

Peculiarities of the Epidemiology of Chronic Myelogenous Leukemia in the Republic of Uzbekistan

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Abstract The purpose of this study is to analyze the prevalence and dynamics of chronic myeloid leukemia among the population of the Republic of Uzbekistan. A retrospective analysis of the statistical material on the detection of myeloid leukemia for 2010-2020, obtained in the Department of Statistics of the Republic of Uzbekistan and case histories of patients with myeloid leukemia registered in the consulting polyclinic of the Research Institute of Hematology and Blood Transfusion under the humanitarian program "GIPAP", was carried out. The results of the analysis showed that in 2020 0.11 cases (per 100,000 population) of primary myeloid leukemia incidence were registered, including the incidence of chronic myeloid leukemia was 30% (the largest share of registered cases was noted in the age group 50-69 years - 37%) (urban residents - 46.9%, rural residents - 53.1%, men - 56.6%, women - 43.4%). The largest share of primary morbidity was recorded in 2010, the smallest in 2011, and by 2019 it had decreased 2.8 times. In the period 2010 to 2014, there is an uneven distribution of morbidity rates by year from 0.26 to 0.65 cases per 100,000 population (average 0.4 ± 0.075). From 2015 to 2019, there is an uneven distribution of incidence rates by year from 0.34 to 0.6 cases per 100,000 population (on average 0.5 ± 0.04). Compared to 2010, by 2019 it has doubled. The results indicate an improvement in diagnostics as a result of improvements in cytogenetic and molecular genetic diagnostic methods.

Keywords Chronic myeloid leukemia, Epidemiology, Morbidity, Prevalence

1. Introduction

Relevance of the topic: Malignant neoplasms of hematopoiesis and lymphoid tissues are now common pathologies, with chronic myelogenous leukemia (CML) leading the way. CML forms a group of dangerous diseases of the blood and bone marrow and is characterized by an overproduction of granulocytes (neutrophils, eosinophils, and basophils). There are two main types of this pathology: acute myeloblastic leukemia and chronic myeloid leukemia (chronic myelogenous leukemia) [1,3].

It is known that CML is a clonal myeloproliferative disease caused by reciprocal translocation of t(9; 22)(q34; q11) translocation between chromosomes 9 and 22, resulting in high tyrosine kinase activity *bcr-abl* on chromosome 22 (Philadelphia chromosome, Ph) -ABL chimer gene is formed. This pathology: characterized by disruption of cell life activity processes such as increased proliferation, slowing of apoptosis, decreased adhesion in the stroma [2,8,17,18].

Studies in Russia and abroad have shown that the detected changes are manifested by changes in blood analysis in the form of neutrophil leukocytosis with rejuvenation of the leukocyte formula to blast cells [5,7,19].

In the recent scientific literatures, scientists have proposed the introduction of end-of-life observations and a mandatory identification system on patients with malignant tumors, including patients with chronic myelogenous leukemia, with the inclusion of multiple nosological registers. All this allows to study the condition of patients and the degree of disease prevalence in the dynamics [11,15,16].

The purpose of the study is to analyze the prevalence of chronic myelogenous leukemia among the population of the Republic of Uzbekistan.

2. Materials and Methods

Materials from the Department of Statistics of the Republic of Uzbekistan, as well as the results of retrospective analysis of medical records of patients with acute and chronic myelogenous leukemia registered and treated in the consulting clinic of the Scientific Research Institute of Hematology and Blood Transfusion under the

humanitarian program “GIPAP” for 2010-2020. The incidence of CML disease and its dynamics over the last 10 years were analyzed. Primary morbidity and prevalence rates were calculated per 100,000 populations per year. In calculating the prevalence indicators, all cases of the disease recorded in the same year were taken into account, regardless of the initial diagnosis and the time of their occurrence. Data on the quantitative composition of the population were obtained from the State Statistics Committee of the Republic of Uzbekistan. Statistical processing of data was carried out using a practical statistical analysis program MS Excel for Windows XP. It involves calculating the arithmetic mean of the figure and the standard deviation. Assessment of the reliability of the difference in performance was conducted using the Student’s parameter criterion. When $R < 0.05$, the differences were considered reliable.

