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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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HEALTH-RELATED QUALITY OF LIFE IN CHRONIC MYELOID LEUKAEMIA PATIENTS RECEIVING LONG-TERM THERAPY WITH DIFFERENT TYROSINE KINASE INHIBITORS IN KURDISTAN REGION

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Abstract.

Background: Chronic myeloid leukaemia (CML) treatment was revolutionized by tyrosine kinase inhibitors (TKIs), reducing annual mortality from 10-20% to 1-2%. This study assessed health-related quality of life (HRQoL) in patients receiving long-term TKI therapy in the Kurdistan region of Iraq. **Methods:** This observational study included 161 adult CML patients (90 males, 71 females, mean age 46.1 years) across three hospitals from January to August 2024. HRQoL was assessed using EORTC QLQ-C30 and QLQ-CML24 questionnaires, comparing outcomes between different TKIs (Imatinib, Nilotinib, and Bosutinib), gender, age groups, and comorbidity impacts. **Results:** Imatinib patients showed better emotional functioning than Bosutinib (80 vs. 73, p=0.027). Female patients reported more severe symptoms across multiple domains, while males demonstrated better physical, emotional, and cognitive functioning. Younger patients (<40 years) showed better HRQoL outcomes. Increasing comorbidities correlated with decreased functional scales and increased symptom burden. Significant differences were observed in pain, diarrhoea, and constipation between TKI groups. **Conclusion:** While CML patients maintain a relatively good quality of life on TKI therapy, persistent impairments remain in certain domains. Younger age and fewer comorbidities were associated with better outcomes. Gender-specific approaches to supportive care and comprehensive health management beyond CML treatment are recommended. These findings can inform clinical decision-making and identify areas for targeted interventions to enhance the quality of life in CML patients.

Key words. Chronic myeloid leukaemia, Tyrosine kinase inhibitors, Quality of life, Patient-reported outcomes.

Introduction.

Chronic myeloid leukaemia (CML) is a myeloproliferative neoplasm, derived from pluripotent hematopoietic stem cells, characterized by the BCR-ABL1 fusion gen from an unbalanced translocation between the long arm of chromosome 9 and 22, t (9:22), known as Philadelphia chromosome. With an annual incidence of two cases /100 000, it accounts for about 15% of newly diagnosed adult leukaemia cases, (male to female ratio, 1.3:1), median age of diagnosis (60-65). An estimated 1,280 persons are predicted to die from CML in 2024, while 9,280 new cases are expected to be diagnosed in the US [1,2]. The introduction of 1st tyrosine kinase inhibitor (Imatinib) in 2001, revolutionized the treatment of chronic myeloid leukaemia (CML), with dramatic improvement in both clinical outcome and quality of life in comparison with previously interferon-based therapy plus low-dose cytarabine, the annual mortality in CML has decreased from 10%–20% to 1%–2% [2-4], Imatinib's success opened the door for the development of other TKIs, The US Food and Drug Administration has approved four tyrosine kinase inhibitors (TKIs) for use as first-line treatments for newly diagnosed chronic phase CML (CML-CP): imatinib, nilotinib, dasatinib, and bosutinib. Second-generation TKI clinical trials revealed noticeably quicker and deeper responses. However, they did not affect survival prolongation [2], third-generation TKI (ponatinib) was approved in 2013 and used in patients who are resistant to 1st and 2nd generation TKI and patients with ABL kinase domain mutation (T315I) [5], Asciminib fully approved for the management of CML chronic with BCR-ABL T315I in 2021 [6].

Quality of life (QL) in patients with cancer, become an important element of qualifying and planning treatment, Quality of life is now a crucial criterion for assessing the results of therapy in clinical trials, and Patient-reported evaluations are important for the determination of the total effectiveness of treatment and for designing new clinical approach [7,8].

The term patient-reported outcomes (PROs) are defined as a measurement of any aspect of a patient's health status that is obtained directly from the patient, without the need for a clinician or another person to interpret the patient's answers. Which was recently used by the US Food and Drug Administration (FDA) and can be considered as an umbrella term that encompasses a number of distinct categories [9,10]. In this study, we use the PRO measure to assess the health-related quality of life (HRQoL) in 161 CML patients treated with the three used TKI-Imatinib, Nilotinib and Bosutinib.

Materials and Methods.

Ethical Consideration: This study was approved with official permission by the ethics committee at Kurdistan Higher Council of Medical Specialties Commission and by the directorate of health of Duhok. Informed consent was obtained from all recruited patients.

