Assessment of factors affecting the mental condition of patients with chronic myeloid leukemia treated with tyrosine kinase inhibitors

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Summary

Aim. The aim of the study was to make a general assessment of mental health, including signs of somatization, depression, anxiety, and functional disorders, in patients with chronic myeloid leukemia (CML) treated with tyrosine kinase inhibitors (TKIs) and to assess the impact of factors such as the duration of the disease, side effects of therapy, age, and gender on the occurrence of the above-mentioned disorders. Another goal was to identify patients at risk of developing mental disorders.

Method. The study involved 91 patients and was conducted at the Hematology Clinic of the University Hospital in Krakow. The following questionnaires were used to assess mental health: survey created by the author, David Goldberg's questionnaire GHQ-28, and the four-dimensional 4DSQ, measuring four dimensions of the mental condition.

Results. The average level of the mental condition of the studied group was demonstrated. 29 people with mental disorders were identified. Women and people living alone obtained worse results in almost all dimensions of the questionnaires. The analysis revealed that factors such as age, number of side effects and gender significantly affect mental disorders in the studied group. A significant and positive correlation has been found between the number of side effects and the presence of somatization signs. Mediocre correlations occurred between age and mental disorders and all dimensions of the GHQ-28.

Conclusions. The obtained results indicate that attempts should be made to reduce side effects among CML patients. Visiting the psychologist to work on the acceptance of the disease, psychoeducation, behavioral therapy, and contact with a psychiatrist to consider the introduction of pharmacotherapy is recommended. All of these methods may improve a patient's quality of life.

Key words: cancer, leukemia, psychiatric disorders

Introduction

Chronic myeloid leukemia (CML) is a disease characterized by a varied clinical course and a diverse prognosis, dependent at the time of diagnosis mainly on the phase of the disease, and during its course on the response to therapy. There are three phases in the course of CML: chronic, acceleration and blast crisis.

Treatment of chronic myeloid leukemia depends on the phase of the disease, general health, age, and fitness level. The treatment of CML includes: pharmacotherapy (mainly tyrosine kinase inhibitors – TKI), chemotherapy, radiotherapy, and hemopoietic stem cell transplantation [1].

The most commonly reported side effects caused by TKI are: increased risk of infection, skin changes, severe fatigue (fatigue), bruising, diarrhea, loss of appetite, water retention, mainly occurring in the first weeks of pharmacotherapy. Long-term side effects include complications in the cardiovascular system (occlusive arterial disease, thromboembolic complications) in the case of nilotinib and ponatinib, the occurrence of cardiac failure, pleural effusions and pulmonary hypertension in patients receiving dasatinib [2].

Mental disorders among patients with neoplasms may lead to lowering of the quality of their life and negatively affect the treatment process [3]. It is believed that the development of depression among people suffering from different neoplasms is up to three times more common in comparison with the general population. Modern research as well as general practice indicate that about half of cancer patients have various mental disorders. Those patients require diagnosis and treatment [4]. Anxiety and depression are very common among those patients [5, 6], although it happens that depression is a side effect of other diseases – then it is not treated as a reaction to an oncological disease [7]. There is also evidence that symptoms of affective and somatic depression may occur also before cancer is diagnosed.

Each stage of cancer may have an impact on the patient's mental condition. Both a sense of loss of safety and health which is at risk increase patients' anxiety. As shown by Kieszkowska et al. [8], the treatment process leads to the reduction of anxiety. Patients have feeling that they partially control the course of their disease and the risk caused by the disease. Kuty-Pachecka et al. [9] indicate that the most common sources of the mental problems occurring among patients with diagnosed cancer are side effects of the treatment, their impact on the patients' functioning, and a long-term stay in the hospital ward.

A common reaction to the oncological disease is the so-called 'emotional distress' which can be understood as a mental breakdown, mental suffering, or emotional disturbance. Long-term exposure to many disease-related stressors contributes to an increased risk of mental disorders, in particular symptoms of anxiety, depression, and to the development of clinically significant anxiety and depressive disorders [10–12]. Sadness and regret are normal reactions to the various crises that a person with cancer has to face. The intensification and the persistence of cancer-related mental distress

are mainly associated with physical, psychological and social stressors associated with the disease [12, 13].