3. The Main Findings and Results

3.1. Results and Discussion

According to the plan of research, on the basis of materials first obtained from the Department of Statistics, the incidence of chronic myelogenous leukemia in Uzbekistan in 2020 and the age structure of patients suffering from this disease were analyzed.

According to the results, in 2020, the incidence of acute myelogenous leukemia was recorded in 109 cases, and the incidence of chronic myelogenous leukemia in 36 cases. The proportion of patients living in urban and rural areas was 77 (53.1%) compared to 68 (46.9%) patients. Among the registered patients with CML, men accounted for 82 (56.6%) and women for 63 (43.4%) (55.6% of patients with CML - men, 44.4% - women).

Today, it is known that CML disease can develop at any age. The results of the study of the peculiarities of the age structure of CML disease in Uzbekistan; regardless of gender, allowed to determine the relationship between the age of patients and the increase in morbidity. During our study, the highest incidence of reported cases of CML at the time of diagnosis was reported in the 50-69 age groups, with a share of 37%. The incidence was found to decrease after the age of 80, although according to world statistics, this figure is more common in the adult group (Figure 1).

In 2020, the incidence of primary disease with CML in the Republic of Uzbekistan was 0.08 cases per 100,000 population and 0.14 cases per adult population. The average incidence in Uzbekistan over the past 5 years was 0.1 ± 0.01 (according to WHO - 0.7). The data obtained on the dynamics of primary disease with CML over the years studied are presented in Figure 2.

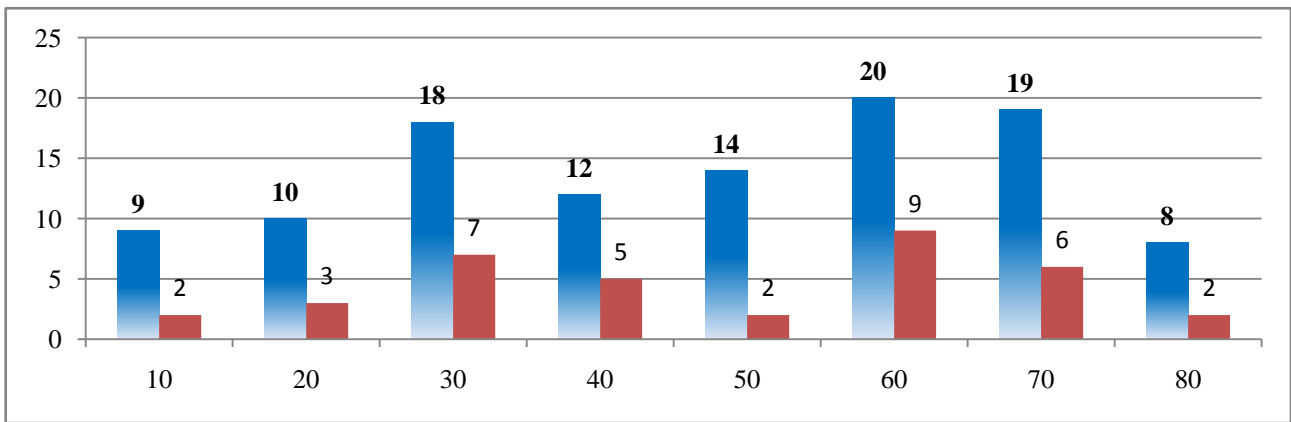


Figure 1. Age structure of patients with myelogenous leukemia in Uzbekistan in 2020 (abs number)

