EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 7
01-04
Year: 2021

HEMATOLOGICAL PARAMETERS OF CHRONIC MYELOID LEUKEMIA PATIENTS IN SUDAN TREATED WITH IMATINIB

Noah Awad[1]*, Aboalgasim Abaas[2], Nawal Altayeb[3] and Hiba Khalil[4]

[1]Medical Laboratory Specialist, Alribat Hospital, Khartoum, Sudan Sudan.
[2]Assistant Professor, of Medical Laboratory Sciences, Sudan University of Science and Technology, Sudan
[3]Assistant Professor of Hematology, Ibn senna University, Sudan.
[4]Associate Professor of Hematology and Stem Cells Technology, Al-neelain Stem Cells Center, Al-Neelain University, Sudan.

***Corresponding Author: Noah Awad**
Medical Laboratory Specialist, Alribat Hospital, Khartoum, Sudan Sudan.

Article Received on 24/04/2021 **Article Revised on 14/05/2021** **Article Accepted on 04/06/2021**

ABSTRACT

Background and Objectives: Chronic myeloid leukemia (CML) is disease that differentiated by gene called the bcr-abl fusion gene which produced bcr-abl fusion protein. The detection of tyrosine kinase inhibitor (TKI), imatinib, enhancement the treatment of CML patients. Our general objective is to determine the Hematological parameters in Sudanese patients with chronic myeloid leukemia treated with Imatinib, the specific objectives to correlate the hematological parameters with phases. **Methods:** Descriptive study conducted from June 2017 to October 2019 at Alneelain University, faculty of Medical Laboratory Sciences, Khartoum, Sudan. All CML patients were diagnosed Positive of Philadelphia chromosome from Hematology oncology at Radio and Isotope Center at Khartoum, Sudan after the approval of study. Patients were included sexes, Philadelphia chromosome result, bone marrow report, clinical feature, WHO criteria for phases of disease and treatment. **Results:** The numbers of male patients were 67 (67%), while the numbers of females were 33 (33%) as can be seen in Fig.1. Ages of the studied patients ranged from 10 to 70 years. The mean ages of the population were 43.89 years. The mean ages of males were 46.22years; and that of females were 41.75 years. The ratio of male to female is 2:1. **Interpretation & conclusions:** It can be concluded that treatment of CML patients with Imatinib mesylate caused complete WBCs decrease to normal range. The major hematologic and cytogenetic response was noticed when using a higher dose of Imatinib mesylate.

KEYWORDS: Chronic Myeloid Leukemia, Imatinib, Myeloproliferative disease.

INTRODUCTION

Chronic myeloid leukemia (CML) is a neoplasm disease distinguish by single expansion of hematopoietic stem cells, leading to an increase in peripheral blood myeloid, erythroid, and platelet cells, with bone marrow (BM) change a myeloproliferative condition characterized by chromosomal change t (9; 22) (q34; q11),[1] also sometimes called Philadelphia chromosome. The result of this translocation case is a bcr-abl oncogenic fusion gene that resulting bcr-abl protein which lead to tyrosine kinase activity. More medical information's knowledge about CML and the discovery of the pathogenesis of tyrosine kinase has led to the creation of a good drug called imatinib mesylate (IM) that binds at the ATP binding site and specifically stopped bcr-abl kinase action. The Imatinib treatment of CML gives high rate of cytogenetic and molecular attenuation in the majority of patients. Treatment protocol of CML patients whom in chronic phase is 400 mg IM per day that including the bcr-abl transcript level using real time quantitative PCR (RQ-PCR) and Philadelphia chromosome positive cells percentage using cytogenetic techniques farther more, some leukemic patients not respond to IM therapy. One of the real causes for that are ABL kinase mutations actually represent more than 50% of Imatinib unsuccessful in CML patients.[3]

Over the world Chronic myeloid leukemia (CML) patients representive 15%–20% of all adult leukemia's.[4]

METHODS

Descriptive study conducted from June 2017 to Oct 2020 at Alneelain University, faculty of Medical Laboratory Sciences, Khartoum, Sudan. All CML patients were diagnosed Positive of Philadelphia chromosome from Hematology oncology at Radio and Isotope Center at Khartoum, Sudan after the hospital approved the study. Patients were included both sexes with their clinical data such as Philadelphia chromosome result, bone marrow

report, clinical features, WHO criteria for phases, age, sex, occupations, duration of disease and treatment.