The psychological situation of people with cancer is the subject of many multidisciplinary studies carried out in Poland and all over the world [14–18]. Such studies are carried out both with children [19, 20] and adults [21, 22] with myeloid leukemia.

Although the scientific literature and numerous studies provide a lot of information about mental disorders among cancer patients, there are still missing data about some aspects such as the relationship between side effects of treatment and the duration of the disease and depression, anxiety, somatization, and general disorders of the patient's functioning. Therefore, the presented research is devoted to these issues.

The research was conducted in a group of patients with chronic myeloid leukemia, as these are patients who require long-term treatment. The treatment of choice for this group of patients is the use of tyrosine kinase inhibitors, the administration of which is sometimes complicated by a number of side effects, although most of them are of a minor intensity, but they are sometimes persistent and last long enough that they may predispose to anxiety, depressive and somatic symptoms.

Aim

The aim of the study was to assess the presence of mental health disorders among patients with chronic myeloid leukemia (CML) treated with tyrosine kinase inhibitors (TKIs). The mental health issues in our study were as follows: somatization, depression, anxiety, and social dysfunction. The other aim was the assessment of the impact of factors such as the duration of the disease, side effects of treatment, age, and gender on the occurrence of mental health disorders.

The final aim was the identification of patients being at risk of developing mental disorders.

Material and method

91 patients with CML treated with TKIs were examined. The study group consisted of 53 women and 38 men. The mean age in the research group was 57 years (range 20–82 years) (*SD*: 12.46). The most commonly mentioned side effects of treatment were bone and joint pain and muscle cramps and pain (68.1%), water retention (64.8%) and tiredness (53.8%). The average length of the disease was 10 years. The detailed characteristics of the examined group are presented in Table 1.

Table 1.**Characteristics of the studied group**

Feature		N	Percent
Sex	Women	53	58.2
	Men	38	41.8

Education	Primary	5	5.5
	Vocational	25	27.5
	Secondary	32	35.2
	Higher	29	31.8
Place of residence	City	63	69.2
	Village	28	30.8
Marital status	Single	8	8.8
	Widowed	11	12.1
	Divorced	5	5.5
	Married	67	73.6
Residence status	Living alone	15	16.5
	Living with family	76	83.5
Number of side effects	0–4	49	54.0
	5–10	42	46.0
Duration of the disease	<1 year	4	4.4
	1–5	15	16,5
	6–10	30	33.0
	11>	42	46.1

This study is a retrospective analysis of adult patients with CML treated with TKIs. People for the study were recruited from among patients who were consecutively admitted to the outpatient hematology department of the University Hospital (US) in Krakow in the period from 01.2017 to 09.2019, who met the inclusion criteria: diagnosis of chronic myeloid leukemia, treatment with tyrosine kinase inhibitors, age over 18 years. The clinical diagnosis of CML was confirmed by cytogenetic and molecular bone marrow examination, information on the method of treatment was obtained from the patients' medical records. People who did not voluntarily consent to participate in the study were excluded from the study. The study was approved by the Bioethics Committee of the Jagiellonian University (No. 1072.6120.113.2020).

The survey was questionnaire-based. Patients were informed about the purpose of the study and permission to conduct it was obtained.

In order to assess mental health, the following questionnaires were used: survey created by the author, GHQ-28 by David Goldberg in the adaptation of Zofia Makowska and Dorota Merecz [23], and the four-dimensional 4DSQ, measuring four dimensions of the mental condition [24].

The questionnaire created by the author included sociodemographic questions as well as the questions about the duration of the disease and the side effects of treatment.

Using David Goldberg's GHQ-28, it is possible to detect mental disorders in four dimensions: somatic symptoms (scale A),anxiety/insomnia (scale B), social dysfunction (scale C), and severe depression (scale D). The GHQ-28 is one of the most commonly

used and tested tools for screening emotional stress and detecting mental disorders. It contains 28 items which are divided into 7 in each dimension. It has several scoring systems [25]. In the following study, the results are shown using two methods. The first uses the Likert scale modified by the authors of the tool – from 0 to 3 (where 0 is "less than usual", 1 – "not less than usual", 2 – "rather more than usual", and 3 – "much more than usual"), and the results are presented in the form of sten scores, where the result between a sten score of 1 and 4 means low level of disorder, a sten score of 5–6 indicates the medium level and a sten score higher than 7 – high level. This method is used to assess the area and severity of mental health disorders. In the second scoring system, the GHQ method was used, which uses a zero-one scale (0 – "no symptom", 1 – "symptom occurrence"). This method detects only cases of deviation from the norm. The cut-off threshold used to identify cases in the group of patients is 5 points. The subscales of the questionnaire assess the contribution of individual factors to the overall test result.