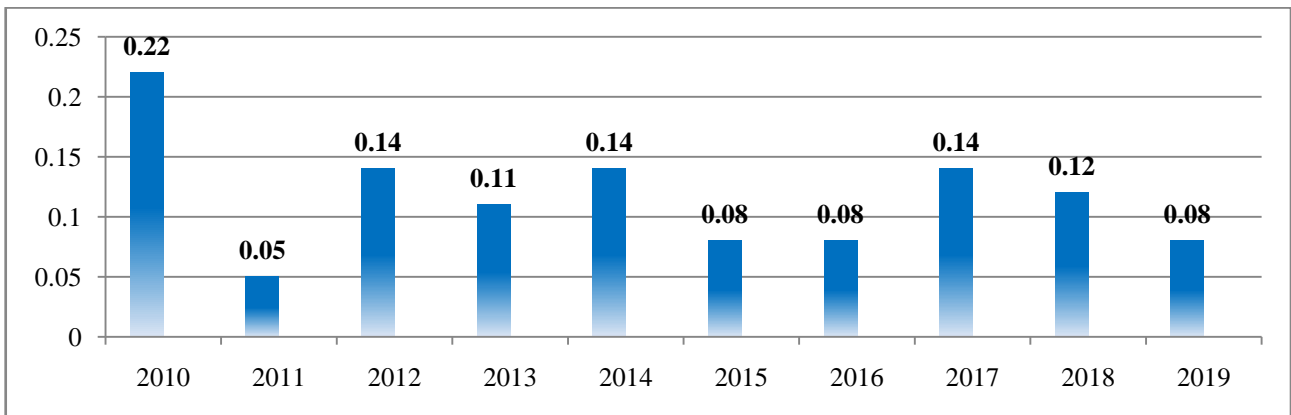


Figure 2. Indicators of primary morbidity with chronic myelogenous leukemia in the Republic of Uzbekistan (per 100,000 populations)

According to the statistics, the average incidence of primary disease for the first 5 years of the 10-year period decreased from 0.13 ± 0.03 per 100,000 population (2010-2014) to 0.1 ± 0.01 (2015–2019) (1, 5 times). During the first five years, the absolute value of primary morbidity was unevenly distributed from 62 to 44 cases, and over the next two years (2015-2016) the primary morbidity rate was 0.08 cases per 100,000 populations. This figure increased 1.75 times in 2017, and from 2018, the primary morbidity rate has been declining to 0.12. In 2019, it was found to be 1.5 times lower than in 2018.

It was found that the mean value of the absolute incidence of primary disease over the 10-year period studied (35.6 ± 7.08) was 1.1 times lower than the mean value of the mean five-year average (32.4 ± 4.04) ($p < 0.05$). The highest figure for the years studied was recorded in 2010, the lowest in 2011, and by 2020 it had decreased by 2.8 times.

Recent advances in the treatment of CML, depending on the new drugs used in the treatment, have radically changed the epidemiology of the disease, as well as the possibility of diagnosis. According to N.R. Ryabchikova and co-authors (2018), the use of first-generation tyrosine kinase inhibitor (TK1) imatinib in clinical practice significantly improves the survival rate of patients with CML [7]. The overall 8-year survival rate was 85%. It shows that in 5-8 years of long-term imatinib therapy the incidence of disease development does not exceed 0.5% per year [6,12-14]. Satisfactory quality of life and ability to work have been reported in the majority of patients with CML during treatment with imatinib [1,8].

In 2016, Uzbekistan introduced new, more effective drugs for the treatment of CML - second-generation TKI (TKI2) nilotinib and dasatinib [8]. The results of clinical studies on the use of nilotinib and dasatinib in the first line of CML therapy showed a much higher efficacy compared with imatinib. Deep molecular remissions have been achieved in the past. In addition, the probability of CML progression decreased [6,7].

The overall incidence rate was unevenly distributed from 0.26 to 0.65 cases per 100,000 populations from 2010 to 2014. The mean for the first 5 years was 0.4 ± 0.075 per 100,000 populations. Over the next 5 years (2015-2019), the incidence rate ranged from 0.34 to 0.6 per 100,000 populations, with an average of 0.5 ± 0.04 per 100,000 populations. Compared to 2010, the incidence has doubled. These results indicate an improvement in the identification and registration of patients in recent years, which is associated with the improvement and introduction of cytogenetic and molecular methods of diagnosis in the regions.