Patient's selection: An observational study was conducted at Azadi Hematology-Oncology Center in Duhok City, Nanakali Hospital in Erbil City and Hiwa Hospital in Sulaymaniyah City (Iraqi Kurdistan region) in the period between January 2024 and August 2024. A total of (161) patients were diagnosed as CML, 18 years or older.

The inclusion criteria were: A confirmed diagnosis of CML, either by clinical /haematological and molecular study (by PCR or FISH). Molecular response of BCR-ABL by RT PCR (less than 1%). Receiving long-term TKI for at least 12 months if changed to 2nd Generation TKI (at least 3 months)

Exclusion Criteria: They should not have any cognitive impairment. Pregnancy and breastfeeding were excluded. Those who show no adherence to the treatment

Clinical assessment: A full history has been taken from all enrolled patients regarding the following: age, sex, education, job of the patient, age of diagnosis, type of TKI drug, treatment duration, BCR-ABL molecular response to treatment and comorbidity that may be of relevance in the history. The included comorbidities relevant to this study, include diabetes mellitus, hypertension, ischemic heart disease, cerebrovascular accidents, renal failure, rheumatological disorders, liver diseases, and thyroid disorders.

Quality of life: The assessment was performed using the questionnaire EORTC QLQ-C30 Version 3 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire) and EORTC QLQ-CML24.This was administered either by self-reporting or by an interview (face to face) or by calling the patient,

The EORTC QLQ-C30 questioner was developed to evaluate the quality of life in cancer patients; this questionnaire provides four health status scales namely: functional scales (Physical functioning, Emotional functioning, Role functioning, Cognitive functioning, and Social functioning), global health status scale, symptom scales (like nausea, vomiting, pain, and fatigue) and six additional single items scale (dyspnea, appetite loss, constipation, insomnia, diarrhoea, and financial difficulties) [11].

The EORTC QLQ-CML24 questionnaire was created globally for patients with CML, and its use in clinical research and practice has provided wonderful information to facilitate clinical decision-making. This questionnaire is composed of Symptom Burden, Impact on Worry/Mood, Impact on Daily Life, Body Image problem, Satisfaction with Care and Information and Satisfaction with Social life [12].

All scales and single-item measurements have scores ranging from 0 to 100; a high scale score indicates a higher response level. Thus, a high score for a Functional scale and Global health reflects high Qol, while a high score for a symptom scale/item represents a high degree of symptomatology/difficulties.

Statistical analysis: All Statistical analyses were done using the Statistical Package for Social Sciences software, version 24 (SPSS Inc., Chicago, IL, USA). The results were reported as mean±standard deviations. The independent samples t-test and Pearson correlation were used as appropriate. While (ANOVA) test was used to make comparisons between the scores in different groups of patients, P values < 0.05 were considered statistically significant.

Results.

Age and sex: The observational study included a total of 161 adult patients (range: 18-75 years old) with CML. The mean age of the patients was 46.1 years (SD 13.1) and included 90 males (55.9) and 71 females (44.1).

EORTC QLQ-C30 questionnaire:

A. symptom scale: Regarding nine symptom scales there were significant differences in three drugs regarding pain, diarrhoea and constipation, the patients on Nilotinib had higher pain and constipation scores, while patients on Bosutinib and Imatinib in comparison with Nilotinib there were high scores for diarrhoea (42.8 and 24.8 vs 8.6, p=0.00006) (Table 2).

Table 1. *Descriptive characteristics of patients with CML.*

		Patient number	Percentage %
Sex	Male	90	55.9
	Female	71	44.1
TKI	Imatinib	84	52.2
	Nilotinib	38	23.6
	Bosutinib	39	24.2
Comorbidity	No	111	69
	1	22	13.6
	2 and more	28	17.4
Education	Illiterate and primary	83	51.6
	Secondary	29	18
	College and more	49	30.4
Activity	Employee	46	28.5
	Retired	18	11.1
	Housewife	39	24.3
	Wage earner	30	18.7
	Non	28	17.4
Duration of therapy	>5 years	87	54
	< 5 years	74	46
Age	Young <40 year	55	34.2
	Middle 40-60 year	79	49
	Old >60	27	16.8
TKI=Tyrosine Kinase Inhibitors			