The last tool used in the study was a four-dimensional 4DSQ, which measures four dimensions of mental health: distress, anxiety, depression, and somatization. It includes 50 items located on four scales. The categories of answers are formulated as "no", "sometimes", "regularly", "often", and "very often or constantly". To get results, the answers are rated as 0 for "no", 1 for "sometimes" and 2 for other categories of responses, and the item scores are added together to scale the results. The distress scale contains 16 items and the range from 0 to 32 points, the depression scale contains 6 items and a range from 0 to 12 points, the anxiety scale contains 12 items and a range from 0 to 24 points, and the somatization scale contains 16 items and a range from 0 to 32 points. The cut-off points for individual scales are presented in Table 2.

Table 2. **The cut-off points for individual scales of the 4DSQ**

Factors	Distress	Depression	Anxiety	Somatization
Moderate	>9	>2	>3	>10
High	>20	>5	>9	>20

These tools have been used in many studies of chronically ill patients [26–31].

The research tools used in this work did not make it possible to determine the diagnosis of depressive, anxiety or somatic disorders, which requires fulfilling certain diagnostic criteria of the ICD-11 [32] or/and DSM-V [33]. Therefore, in the following publication, the terms 'depression', 'anxiety' and 'somatization' have been used as a slogan and should be understood as a set of depressive, anxiety, and somatic symptoms, respectively.

Statistical analysis was performed using the IBM SPSS Statistics version 25 The nonparametric tests were used: Mann-Whitney U test and Kruskal-Wallis test. The significance level of $p < 0.05$ was adopted. The normality of the distribution was verified by the Kolmogorov-Smirnov test. Spearman's correlation coefficient was used

to identify the relationship between the studied variables while multiple linear regression analysis was used to identify predictors of mental disorders.

Results

The mean GHQ-28 result among all respondents was 24 points; 29 points in women and 17 points in men (sten score of 6 in all cases). This result indicates the average mental condition of the studied group.

Using the GHQ-28 scoring (0 – no symptom, 1– symptom occurrence), there were 29 (32%) people identified with symptoms of mental disorders who crossed the threshold of 6 points.

The mean results of the 4DSQ for the whole study group were normal. Table 3 presents the cases of people who obtained moderate or high results in the individual scales of the 4DSQ.

Table 3.**The results of the 4DSQ in the examined group of patients**

Factors	Distress N (%)	Depression N (%)	Anxiety N (%)	Somatization N (%)
Moderate	21 (23)	9 (9.9)	13 (14.3)	29 (31.9)
High	6 (6.6)	7 (7.7)	6 (6.6)	3 (3.3)

Out of the 91 respondents, 27 patients obtained high results on the Distress scale (29.6%), 16 on the Depression scale (17.6%), 19 on the Anxiety scale (20.9%), and 32 patients in the Somatization scale (35.2%).

The results of the Mann-Whitney U test revealed differences in individual results of mental condition among women and men. Data are presented in Table 4.

Table 4. **Mental condition of cancer patients by gender**

Mental condition	Women (n = 38) Me (Q1–Q3)	Men (n = 53) Me (Q1–Q3)	p
GHQ-28			
GHQ-28	27.0 (15.5–39.5)	16.0 (7.75–23.25)	<0.001
Somatic symptoms	7.0 (4.5–10.5)	4.0 (3.0–6.0)	<0.001
Anxiety, insomnia	7.0 (5.0–10.0)	4.0 (2.0–6.0)	<0.001
Social dysfunction	7.0 (3.0–9.5)	4.0 (1.0–6.0)	0.001
Symptoms of depression	7.0 (3.0–9.0)	4.0 (1.0–6.0)	0.002
4DSQ			
Distress	6.0 (3.0–12.0)	4.0 (0.75–7.00)	0.003
Depression	0.0 (0.0–1.0)	0.0 (0.0–0.0)	0.115

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| Anxiety | 1.0 (0.0–3.5) | 0.0 (0.0–1.0) | 0.002 |
| Somatization | 10.0 (4.0–14.0) | 4.0 (2.0–7.0) | <0.001 |

Me – median; Q1 – lower quartile; Q3 – upper quartile.