As a result of studying the number of registered CML patients in the regions of the country, it was possible to determine that the highest incidence was observed in Fergana (28.83%), Navoi (18.09%) and Samarkand (18.08%) regions. In Khorezm region, the figure was 4.77%; Tashkent city - 3, 71%; Syrdarya region - 3.47% in Surkhandarya region and the Republic of Karakalpakstan - 3.34%; In the Tashkent region - 3.32%. Small indicators were found in

Kashkadarya, Namangan, Andijan and Jizzakh regions: 3.0%; 2.81% 2.58%; Respectively, 2.55%, the lowest incidence was observed in Bukhara region (0.03%).

Thus, the observation of the long-term dynamics of the disease shows that the incidence rate in the country has increased significantly in recent years. The main epidemiological indicators of CML in Uzbekistan did not differ significantly from the data provided by international researchers.

According to the literature, CML accounts for approximately 20% of all leukemias. CML ranks third in Europe and North America in terms of prevalence after acute leukemia and chronic lymphocytic leukemia (CLL). In Japan, India, Indonesia, and many other countries, CLL is less common, with CML ranking second [6].

According to a study by E.G. Ovsyannikova and co-authors (2010), the incidence of CML is 1-1.5 cases per 100,000 population in all countries, although the disease occurs in all age groups and is more common among men than women. [10]. According to S.M. Kulikova (2014), the incidence of CML among the population of the Russian Federation is 0.7-0.8 cases per 100,000 populations [9].

4. Conclusions

Thus, based on the materials received from the Department of Statistics of the Republic of Uzbekistan and the results of retrospective analysis of medical records of patients with acute and chronic myelogenous leukemia registered and treated in the consulting clinic of the Research Institute of Hematology and Blood Transfusion under the international humanitarian program “GIPAP” retrospective analysis of data on the prevalence rate allowed to draw the following conclusions:

1. In 2020, the incidence of primary myelogenous leukemia in Uzbekistan was registered in 109 cases (0.11 per 100,000 populations), including the incidence of chronic myelogenous leukemia is 30%. The proportion of patients living in urban and rural areas was 53.1% per 46.9% of patients. Among the patients with CML, 56.6% were men and 43.4% were women (55.6% of patients with CML were men and 44.4% were women). The highest incidence of CML was reported in the 50-69 age groups, with a share of 37%.
2. It was found that the average incidence of primary disease for the first 5 years of the 10-year study decreased from 0.13 ± 0.03 per 100,000 population (2010-2014) to 0.1 ± 0.01 (2015–2019). The highest figure for the years studied was recorded in 2010, and the lowest in 2011.
3. The overall morbidity rate from 2010 to 2014 was unevenly distributed from 0.26 to 0.65 cases per 100,000 populations. The 5-year average was 0.4 ± 0.075 per 100,000 populations. Over the next 5 years (2015-2019), the incidence rate ranged from 0.34 to

0.6 per 100,000 populations; the average was 0.5 ± 0.04 per 100,000 populations. Compared to 2010, the incidence has doubled. These results indicate an improvement in the identification and registration of patients in recent years, which is associated with the improvement and introduction of cytogenetic and molecular methods of diagnosis in the regions.