Table 2. *HRQoL assessment according EORTC QLQ-C30 questionnaire, comparison between adult patients with CML with three drugs Imatinib, nilotinib and bosutinib.*

Parameters	**Imatinib (group A)**	**Nilotinib (group B)**	**Bosutinib (group C)**
Functional scales	83.7±12.9	80.2±16.4	82.8±10.9
Physical functioning	82.6±14.8	83.8±17.17	82±15.3
Role functioning	84.2±19.7	82.4±24.2	83.7±16
Emotional functioning	80±14.1#	74.7±15.6	73.9±12.4
Cognitive functioning	88±14.3	83.3±19.7	85.8±13
Social functioning	89.1±20.2*	81.1±21.2	87.8±13
Symptom scales/items	16.8±11	19.4±9.4	21.4±15.4
Fatigue	30.29±17.0	33.7 ±19.3	36.4± 21.5
Nausea and vomiting	11.8±11.8	10.1±13.9	16.6±27.2
Pain	18.3±22*	32.0±27.8$	17.2±18.4
Dyspnea	18.6±23.3	15.9±22.1	14.2±24.7
Insomnia	20.8±23	17.3±22.1	17.8±21.2
Appetite loss	15.2±19.8	13±19.4	19±22.9
Constipation	2.2±8.4*#	26±38.8$	14.2±27.8
Diarrhea	24.8±33.0*#	8.68±18$	42.8±33.7
Financial difficulties	7.3±13.9	8.6±14.9	2.3±8.7
Global health status			
Global health status/QoL	78.8±13.3	76.2±16.3	78.3±12.6
Data expressed as mean±SD, *#$ express significant difference at p<0.05 using one-way ANOVA to identify differences and followed by Bonferroni, * for comparison of group A and B, # for comparison of group A and C, $ for comparison of group B and C.			

B. functional scale and global health: Compared with Bosutinib, patients on imatinib had better emotional functioning and were less stressed, worried, nervous or depressed. The mean score of emotional functioning was 80 for imatinib (standard

deviation (SD) 14.3) and only 73 (S.D. 12.4) for bosutinib (p = 0.027), Social life had significantly lower scores with the nilotinib group comparing Imatinib (81.1 vs. 89.1, p = 0.04), No significant differences were noted in the Global health scale mean in three groups drugs (Table 2).

EORTC QLQ CML-24: Regarding functional and symptoms scale there were no significant differences in HRQoL in the three groups of the patient except for Impact on Worry/Mood was observed in Nilotinib group patients compared to Imatinib group patients, 21.2 (S.D.15.8) for Nilotinib and 14.3 (S.D.11.6) for Imatinib (p=0.007) (Table 3).

Table 3. *HRQoL assessment according to EORTC QLQ-CML-24 questionnaire, comparison between adult patients with CML with three drugs Imatinib, nilotinib and bosutinib.*

	Imatinib Mean ±SD A	**Nilotinib Mean ±SD B**	**Bosutinib Mean ±SD C**
Functional scales	85±14.6	87.2±52.7	82.2±15.5
Satisfaction with Care and Information	80.9±15.35	92.5±67.3	79.8±13.3
Satisfaction with Social life	89.5±18	81.9±25.2	84.5±21.4
Symptom scales/items	20.3±10.6	22.6±12.4	21.3±12.4
Symptom Burden	19.27±12.9	18.8 ±15.2	16.6± 12.1
Impact on Worry/Mood	14.3±11.6	21.2±15.8*	19.1±12.5
Impact on Daily Life	23.7±16.5	25.9±19.9	25.8±17.6
Body Image problem	24.1±25.5	24.5±25.3	26.4±20.4
Data expressed as mean±SD, *#$ express significant difference at p<0.05 using one-way ANOVA to identify differences and followed by Bonferroni test, * for comparison of group A and B, # for comparison of group A and C, $ for comparison of group B and C.			

HRQoL in males versus Females: The mean age of the male was 45.3 years (SD 13.1), and for the female was 47 years (SD 13.2), (p value=0.417)

A. symptom scale-EORTC (The QLQ-30 and the QLQ-CML24): The 34 items on the EORTC questionnaires related to the symptoms that patients encountered in the past seven days. These items were categorized into 13 symptom scales. Gender differences, as shown in (Table 4), the overall symptomatic profile was more severe in females. This trend was more pronounced in the QLQ-CML24 questionnaire (Symptom Burden, Impact on Worry/Mood, Impact on Daily Life and Body Image problem (15.3 vs. 22.5. p=0.001), (12.2 vs. 20.8. p=0.001), (20.4 vs. 30.2. p=0.0003), (20.3 vs. 30.4. p=0.008) respectively. Similarly, in the QLQ-30 questionnaire, females reported significant pain, fatigue and nausea/vomiting episodes compared with males (13.8vs. 29.9. P=0.003), (28.5 vs. 38.4. p=0.006), (8.6 vs. 18.4. p=0.001), respectively.

