p*-value
Age			
60year or less	54(62.7%)	10(62.5%)	0.982
>60 years	32(37.3%)	06(37.5%)	
Gender			
Male	62(72.1%)	12(75.0%)	0.809
female	24(27.9%)	04(25.0%)	
Deranged β2-microglobulin			
levels	55(63.9%)	4(25.0%)	0.004
No	31(36.1%)	12(75.0%)	
Yes			
Receiving treatment			
No	40(46.5%)	07(43.7%)	0.839
Yes	46(53.5%)	09(56.3%)	

suggests that Pearson chi-square analysis established the association between elevated levels of β2-microglobulin and 17p deletion (*p*-value-0.004).

DISCUSSION

Cancers of all types have been taking the lives of people or impacting the quality of life negatively all around the world. 1 Hematopoietic malignancies have been no exception to it. Chronic lymphocytic leukaemia is one of the most common malignancies in our part of the world, draining many health budgets and affecting the lives of hundreds of individuals of all age groups each year.[15,16] Molecular genetics is an emerging field in developing countries. A lot of them lack the facilities to conduct these studies. Pakistan has facilities to detect certain mutations related to various

malignancies, and 17p deletion is one of the mutations that can be detected in various laboratories in our country. Therefore, we planned this study to assess the frequency and factors related to 17p deletion among patients diagnosed with Chronic lymphocytic leukaemia at our oncology department.

Yu *et al*. conducted a study in 2017 intending to look for the genomic complexity related to 17p deletion and affecting the response to treatment and prognosis of CLL. They concluded that 17p deletion has a unique genomic profile and that clonal TP53 mutation, 3p, 4p or 9p deletions, and genomic complexity are associated with shorter overall survival.[17] We did not study the prognosis among our study participants. We had no facilities to study other mutations along with 17p deletion, but we found that 17p deletion was common for our study participants. Buccheri *et al*. They found that both these mutations have been linked with poor treatment response and grave prognosis.[18] Studies like these gave us the basis to perform our study, which revealed that around 17% of the patients with CLL had 17p deletion in our population. If this alarming number of patients were going to have poor responses to conventional treatment, then treating teams should be alarmed right from the beginning.

Greipp *et al*.[19] They tried to study various mutations related to chronic lymphocytic leukaemia along with the impact of these mutations on prognosis. Their findings were that around 1% had both 17p- and 11q- in the same cells ("double hit") at some point during their disease, 7% had 17p- deletion, 11% had 11q-, and 81% had neither 17p- nor 11q-. Our objective was to only look for 17p deletion among patients suffering from CLL, and we found that around 17% of patients had the presence of 17p deletion, which was higher than found by Greipp et al. A study published by Mahmood *et al*. in 2018 included 130 patients with CLL. Of these, 24(18.5%) had 17p deletion, and elevated beta 2 macroglobulin was related to 17p deletion in their study.[10] Our findings were similar to those of their study, as around 17% of our patients had 17p deletion, and elevated beta 2 macroglobulin was related to the presence of 17p deletion in our study.

LIMITATIONS OF STUDY

Patients were not evaluated for other mutations or short-term and long-term prognoses. Future studies with better design may generate better and generalizable results.

CONCLUSION

17p deletion was a fairly common finding among patients of chronic lymphocytic leukaemia presenting to our department. Patients with elevated β2-microglobulin levels were more at risk of having this genetic mutation than those with normal β2-microglobulin levels.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

AUR & RA: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

MNU & TA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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