REFERENCES

- [1] Abdulkadyrov K.M., Abdullaev A.O., Avdeeva L.B. and other. (2013) Federal clinical guidelines for the diagnosis and therapy of chronic myeloid leukemia. *Bulletin of Hematology*. – Tashkent. IX. No 3. – pp. 4-40.
- [2] Aksenova E.V., Krutov A.A., Soldatova I.N. et al. (2010) Molecular monitoring in patients with chronic myeloid leukemia: correlation with cytogenetic response, prognostic value, assessment of response to therapy. *Clinical Hematology Oncology*; No. 2: - pp. 151–159.
- [3] Varshavsky A. V. (2011) Clinical - epidemiological characteristics of hematological malignancies in the Republic of Bashkortostan. Abstract of thesis. Dis. Candidate of Medical Sciences. – Ufa. – p. 24.
- [4] Volkova S.A., Kovalishena O.V., Gostyuzhova E.A. et al. (2011) Effect of imatinib therapy according to clinical and epidemiological monitoring of chronic myeloid leukemia in the Nizhny Novgorod region for the period 2000–2010. *Hematology and transfusiology*; 56 (4): - pp. 17-22.
- [5] Vinogradova O.Yu., Kulikov S.M., Kutsev S.M. and other. (2011) Problems of organization of treatment of chronic myeloid leukemia in Russia. *Clinical hematology oncology*; 4 (4): - pp. 292–297.
- [6] Zaritsky A.Yu., Lomaia E.G., Vinogradova O.Yu. (2007) Prognosis factors for imatinib mesylate therapy in patients in the chronic phase of Ph-positive chronic myeloid leukemia: data from a multicenter non-randomized study in Russia. *Therapeutic archive*; 79 (8): - pp. 17-22.
- [7] Ryabchikova N.R., Minniakhmetov I.R., Safuanova G.Sh. et al. (2013) Chronic myeloid leukemia: molecular monitoring in clinical practice. *Oncohematology*; 8 (1): - pp. 1–16.
- [8] Kazakbaeva Kh.M., Saidkhanova Kh.K., Yakubova A.K. (2015) Analysis of the detection rate of chronic myeloid leukemia. *Collection of scientific papers*; - pp. 60-64.
- [9] Kulikov S.M., Vinogradova O.Yu., Chelysheva E.Yu., and others. (2014) The incidence of chronic myeloid leukemia in 6 regions of Russia according to a population study of 2009–2012. *Therapeutic archive*; 86 (7): - pp. 24-30.
- [10] Ovsyannikova E.G., Kovalinskaya I.S., Israpilova Z.M., et al. (2010) Analysis of the cytogenetic response of patients with chronic myeloid leukemia in the Astrakhan region. *Astrakhan Medical Journal*. – Tashkent: 5. No. 3. – pp. 97-99.
- [11] Ryabchikova N.R., G.Sh. Safuanova, V.I. Nikulichev. (2018) Epidemiology of chronic myeloid leukemia in the Republic of Bashkortostan. *Clinical hematology oncology*. No. 11 (4). – pp. 349-53.
- [12] Turkina A.G., Golenkov A.K., Napso L.I. and other. (2015) Russian register for the treatment of chronic myeloid leukemia in routine clinical practice: the results of many years of work. *Effective pharmacotherapy*; 10 (1): - pp. 8-13.
- [13] Turkina A.G., A.Yu. Zaritsky, V.A. Shuvaev, E.Yu., and others. (2017) Clinical guidelines for the diagnosis and treatment of chronic myeloid leukemia. *Clinical hematology oncology*. No 10 (3). – pp. 294-316.
- [14] Deininger M, O'Brien SG, Guilhot F, et al. (2009) International randomized study of interferon vs STI571 (IRIS) 8-year follow up: sustained survival and low risk for progression or events in patients with newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP) treated with imatinib. *Blood*; 114(22): - p. 462.
- [15] Pasguini R, Cortes J, Kantarjian HM, et al. (2010) A worldwide observational registry collecting longitudinal data on management of chronic myeloid leukemia patients (The WORLD CML Registry)-2nd Annual interim analysis. *Blood*; 116 (21): 2292.
- [16] Jabbour J., Hagop Kanterjian. CME Information: Chronic myeloid leukemia: 2014 update on diagnosis, monitoring, and management. *American Journal of Hematology*, Vol. 89, No. 5, May 2014. – pp. 547-556.
- [17] Baccarani M, Cortes J, Pane Fetal. Chronic myeloid leukemia: an update of concepts and management recommendations of European Leukemia Net. *J Clin Oncol* 2009; 27: 6041–6051.
- [18] Jain, P. et al. Early responses predict better outcomes in patients with newly diagnosed chronic myeloid leukemia: results with four tyrosine kinase inhibitor modalities. *Blood* 121, 4867–4874 (2013).
- [19] Mahon F-X. Discontinuation of tyrosine kinase therapy in CML, *Ann Hematol*. 2015; 94 (Suppl 2): 187. doi: 10.1007/s00277-015-2320-4.