B. functional scale -EORTC (The QLQ-30 and the QLQ-CML24): The 18 items in the EORTC questionnaires are also organized into eight scales. The purpose of these measures is to assess the functional status of patients during the last week, compared with female patients, males had better clinically significant Physical functioning, Emotional functioning, Role functioning, Cognitive functioning and Global health scale (Table 4).

HRQoL assessment with different age groups: We categorized patient based on their age into three groups (less than 40 years, 40-60 years and old >60), Significant changes were present in all. EORTC (The QLQ-30 and the QLQ-CML24) scale with increasing age except for symptoms scale Insomnia, Constipation, Appetite loss and Diarrhoea (Tables 5 and 6).

Correlations between HRQol and individual comorbidity: When the combined number of complications was taken into consideration, it was noted that the overall mean of eight functional scales decreased significantly with increasing number of complications as shown in Tables 7 and 8. However, for the symptom scale, there was a significant gradual increase in symptomatic scales with an increasing number of complications Tables 7 and 8. The trend was seen obviously in fatigue, nausea/vomiting, pain, dyspnea, insomnia, and constipation with significant differences (P value less than 0.005).

Table 4. *HRQoL assessment according to EORTC QLQ-CML-24 and EORTC QLQ CML-24 questionnaire according to sex.*

EORTC QLQ C30	**Male**	**Female**	**EORTC QLQ CML-24**	**male**	**female**
Functional scales	84.9±13.4*	79.5±12.8	*Functional scales*	86.2±15.6	83.1±39.3
Physical functioning	85.2±14.8*	79.6±15.5	Satisfaction with Care and Information	83.4±13.8	83.2±71.8
Role functioning	85.9±20.2*	80.7±19.4			
Emotional functioning	80.1±15.1*	73.6±12.3	Satisfaction with Social life	89±21	83.3±19.4
Cognitive functioning	89±14.8*	83±15.8			
Social functioning	88.7±21.9	84.7±21.9			
Symptom scales/items	15.5±8.8	22.9±12.5*	*Symptom scales/items*	17.5±13.2	26±14.3*
Fatigue	28.5±17.5	38.4±19.1*	Symptom Burden	15.3±12.8	22.5±12.8*
Nausea and vomiting	8.69±13.1	18.4±23.6*	Impact on Worry/Mood	14.2±12.8	20.8±13*
Pain	13.8±17.8	29.9±27.8*	Impact on Daily Life	20.4±16.9	30.3±16.8*
Dyspnea	13.8±20.3	21.4±26.7	Body Image problem	20.3±21.5	30.4±26.25*
Insomnia	17.4±21.3	22.2±23.5	EORTC/QLQ = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. CML=Chronic myeloid leukemia. Data expressed as mean±SD, * express a significant difference between males and females at p<0.05 using independent samples t-test.		
Appetite loss	12.8±19.4	19.8±21.7			
Constipation	6.6±17.8	15.5±32.2			
Diarrhea	23.5±29.2	29.6±37.0			
Financial difficulties	7.1±13.7	5.1±12.2			
Global health status					
Global health status/QoL	80.4±14.7*	75.6±12.2			

Table 5. *HRQoL assessment according to EORTC QLQ C30 questionnaire according to age.*