Women differ significantly from men in individual mental condition outcomes in all scales except the depression scale in the 4DSQ and in the occurrence of mental disorders measured by the GHQ-28. Men scored lower than women in all GHQ-28 dimensions.

Table 5 presents the differences in the individual mental condition scores (tested with the Mann-Whitney *U* test) depending on the residence status.

Table 5. **Differences in individual mental condition depending on the residence status**

Mental condition	Living alone (n = 10)	Living with family(n = 81)	p
	Me (Q1–Q3)	Me (Q1–Q3)	
GHQ-28			
GHQ-28	24.0 (17.0–43.0)	19.0 (9.25–31.0)	0.037
Somatic symptoms	8.0 (5.0–11.0)	5.0 (3.0–7.75)	0.015
Anxiety, insomnia	7.0 (5.0–11.0)	5.0 (3.0–8.0)	0.036
Social dysfunction	6.0 (3.0–11.0)	4.0 (2.0–8.0)	0.069
Symptoms of depression	6.0 (4.0–10.0)	4.0 (2.0–8.0)	0.058
4DSQ			
Distress	7.0 (425–10.50)	5.0 (2.0–9.0)	0.163
Depression	0.0 (0.0–1.50)	0.0 (0.0–1.0)	0.682
Anxiety	0.50 (0.0–5.0)	0.5 (0.0–2.0)	0.325
Somatization	11.0 (8.0–14.50)	5.0 (3.0–12.0)	0.022

People living alone obtained significantly higher results than those living with their families in the questionnaire measuring the occurrence of mental disorders (GHQ-28) and in the following 4DSQ dimensions: somatic symptoms, anxiety/insomnia and somatization.

Table 6 shows the correlations between the mental condition of the patients and their age, length of the cancer and the presence of side effects of treatment in the entire study group.

Table 6. **Mental condition and age, length of the disease and side effects of treatment**

Mental condition	Age		Length of the disease		Number of side effects	
	rho	p	rho	p	rho	p
GHQ-28						
GHQ-28	0.351	0.001	0.145	0.171	0.401	<0.001

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Somatic symptoms	0.316	0.002	0.132	0.185	0.361	<0.001
Anxiety/insomnia	0.314	0.002	0.132	0.211	0.402	<0.001
Social dysfunction	0.363	<0.001	0.145	0.314	0.399	<0.001
Symptoms of depression	0.350	0.001	0.181	0.087	0.409	<0.001
4DSQ						
Distress	0.088	0.408	-0.045	0.673	0.382	<0.001
Depression	0.123	0.247	0.142	0.179	0.196	0.063
Anxiety	-0.074	0.486	-0.008	0.937	0.295	0.004
Somatization	0.185	0.080	0.068	0.524	0.524	<0.001

A significant and positive ($rs = 0.524$) correlation has been found between the number of side effects and the presence of somatization. Moderate correlations occurred between age and mental disorders and all dimensions of the GHQ-28. Moderate and weak correlations were observed between the number of side effects and almost all dimensions of both questionnaires.

The results of linear regression models are presented below.

Table 7. **Predictors of mental disorder occurrence, measured by the GHQ-28**

Mental disorders	Unstandardized coefficients		Standardized coefficients	
	B	Standard error	β	Significance
Duration of the disease	0.032	0.256	0.011	0.901
Age	0.290	0.114	0.229	0.013
Number of side effects	2.673	0.597	0.399	0.000
Male vs. female	-7.376	2.893	-0.232	0.013
Living alone vs. living with family	5.134	3.863	0.122	0.187

$R = 0.611$; $R^2 = 0.373$; $F(5.85) = 10.113$; $p < 0.001$

The analysis revealed that factors such as age, number of side effects and gender significantly affect mental disorders in the studied group. The older a person is, the higher the occurrence and the level of the disorder appears ($\beta = 0.229$; $p = 0.013$). Another conclusion is that the more side effects occur, the greater is the amount of general mental health disorders ($\beta = 0.399$; $p = 0.000$). Men were less likely to develop mental health disorders ($\beta = -0.232$; $p = 0.013$).

