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A DESCRIPTIVE STUDY OF DISTRIBUTION OF BCR – ABL1 FUSION TRANSCRIPTS IN CHRONIC MYELOID LEUKEMIA PATIENTS IN NORTH WESTERN INDIA

Hematology

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ABSTRACT

BACKGROUND: Chronic myeloid leukemia (CML) is a clonal myeloproliferative neoplasm arising from pluripotent stem cells, characterized by a specific chromosomal translocation, t(9;22)(q34;q11). This translocation results in the BCR-ABL1 fusion gene, which encodes an abnormal tyrosine kinase protein that drives the disease. The location of breakpoints within the BCR and ABL1 genes produces various BCR-ABL1 fusion transcripts, leading to proteins of different molecular sizes [1]. We aimed to study the distribution of P210 major transcript, P190 minor transcript and P230 micro transcript in chronic myeloid leukemia in northwestern India. **METHODOLOGY:** This cross-sectional study included 100 clinically newly diagnosed cases of chronic myeloid leukemia (CML). Two vials, each containing 3ml of EDTA peripheral blood samples were received and complete blood count of the samples was performed, followed by the quantitative detection of BCR-ABL1 fusion transcript using multiplex reverse transcriptase polymerase chain reaction (RT-PCR) and statistical analysis was done. **RESULTS:** The median age was 41 years and a male-to female ratio of 1.22:1. The P210 major transcript was predominant, found in 97% of cases, while the P190 minor transcript was identified in 2% of patients and the P230 micro transcript was identified in 1% of the patients. There was no significant correlation between BCR-ABL transcript variants and variables such as age (p=0.828), gender (p=0.194), haemoglobin levels (p=0.880), basophil count (p=0.200), total leukocyte count (p=0.297), packed cell volume (p=0.933), and platelet count (p=0.616). **CONCLUSION:** The frequency of expression of the P210 major transcript in CML patients in our study population was 97 %. The P190 minor transcript variant was identified in 2% of patients and P230 micro transcript was identified in 1% of patients. Both were linked to higher disease progression rates and poorer outcomes, as highlighted in various studies. [2,3,4]

KEYWORDS

P210 major transcript, P190 minor transcript, P230 micro transcript, Chronic myeloid leukemia(CML)

INTRODUCTION :

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative neoplasm of pluripotent stem cells, predominantly composed of proliferating granulocytes. CML is the commonest adult leukemia in India. It is associated with a characteristic chromosomal translocation t (9;22) (q34; q11) leading to BCR – ABL1 fusion gene. Depending upon the location of breakpoints in BCR – ABL1 genome many fusion transcripts have been described which encodes for proteins with different molecular sizes. There are two major BCR-ABL1 fusion transcripts which are e13a2(originally called b2a2) and e14a2 (originally called b3a2) translated to ($p210^{BCR-ABL1}$) protein. The minor BCR –ABL1 fusion transcript e1a2 is translated to ($p190^{BCR-ABL1}$) protein. The micro BCR- ABL1 fusion transcript e19a2 (originally called c3a2) is translated to ($p230^{BCR-ABL1}$) protein.[1]

The study aimed to assess the distribution of BCR-ABL1 fusion transcripts in patients with Chronic Myeloid Leukemia (CML) in northwestern India, addressing a notable gap in existing data for that region.

MATERIALS AND METHOD:

This was a cross-sectional study conducted at the Advanced Hematology Lab, Department of Pathology, SMS Medical College, Jaipur, between May 2023 and April 2024. Elaborate informed consent was obtained from the patients or their attendants before the commencement of the study. Ethical clearance was duly obtained from the Institutional Ethics Committee. All consecutive eligible patients fulfilling the following inclusion criteria (newly clinically diagnosed cases of Chronic Myeloid Leukemia according to WHO 2018 criteria and who were willing to provide consent for the study) were included.

Two vials, each containing 3 ml of EDTA peripheral blood samples, were collected under aseptic precautions after obtaining informed consent. RNA extraction was then performed using the TRUPCR RNA extraction kit, followed by the synthesis of cDNA from the extracted RNA. Quantitative detection of the BCR-ABL1 fusion transcripts was carried out using multiplex RT- PCR with the TRUPCR BCR-ABL1 kit, and statistical analysis was performed thereafter.

RESULTS:

The median age was 41 years, with ages ranging from 12 to 80 years, and a male-to-female ratio of 1.22:1. The P210 major transcript was predominant, found in 97% of cases, while the P190 minor transcript was identified in 2% of patients and the P230 micro transcript was identified in 1% of the patients. There was no significant correlation between BCR-ABL1 transcript variants and variables such as age (p=0.828), gender (p=0.194), hemoglobin levels (p=0.880), basophil count (p=0.200), total leukocyte count (p=0.297), packed cell volume (p=0.933), and platelet count (p=0.616).