Specimen Collection and Preparation

EDTA blood samples of venous blood were collected from the vein under aseptic conditions.

RESULTS

The numbers of male patients were 67 (67%), while the numbers of females were 33 (33%) as can be seen in Fig.1. Ages of the studied patients ranged from 10 to 70 years. The mean ages of the population were 43.89 years. The mean ages of males were 46.22years; and that of females were 41.75 years. The ratio of male to female is 2:1.

The frequencies of hematological parameters for all CML patients were reported as means of TWBCS(12.5), Hb (12.09), RBC 3.92, PLTs, (230.69), HCT (35.900),MCV (94.42) and MCHC (32.84) Table (1.1).

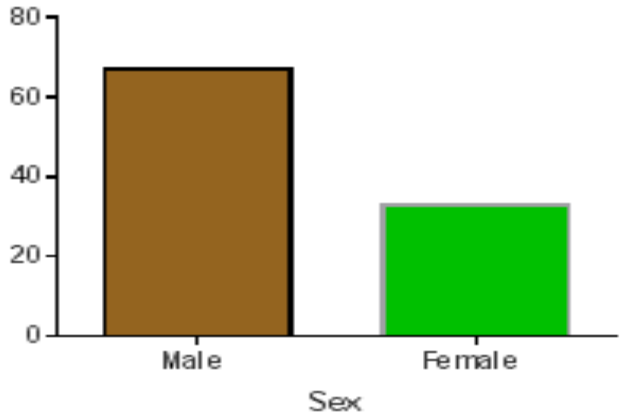

Figure I: Frequencies of sex among population.

Table 1.1: Frequencies of hematological parameters.

	TWBCS	HB	RBC	PLTS	HCT	MCV	MCHC
N Valid	100	100	100	100	100	100	100
Missing	0	0	0	0	0	0	0
Mean	12.5	12.09	3.92	230.69	35.900	94.42	32.84
STD.dieviation	22.9	1.91	.695	146.87	8.241	10.777	2.40
Minimum	2.4	5.70	1.20	13.00	3.50	39.00	26.80
Maximum	166.0	15.80	5.60	883.00	47.50	126.00	43.40

DISCUSSION

This study focus in hematological parameters among Imatinib treatment CML patient in Sudan.

One hundred participants enrolled in this study, all CML patients were diagnosed Positive of Philadelphia chromosome Patients were included both sexes with male/female ratio about 2.1 with their clinical data such as Philadelphia chromosome result, bone marrow report, clinical features, WHO criteria for phases, age, sex, occupations, duration of disease and treatment. In this study The frequencies of hematological parameters for all CML patients were reported as means of TWBCS (12.5), Hb (12.09), RBC 3.92, PLTs, (230.69), HCT (35.900),MCV (94.42) and MCHC (32.84) and In the current study, treatment of CML patients with Imatinib mesylate caused non-significant changes in RBCs count, MCV value, MCH, MCHC, PLTs , HCTand Hb levels, and this may be similar to Study done by Jbireal JM, and Azab Elsayed Azab ,2019 in Libya that found that treatment of CML patients with Imatinib mesylate caused complete WBCs decrease to normal range. Also considered almost the same and similar to study done by Neetu Pandey and Geeta Yadav and others in India 2019 86.21% of patients showed decrease in marrow cellularity with normalization of M:E ratio. 72.42% of patients had decrease in grade of fibrosis and and 17.24% showed no change while 10.34% of patients showed progression of fibrosis grade. Patients with MMR score ≥ 2 (n=4) and those with progression of fibrosis grade (n=3) showed suboptimal molecular response (BCR-ABL transcripts > 10%). Pretherapy mean MVD of patients (14.69 ± 5.28) was higher than that of controls (6.32 ± 1.64). Also hematological parameters decrease to normal range.