Table 8. **Predictors of somatization, depression, social dysfunction, and anxiety, measured by the GHQ-28**

GHQ-28 factors	Somatization		Depression		Social dysfunction		Anxiety	
	B*	p	B*	p	B*	p	B*	p
Duration of the disease	-0.005	0.945	0.032	0.642	-0.002	0.973	0.007	0.915

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Age	0.063	0.035	0.082	0.008	0.086	0.005	0.059	0.043
Number of side effects	0.581	0.000	0.726	0.000	0.698	0.000	0.667	0.000
Male vs. female	-2.043	0.008	-1.517	0.052	-1.746	0.023	-2.071	0.006
Living alone vs. living with family	1.697	0.093	1.082	0.295	0.929	0.358	1.426	0.147

* raw regression coefficients

The predictors of the occurrence of somatization were: age, number of side effects and gender. Women obtained significantly higher results on this scale ($B = -0.581$; $p = 0.008$). The older a person was ($B = 0.036$; $p = 0.035$) and the more side effects were present ($B = 0.581$; $p = 0.000$), the higher was the level of stigmatization.

In the presented model of depression occurrence, two variables were crucial: age and the number of side effects. The older a person was ($B = 0.082$; $p = 0.008$) and the more side effects were observed ($B = 0.726$; $p = 0.000$), the higher likelihood of depression occurred.

The predictors of social dysfunction were: gender, number of side effects and age. A person who was one year older scored 0.086 points higher on the social dysfunction scale. Each increase in the number of side effects caused an increase in the social dysfunction by 0.7 points. Men had a lower risk of developing mental disorders ($B = -1.746$; $p = 0.023$).

Among the examined group, factors such as age, number of side effects and gender turned out to be predictors of anxiety. The older patients with a greater amount of side effects were significantly more likely to experience anxiety.

Discussion

Numerous studies confirm that the mental condition among patients suffering from cancer is specific. The specific nature of cancer disease and the process of its treatment may lead to unpleasant emotional conditions among the patients. The most common and earliest symptom is anxiety which could be the beginning of other conditions, such as depression or various forms of aggression [34]. The vast majority of patients are accompanied by negative feelings, such as tiredness, anxiety, powerlessness, misunderstanding, fear, anger, sadness, bitterness, irritability, and panic [14]. There is a general decrease in mood, feelings of vulnerability, helplessness and hopelessness. Anxiety and depression are also often considered to be factors that cause or intensify pain [15]. This is especially an issue among patients with acute leukemia requiring the use of intensive chemotherapy.

The most common mental disorders in cancer patients are anxiety disorders which are the effects of huge anxiety associated with the disease process. Some studies indicate that the anxiety disorders affect nearly 30% of people in this group [16]. Grabińska et al. [17], when analyzing the need for psychological help in cancer patients, indicated

that since the diagnosis of the disease, already 69% of respondents feel a decrease in mood and anxiety disorders. Researchers indicate that the diagnosis of cancer determines the occurrence of mental disorders in patients [17].

In our study, patients who were tested using the GHQ-28 and 4DSQ obtained an average overall level of mental health, regardless of their gender. Simultaneously, 29 patients with mental disorders were identified using the GHQ-28. This separate group consists mostly of women over 53 years who live alone in the countryside and experience more than two side effects of treatment. Similar results were obtained using the 4DSQ in which 16 to 32 cases were identified in individual scales (Table 4).

Men obtained lower scores than women on the scales of stress, anxiety and somatization as well as in the occurrence of mental disorders (Table 3). Differences in adverse psychological consequences in both sexes are also indicated by longitudinal Wisconsin tests conducted by Pudovska [35] among cancer patients between 1993 and 1994 and in the same people between 2004 and 2005. It has been proved that cancer causes more adverse psychological consequences among men than women. Michałowska-Wieczorek [36] also paid attention to the differences in coping with the disease between groups of men and women. The examination of the group of 150 cancer patients revealed that women were more likely to choose a fighting spirit strategy that is trying to treat the disease as a challenge. On the other hand, men were much more likely to show anxiety which was expressed in the fear of a given situation. Men also experience helplessness and a sense of hopelessness in the disease much more often. Vodeimaier et al. [37] showed that women experience higher levels of anxiety and symptoms of depression than men.