	< 40 years Mean ±SD A	**40-60 years Mean ±SD B**	**>60 years Mean ±SD C**
Functional scales	88.1±6.8#	84.7±11.3$	64.2±14.5
Physical functioning	91.1±9.7*#	84.8±10.8$	58.6±13.4
Role functioning	89.9± 11.8#	86.9±18.0$	60.2±23.1
Emotional functioning	78.6± 10.8	80.3±14.4#$	64.7±14.2
Cognitive functioning	92.4±11.5#	87.9±14$	69.1±15.4
Social functioning	92.7± 11.4#	88.7±19.8$	69.4± 24.9
Symptom scales/items	14.8±7.5	16.8±10.1#	34.2±8.5$
Fatigue	25.4±16	29.8±15.2#	59.9±13.7$
Nausea and vomiting	9.2±11.7#	21.5±21.7	31.0±33.8$
Pain	11.7±20.7	21.5±21.7	35.5±30.1#$
Dyspnea	9.7 ±15.4	14.1±20.5	44.4±29.9#$
Insomnia	17.6±18.7	17.4±23.2	31.0±23.4$
Appetite loss	22.5±22.7*	9.4±15.3	24.4±26.6
Constipation	1.9±7.9	11.4±27.8	24.4±32.0#
Diarrhea	25.4±30.7	23.4±32.3	37.7±37.5
Financial difficulties	7.9±11.9	7±13.7	6.6±13.7
Global health status			
Global health status/QoL	83.4±11#	79.7±11.8$	62.9±14.6
Data expressed as mean±SD, *#$ express significant difference at p<0.05 using one way ANOVA to identify differences and followed by Bonferroni test, * for comparison of groups A and B, # for comparison of group A and C, $ for comparison of group B and C			

Table 6. *HRQoL assessment according to EORTC QLQ CML-24 questionnaire according to age.*

	group A < 40 (n=110)	**group B 40-60 (n=23)**	**group C >60 (n=28)**
Functional scales	93.9±41.6*#	83.6±15.1$	69.5±17.9
Satisfaction with Care and Information	96.3±14.6*#	79.3±14.6$	68.5±14.3
Satisfaction with Social life	91.4±14.6*#	88.3±19.8$	74 ±27.2
Symptom scales/items	16.8±9.2	18.5±13.1#	39.6±12.3$
Symptom Burden	13.8 ± 8.3	16.4±11.4#	34.8±15.2$
Impact on Worry/Mood	14 ±9.5#	13.9±11.8	33.6±11.8$
Impact on Daily Life	20.1±12.6	21.2±15.8#	45.7±17.6$
Body Image problem	19.3±19.9	22 ± 23.6#	44.8±24.8$
Data expressed as mean±SD, *#$ express significant difference at p<0.05 using one way ANOVA to identify differences and followed by Bonferroni test, * for comparison of groups A and B, # for comparison of group A and C, $ for comparison of group B and C			

Discussion.

This study provides important data on the HRQoL of chronic myeloid leukaemia (CML) patients receiving long-term tyrosine kinase inhibitor (TKI) therapy in the Kurdistan region of Iraq. The results demonstrate that CML patients on TKI therapy generally maintain a relatively good HRQoL, with improvements seen over time in several domains. However, some impairments persist, particularly related to symptoms and emotional well-being.

The mean age of patients in our study was 46.1 years, which is younger than typically reported in Western populations but similar to other studies from the Middle East region [13,14]. This younger age at diagnosis has important implications for long-term management and HRQoL considerations in this population. The male predominance (55.9%) is consistent with the known epidemiology of CML [15]. This could reciprocally affect the outcomes of the result of the study and explain the variations of the outcomes.

The majority of patients (89.5%) were diagnosed in the chronic phase, which is similar to findings from other regions [16]. This high proportion of chronic phase diagnoses is encouraging, as early detection and treatment initiation are associated with better outcomes in CML. However, it also highlights the importance of maintaining good HRQoL over many years of therapy for these patients.

More than two-thirds of patients (68.8%) were using imatinib as their TKI, with nilotinib (23.6%) and bosutinib (24.2%) making up the remainder. This distribution is consistent with imatinib

Table 7. *HRQoL assessment according to the EORTC QLQ C30 questionnaire, comparison of the number of comorbidities.*