On other hand this study disagree with study done in Serbia, by Danijela Lekovic., et al. (2017) leukocytosis ≥ 100 × 109/l ($p = 0.001$), blood blasts ≥ 1% ($p = 0.002$), and the presence of additional cytogenetic aberrations ($p = 0.002$) as predictors of Imatinib failure,so high rate of TWBCs count observed may due to different ethnic group.

ACKNOWLEDGMENT

My great thanks to my supervisor Dr. Hiba Badr Eldin Khalil Associate Professor of Hematology and Stem cells Al-Neelain University, for hegreat helping and supporting and encouraging me to do the best by guidance. My thanks and appreciation to Dr. Nawal Eltayeb, Assistant Professor, Ibn Senna University, for her valuable supervision and helping. Deeply grateful to Dr Abu Elgasim Abaas Assistant Professor, of Medical Laboratory Sciences, Sudan University of Science and Technology, Sudan for great help.

Financial support & sponsorship None.

CONFLICTS OF INTEREST

REFERENCES:

1. Guideline] national comprehensive cancer Network. Chronic Myeloied Leukemia, Version, 2015; 1. NCCNAvailableathttp://www.nccn.org/profrssionals /physician_gls/pdf/ml.pdf.Accessed: January 3, 2015.
2. [Guideline] national comprehensive cancer Network NCCN clinical practice Guidelineinoncologychronicmyelogenous Leukemia, 2016; 1. Availableathttp://guidelines.nccn.org/epcguideline/guideline/id/EBA4F5EFBFDD8FA8BF78?jumpTo=false#Accessed: December 30, 2015.
3. Ayala M, Ávila E, Domínguez J, Aquino X, Vela J. Diagnosis and treatment of chronic myeloid leukemia in the imatinib mesylate era: Report of the experience at “La Raza” Medical Center in Mexico. Clinical Lymphoma, Myeloma & Leukemia, 2016; 16(2): 57-62. DOI: 10.1016/j.clml.2015.10.006
4. Soverini S, De Benedittis C, Mancini M, Martinelli G. Best practices in chronic myeloid leukemia monitoring and management. Oncologist, 2016; 21(5): 626–633. [PMC free article] [PubMed] [Google Scholar].
5. Parker WT, Lawrence RM, Ho M, et al. Sensitive detection of BCR-ABL1 mutations in patients with chronic myeloid leukemia after imatinib resistance is predictive of outcome during subsequent therapy. J Clin Oncol, 2011; 29(32): 4250-4259.
6. *Besa EC, Buehler B, Markman M, Sacher RA (27 December 2013). Krishnan K (ed.). "Chronic Myelogenous Leukemia Clinical Presentation". Medscape Reference. WebMD*. Retrieved 3 January Bixby, D., Talpaz, M. (2009). "Mechanisms of resistance to tyrosine kinase inhibitors in chronic myeloid leukemia and recent therapeutic strategies to overcome resistance". Hematology, 2014*;* 461-476.
7. Buffa P, Romano C, Pandini A, et al. BCR-ABL residues interacting with ponatinib are critical to preserve the tumorigenic potential of the oncoprotein. FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology, 2014; 28(3): 1221–1236. [PubMed] [Google Scholar] Cătoi, Alecsandru Ioan Baba, Cornel (2007). Comparative oncology .Bucharest: The Publishing House of the Romanian Academy. p. Chapter 17. ISBN 978-973-27-1457-7.Archived from the original on 10 September 2017.
8. Chari, Chari; Dworkin, Ian "The Conditional Nature of Genetic Interactions: The Consequences of Wild-Type Backgrounds on Mutational Interactions in a Genome-Wide Modifier Screen". PLOS Genetics, 2013; 9(8): e1003661. doi:10.1371/journal.pgen.1003661. PMC 3731224. PMID 23935530.
9. Cimato TR, Furlage RL, Conway A, Wallace PK. Simultaneous measurement of human hematopoietic stem and progenitor cells in blood using multi-color flow cytometry. Cytometry B Clin Cytom, 2016*;* 90: 415–423.
10. Chronic myelogenous Leukemia Treatment (PDQ) - Stages of chronic myelogenous leukemia.Septemper21; 20152013.NIH National Cancer Institute .Avail bleathttp://www. Cancer.gov/ cancer topics/pdq/treatment/CML /patient /stage2.AccessedDecember 30, 2015.
11. Cortes J, Huchhaus A Hughes TKantarjian H .Front-line and saving therapies with tyrosine kinase inhibitors and other treatment in chronic myeloid leukemia. J Clin Oncol, 2011; 10, 29(5): 524-531. Epub2011 Jan10.
12. Culen M, Borsky M, Nemethova V, Razga F, Smejkal J, Jurcek T, Dvorakova D, Zackoval D, Weinbergerova B, Semerad L, *et al.* Quantitative assessment of the $CD26^{+}$ leukemic stem cell compartment in chronic myeloid leukemia: Patient-subgroups, prognostic impact, and technical aspects. Oncotarget, 2016*;* 7*:* 33016–33024.
13. Dhahi MAR, Matti BF, Fadel S. Molecular screening for T315I and F317L resistance mutations in Iraqi chronic myeloid leukemia non-responders patients to imatinib. Cancer Clin Oncol, 2013; 2: 55–61. [Google Scholar]
14. D.L. Gibbons, S. Pricl, H. Kantarjian, J. Cortes, A. Quint_as- Cardama, The rise and fall of gatekeeper mutations? TheBCRABL1 T315I paradigm, Cancer, 2012; 118: 293e299.
15. Elias MH, Baba AA, Azlan H, et al. BCR-ABL kinase domain mutations, including 2 novel mutations in imatinib resistant Malaysian chronic myeloid leukemia patients-Frequency and clinical outcome. Leuk Res, 2014; 38: 454–9. [PubMed] [Google Scholar]
16. Elias MH, Baba AA, Husin A, et al. Contribution of BCR-ABL kinase domain mutations to imatinib mesylate resistance in Philadelphia chromosome positive Malaysian chronic myeloid leukemia patients. Hematol Rep, 2012; 4: e23. [PMC free article] [PubMed] [Google Scholar]
17. Elnahass YH, Mahmoud HK, Ali FT, et al. Abl Kinase Domain Mutations in Imatinib-treated Egyptian Patients with Chronic Myeloid Leukemia. J Leuk, 2013; 1: 1–8. [Google Scholar]