The results of studies conducted on cancer patients differ from each other. This may be due to cultural circumstances in which cancer is a threat to male identity as it entails the lack of control over their own body, which is incompatible with traditionally understood masculinity. However, from the point of view of women who care for the home and household members, the disease may increase their susceptibility to cancer-related stressors [38]. People with different types of cancer participated in each study. In one of them, carried out by Michalska-Wieczorek, there were women with breast and ovarian cancer and men diagnosed with lung and prostate cancer. In our study, there were patients suffering from CML. Each type of cancer is experienced by the patients differently. The side effects of the treatment are different and so is the therapy. That is why the difference in results is not surprising.

The results of the authors' own study showed that the duration of the disease did not have an impact on the development of mental disorders. The study group included people who have struggled with the disease from several months to decades. The acceptance of cancer disease varies depending on age [39]. Furthermore, the perception of the disease changes with its duration [40, 41].

In psycho-oncological literature, topics related to the patient's family situation are often discussed [42–44]. Our study showed that people living alone obtained higher results than those living with their families in the overall occurrence of mental disorders

measured with both questionnaires and in the following dimensions: somatic symp-
toms, anxiety, insomnia, and distress (Table 5). The results of the study conducted by
Ocalewski and Izdebski [45] indicate that the quality of life of patients and minders is
interdependent. Family ties are an important predictor of care – older people want to be
loved and needed. If they do not experience children's attention, they feel loneliness.
They show depressive behavior, sometimes they even give up on life.

Also, a study conducted by Nowicki and Rządkowska [46] indicates that patients
in a relationship suffer less often from depression. Research of Dąbska et al. [47]
shows that marital status significantly affects the condition of cancer patients. Single
patients are much more likely to complain about the symptoms of moderate to severe
depression than those in a relationship. According to Németh et al. [48], patients cope
better with the disease when they experience emotional and instrumental support from
the ones they love. These authors, examining the level of social support, conclude that
women with cancer disease feel mentally better if they have a partner, children, and
they have been ill for at least a year. Therefore, it can be concluded that social support
has a positive impact on the quality of life of the cancer patients, their mental condition
and the ability to deal with the disease.

The correlation between the mental condition of the studied group and age showed
that the older a person is, the greater score in all GHQ-28 scales he/she obtains. There
was also a significant correlation between the number of side effects occurring during
therapy and the presence of somatization (Table 5) and average and low correlations
between the number of side effects of treatments and almost all dimensions of both
questionnaires. Similar results were obtained in numerous regression analyses. The
main predictors of mental disorders were: age and the number of side effects (Table
6–8). It is worth paying attention to the fact that the side effects of TKIs (e.g., diar-
rhea, skin changes, weakness, abdominal pain) could be equated with somatization.

Other studies revealed that older people under palliative and hospice care lose the
sense of life [49] while positive adaptation to cancer can be associated with a sense
of meaning in life. The results of many studies confirm the positive role of meaning
in life in the functioning of cancer patients [50–52]. This is a factor that facilitates
creating of a harmonious "self-image", acceptance of the health situation and find-
ing important goals in their life. In order to fulfill its role, the meaning in life must
be adequately satisfying; lack of meaning in life contributes to maladjustment to the
disease, i.e., to a low level of psychological well-being and the presence of negative
emotional reactions [50].

Constanzo et al. [53] pointed out that differences in experiencing cancer (its impact
on mood, mental health, spirituality, and social well-being) depend on age. The results of
that research were similar to ours in which older people performed worse than younger
ones. The results of the study conducted by Dąbska et al. [47] were completely differ-
ent than in our study. They examined 63 patients with malignant cancer. According
to that research, she revealed that younger people were more likely to have a worse
mental condition. Vodeimaier et al. [37], however, indicated that older patients were

more likely to experience anxiety. The discrepancy in the results may be caused by the different types of cancer that the patients suffered from, which is confirmed by a study of Kozak [54].

Conclusions

The study showed that age, gender and side effects of treatment are the factors significantly affecting the mental state of patients with chronic myeloid leukemia treated with tyrosine kinase inhibitors and increasing the risk of mental disorders. It should be noted that the symptomatic, non-nosological approach is one of the significant limitations of the conducted study, as well as small number of patients in the studied groups.

Despite the above-mentioned limitations, the study allowed for the identification of patients at risk of developing mental disorders and referring them to the Mental Health Clinic for further diagnosis and possible psychological help or treatment.

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