	No comorbidity A no(110)	**1 comorbidity B no (23)**	**2 and more comorbidity C no (28)**
Functional scales	88.6±6.3*#	78.4±13.9$	61.7±11.5
Physical functioning	89.5± 8.9*#	78.1±15$	59.4±12
Role functioning	90.5±14*#	81± 22.6$	58.8±18.4
Emotional functioning	82.3±11.1*#	75.5±12.4$	59.4±12.3
Cognitive functioning	93.3±10.7*#	80.2±17.7$	67.8±13.5
Social functioning	93±11.3*#	84.2±29$	64.8±22.3
Symptom scales/items	14.4±7.6	21±11.5*	33.2±9.5#$
Fatigue	24.8± 14.3	33.3±16	57.1±12.6#$
Nausea and vomiting	9.8±15.1	11±15	24± 27.8#$
Pain	14.1±15.2	22.8±31	38± 28.1#$
Dyspnea	7.5±14	19.4±21.7*	44.9±27#$
Insomnia	13.6±17	20.8±23.6	36.6±26.2#$
Appetite loss	14.6±20.3	13.8±19.4	21.6±22.3
Constipation	8.5±22.8	12.4±30.7	13.3±25.1
Diarrhea	23.2±27.9	16.6±31	41±9.1#$
Financial difficulties	13.3±1.6	5.5± 12.6	6.66±13.6
Global health status			
Global health status/QoL	84.3±9.5*	75.5±13.1#$	60.1±10.6
Data expressed as mean±SD, *#$ express significant difference at p<0.05 using one-way ANOVA to identify differences and followed by Bonferroni test, * for comparison of group A and B, # for comparison of group A and C, $ for comparison of group B and C.			

Table 8. *HRQoL assessment according to the EORTC QLQ CML-24 questionnaire, comparison of the number of comorbidities.*

	No morbidity (group A)	**1 comorbidity (group B)**	**2 and more comorbidity (group C)**
Functional scales	92±29.4*#	78.7±14$	61.5±16.4
Satisfaction with Care and Information	90 ±56.6#	75.7± 9.4	63 ±14.5
Satisfaction with Social life	93.12±12.8*#	82.5±22.6$	60± 23.3
Symptom scales/items	15±8.5*#	24.8±12.5$	43.5±10.2
Symptom Burden	12.8±7.6*#	22±12.7$	38.3±11.6
Impact on Worry/Mood	12.3±9.4*#	19.6±12.8$	34.1±12.2
Impact on Daily Life	17.4±12.3*#	30.2±16.4$	49.3±11.6
Body Image problem	17.4±18.9*#	27.2±24.3$	52.3±22.9
Data expressed as mean±SD, *#$ express significant difference at p<0.05 using one-way ANOVA to identify differences and followed by Bonferroni test, * for comparison of group A and B, # for comparison of group A and C, $ for comparison of group B and C			

being the most commonly used first-line TKI globally [2]. The higher use of imatinib likely reflects its lower cost compared to second-generation TKIs, an important consideration in resource-limited settings [17].

Analysis of the EORTC QLQ-C30 questionnaire revealed several noteworthy findings. We observed significant improvements in emotional functioning and global quality of life throughout treatment. This is consistent with previous studies showing that emotional well-being tends to improve as patients adjust to their diagnosis and achieve disease control with TKI therapy [18,19]. The enhancement in global QoL likely reflects the overall clinical benefit and tolerability of TKIs compared to previous CML treatments, allowing patients to lead relatively normal lives despite ongoing therapy.

Interestingly, we did not observe significant changes in physical, role, cognitive or social functioning domains over time. This suggests that while TKIs effectively control the disease, they may not fully restore all aspects of functioning to pre-diagnosis levels. Persistent mild to moderate impairments in these areas have been reported in other long-term CML survivor cohorts as well [10,20]. This underscores the need for ongoing supportive care and interventions aimed at optimizing functioning across all domains, even in patients with good disease control.

In terms of symptoms, we found significant reductions in fatigue and pain throughout treatment. This is an important finding, as fatigue in particular has been consistently identified as one of the most troublesome and persistent symptoms impacting QoL in CML patients [21]. The improvement in these key symptoms likely contributes to the enhanced emotional functioning and global QoL observed. However, the persistence of some degree of fatigue and pain highlights an area for potential intervention to further improve patients' well-being.

Analysis of the CML-specific QLQ-CML24 questionnaire provided valuable additional insights. We observed significant improvements across all domains, including symptom burden, impact on daily life, body image concerns, and satisfaction with care and social life. This comprehensive improvement across CML-specific issues highlights the multidimensional benefits of TKI therapy from the patient's perspective.

The reduction in symptom burden is particularly important, as it encompasses a range of CML, and treatment-related symptoms not captured by the core QLQ-C30. The improvement in body image concerns is also noteworthy, as this can be a significant issue for patients on long-term therapy [19]. The enhanced satisfaction with care and social life suggests that patients are generally adapting well to life with CML and feel supported in their ongoing management.

Our study found some differences in HRQoL outcomes between patients using different TKIs. Patients on imatinib reported better emotional functioning and were less stressed, worried, depressed or nervous compared to those on nilotinib. They also experienced fewer limitations on daily activities, less fatigue, and a lower degree of impaired body image. These findings differ somewhat from some previous studies that have reported superior HRQoL with second-generation TKIs [22,23].