Table -1 : Association Between BCR ABL Transcript And Various Parameter

Parameters	P210 major	P190 minor	P230 micro	P value
Age (years)	42.69 ± 15.36	51 ± 4.24	43 ± 0	0.828
Gender (M/F)	54/43	0/2	1/0	0.194
Hb level (g/dl)	9.53 ± 2.16	10.1 ± 2.4	10.3 ± 0	0.880
Basophil count ($x10^3/mm^3$)	6.24 ± 5.71	2.20 ± 0.47	14.78 ± 0	0.200
TLC count ($x10^3/mm^3$)	180.24 ± 147.73	105.12 ± 7.75	384.74 ± 0	0.297
PCV (%)	31.25 ± 7.38	33.2 ± 7.64	31.6 ± 0	0.933
Platelet count ($x10^3/mm^3$)	368.24 ± 329.24	243 ± 202.24	92 ± 0	0.616

DISCUSSION:

The median age of CML patients in present study was 41 years with a range of 12 – 80 years. Temilola O. Owojuyigbe et al. [5] in a similar study, reported the aged range of CML patients from Nigeria to be 10-87 years, with a median of 38 years. Hossein Ayatollahi et al. [6] in a study from Iran reported patients age range was 21 to 77 years and

mean age was 45.89±15.60 years. Khazaal et al.[7] in a study from Iraq reported a mean age of CML patients of 51.7 ± 12.2 years, with age range of 18–71 years.

In present study CML showed a male preponderance with the male: female ratio of 1.22: 1. Similar to our study, Temilola O. Owojuyigbe et al. [5] found the male: Female ratio of CML patients was 1.2: 1. In another study, Deb et al.[8] reported a male : Female ratio of CML patients was 2.3 : 1. Khazaal et al.[7] in a study from Iraq reported M:F ratio of 1.38:1 These findings reveal a slight male preponderance of CML.

In the present study, the P210 major transcript was identified in 97% of cases, aligning with previous research highlighting its prevalence in Chronic Myeloid Leukemia (CML). For instance, Osman et al. [9] reported that 95.4% of 43 Sudanese patients had the P210 major transcript. Similarly, Ayda Bennour et al. [10] found that 97.77% of 60 Tunisian patients expressed a form of the P210 transcript. Additionally, Abdelrahim M. Muddathir et al. [11] documented that 32.1% of 109 Sudanese patients expressed one or both P210 BCR-ABL1 rearrangements, while Deb et al. [8] reported that 97.5% of 80 CML patients had the P210 major transcript and K.Chootawiriyasakul et al.[[12] reported that 93.79 % of 177 CML patient had the P210 major transcript . A.K. Arun et al. [2] noted that 94.2% of a cohort of 1,260 CML patients had the P210 major transcript. Further studies, including those by Hossein Ayatollahi et al.[6] and Khazaal et al.[7] confirmed the P210 transcript's presence in 91.76% and 98% of cases, respectively.

In contrast, the P190 minor transcript was found in 2% of cases in the current study. A.K. Arun et al. [2] reported the minor transcript in 1.2% of cases, while Hossein Ayatollahi et al. [6] found it in 1.17%. Additionally, Chootawiriyasakul et al. [12] detected the P190 minor transcript in 4.52% of cases, and Temilola O. Owojuyigbe et al. [5] detected the P190 minor transcript in 0.4% of cases.

The P230 micro transcript was found in 1% of cases in the current study. Ayda Bennour et al.[10] reported one patient with the P230 micro transcript, indicating its presence among CML patients in Tunisia. Deb et al.[8] reported this P230 micro variant in 2.5% of patients. A.K. Arun et al. [2] reported the P230 micro variant in 0.3% of cases. Chootawiriyasakul et al.[12] in a study from Thailand, reported that the P230 micro transcript was found in 1.14% of patients. Another similar study by Temilola O. Owojuyigbe et al. [5]24 found the P230 micro transcript in 1.3% of cases from Nigeria. These findings underscore the notable differences in the expression of BCR-ABL1 transcripts, which may be influenced by ethnic and genetic factors, with the P210 major transcript being significantly more prevalent in CML cases compared to the minor P190 minor and P230 micro transcript.

The present study found no significant association between transcript variants and various parameters, such as age, gender, haemoglobin levels, basophil count, total leukocyte count, packed cell volume, and platelet count. These results were consistent with findings from studies by Hossein Ayatollahi et al.[6] and Khazaal et al.[7]

CONCLUSION:

The frequency of expression of the P210 major transcript in CML patients in our study population was 97 %. The P190 minor transcript variant was identified in 2% of patients and P230 micro transcript was identified in 1% of patients. Both were linked to higher disease progression rates and poorer outcomes with tyrosine kinase inhibitor therapy, as highlighted in various studies.[2,3,4] These results emphasize the importance of identifying distinct fusion transcripts in CML patients, offering valuable insights into prognosis and therapeutic responses.

Conflict Of Interest:

There was no conflict of interest in the study undertaken.

Ethics Approval:

Ethics Clearance was obtained from Institutional Ethics Committee – S.M.S. Medical College & Attached Hospitals, Jaipur.

Informed Consent:

Written Informed Consent was obtained from all the patients or their attendants before the study.

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