18. F, Sgambato A, Maione P, Rossi A, Ferrara C, Napolitano A, Palazzolo G, Casaluce Ciardiello F, Gridelli C. ALK inhibitors: a new targeted therapy in the treatment of advanced NSCLC. Target Oncol, 2013; 2(1): 55–67. doi: 10.1007/s11523-012-0250-9. [PubMed] [CrossRef] [Google Scholar].
19. Gandhi L, Janne PA. Crizotinib for ALK-rearranged non-small cell lung cancer: a new targeted therapy for a new target. Clin Cancer Res, 2012; 2(14): 3737–3742. doi: 10.1158/1078-0432.CCR-11-2393. [PubMed] [CrossRef] [Google Scholar].
20. Khoury HJ, Cortes JE, Kantarjian HM, et al. Bosutinib is active in chronic phase chronic myeloid leukemia after imatinib and dasatinib and/or nilotinib therapy failure. *Blood*, 2012; 12, 119(15): 3403-3412. Epub 2012 Feb 27.
21. Hochhaus A, La Rosee P, Muller MC, Ernst T, Cross NC. Impact of BCR-ABL mutations on patients with chronic myeloid leukemia. Cell Cycle, 2011; 10(2): 250-60 [PubMed] [Google Scholar]
22. Jiang H, Xue Y, Wang Q, Pan J, Wu Y, Zhang J, Bai S, Wang Q, He G, Sun A. et al.The utility of fluorescence in situ hybridization analysis in diagnosing myelodysplastic syndromes is limited to cases with karyotype failure. Leuk Res, 2012; 2(4): 448–452. doi: 10.1016/j.leukres.2011.10.014. [PubMed] [CrossRef] [Google Scholar].
23. J. Waclaw, T. Sacha, T. Stoklosa, Imatinib in the treatment of chronic myeloid leukemia:current perspectives on optimal dose, Blood Lymphat. Cancer Targets Ther, 2015; 5: 101e108.