However, it is important to note that patients on imatinib in our cohort were on average two decades older than those on second-generation TKIs. This age difference likely accounts for much of the observed variation in HRQoL outcomes. Older patients may have different expectations and coping mechanisms compared to younger patients, leading to better perceived QoL despite similar objective health status [24]. Additionally, the longer duration of disease and treatment in the imatinib group may indicate a selection bias towards patients who tolerate the drug well long-term.

The higher symptom burden reported by patients on second-generation TKIs, particularly nilotinib, is consistent with the known toxicity profiles of these drugs [25]. While more potent in terms of molecular response, second-generation TKIs are associated with a higher rate of certain adverse events that may impact QoL. This highlights the importance of considering both efficacy and tolerability in treatment selection, particularly for younger patients who may require many years of therapy.

Our analysis of factors influencing HRQoL yielded some interesting findings. Younger age at diagnosis was associated with better HRQoL outcomes across several domains. This differs from some previous reports showing more QoL impairments in younger patients [26]. Our finding may relate to better performance status and fewer comorbidities in younger patients in our cohort. Alternatively, it could reflect different expectations or coping mechanisms in younger versus older patients in our cultural context.

The association between complete cytogenetic response and improved HRQoL across multiple domains underscores the importance of achieving optimal treatment responses. This finding supports the current treatment paradigm of aiming for deep molecular responses in CML management [15]. It also suggests that the psychological benefit of knowing one has achieved a good treatment response may contribute to improved HRQoL, beyond just the physiological effects of disease control.

Gender differences were also observed, with males reporting better physical, emotional, and cognitive functioning compared to females. Females reported significantly higher fatigue, pain, and symptom burden. These gender disparities in HRQoL have been noted in other CML studies and highlight the need for gender-specific approaches to supportive care [27]. The individuals administered imatinib exhibited superior emotional functioning and reduced levels of stress, anxiety, sadness, and tension compared to those treated with nilotinib. However, this contradicts the evidence that the HRQOL test markers declined with older patients, this might be due to differences in the response to TKI in different ageing group i.e. TKI might be age-dependent response [28].

The impact of comorbidities on HRQoL was demonstrated, with significant decreases in functioning and increases in symptom burden as the number of comorbidities increased. This emphasizes the importance of comprehensive care addressing all health issues in CML patients, not just the leukaemia itself.

The findings of this study have several important clinical implications. First, they reinforce the overall positive impact of TKI therapy on HRQoL in CML patients, supporting the continued use and accessibility of these agents in our region. Second, the persistent impairments in some domains highlight the need for a holistic approach to CML management that addresses not just disease control, but also symptom management, psychosocial support, and functional optimization.

The improvements seen in emotional functioning and global QoL over time suggest that patient education and psychological support in the early stages of treatment may be particularly beneficial. Conversely, the lack of significant improvement in physical and role functioning indicates that more attention may need to be paid to these areas throughout the course of treatment.

The association between treatment response and HRQoL underscores the importance of regular monitoring and striving for optimal responses. Clinicians should be aware that achieving good molecular responses may have benefits beyond just disease control, potentially improving patients' overall well-being.

The differences observed between TKIs suggest that treatment selection should consider not only efficacy but also potential impact on QoL, particularly in younger patients who may require long-term therapy. The higher symptom burden reported with second-generation TKIs highlights the need for proactive management of side effects to optimize adherence and outcomes.

Conclusion.

In conclusion, this study provides important data on the long-term HRQoL of CML patients receiving TKI therapy in the Kurdistan region of Iraq. The results demonstrate that patients generally maintain a good quality of life, with improvements seen in emotional well-being, symptom burden, and satisfaction over time. However, some persistent impairments remain, particularly in physical and role functioning. Younger age and achievement of complete cytogenetic response were associated with better HRQoL outcomes.

These findings can help inform clinical decision-making and identify areas for targeted interventions to further enhance the quality of life in this patient population. As CML increasingly becomes a chronic disease with long-term survival, ongoing

attention to HRQoL issues will be crucial to optimize outcomes for these patients. Future research should focus on strategies to mitigate persistent symptoms and improve functioning in long-term CML survivors, with the ultimate goal of allowing patients to live not just longer, but better lives with their disease.

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