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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.

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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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CLINICAL AND LABORATORY CHARACTERISTICS OF THE LATENT FORM OF POLYCYTHEMIA VERA

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Abstract.

A high level of hemoglobin and hematocrit is one of the most important laboratory indicators of polycythemia vera (PV). Nevertheless, in some cases, these indicators may be normal or below the norm. This form of the disease is called latent or masked PV (LPV). It has been found that thrombohemorrhagic complications (THC) are more common in LPV patients than in classic PV (CPV) patients. The relationship between JAK2 gene mutation allele burden, thrombocytosis, leukocytosis level and the occurrence of thrombosis during LPV was analysed in different studies. The results some of them were conflicted. It is also possible that this situation occurs due to the delay in diagnosis and treatment of patients with LPV.

Aim: investigate the laboratory and clinical features of the latent form of PV.

Materials and methods: An analysis of PV patients registered in 2019-2020 was conducted. Out of them patients with LPV were distinguished. During diagnosis of the disease, general blood analysis, trepanobiopsy and histological examination of bone marrow, molecular genetic examination of peripheral blood and bone marrow were performed. All numerical indicators obtained in the course of the research were statistically analyzed taking according to the modern recommendations. Indicators in the groups were arranged in the order of variation, and the average indicator, standard error of this indicator, confidence interval for the 95% confidence level (CI-confidence interval) were calculated for each order. For comparing the groups, the integrity criterion p was taken into account. Calculations were performed using ONE-WAY-ANOVA calculation software.

Results: We study 101 patients. Out of them 36 patients with latent polycythemia were identified. The clinical and laboratory parameters of patients with LPV and CPV were compared. In latent PV the complaints of patients were less intense; the size of the spleen was smaller; thrombotic complications were more often; hemoglobin, hematocrit, erythrocytes count was lower; the number of platelets was higher; leukocytes count and JAK2M617F gene allel burden were not statistically different. The most part of LPV patients, in contrast to CPV patients, was in a high-risk group of THC.

Conclusion: According to the obtained results, it can be concluded that timely and correct diagnosis of LPV is very important. Despite the fact that disease passes in a latent, masked form, THC are more likely to occur. This can be attributed to the high platelet count in the blood and the lack of timely treatment of the disease.

Key words. Polycythemia vera, latent polycythemia vera, JAK2V617F.

Introduction.

Polycythemia vera (PV) belongs to the group of myeloproliferative diseases and develops as a result of triple hyperplasia of the bone marrow due to a known genetic mutation. As a result, erythrocytosis, leukocytosis and thrombocytosis are noted in the peripheral blood, which leads to relevant clinical symptoms [1-3]. A high level of hemoglobin and hematocrit is one of the most important laboratory indicators during this disease. Nevertheless, in some cases, these indicators may be normal or below the norm. This form of the disease is called latent or masked PV (LPV) [4,5]. It is no coincidence that in 2016, the diagnostic criteria of PV were changed in the classification of the World Health Organization and the diagnostic level of hemoglobin and hematocrit was lowered. One of the examinations that facilitate the diagnosis of PV is bone marrow trepanobiopsy and JAK2 gene mutation testing. That is why the results of these examination methods were included in the major criteria in the last classification [6,7].

Mutation of the JAK2 gene in PV has a high specificity. JAK2V617F mutation is positive in 97% of cases, and JAK2exon12 gene mutation is positive in 3% of cases [8]. Testing for JAK2V617F mutation in Azerbaijan has been started since 2014, which greatly facilitated the accurate diagnosis of the disease and timely detection of LPV.

During PV, clinical symptoms manifest themselves mainly due to a sharp increase in the mass of circulating erythrocytes. So, at this time, aquagenic itching, hyperemia of the face, reddening of the sclera, high blood pressure, headache, dizziness, erythromelalgia are noted on the skin related to plethora, and in some cases, spleen enlargement is observed [9]. As the disease progresses, thrombohemorrhagic complications (THC) can be found in patients. There are different opinions about the cause of THC, and the results of research differ. Thus, a group of scientists indicate a high erythrocyte count as the cause of thrombosis, and some indicate a high platelet and leukocyte count. In some studies, the frequency of thrombosis during PV was found to be related to allelic burden of JAK2 gene mutation [10-12]. The hemorrhagic complications noted during PV are associated with the occurrence of acquired Willebrand's syndrome when the platelet count exceeds 1 million.

The presence of chronic diseases anemia in patients can be mentioned as the cause of LPV. At this time, the level of hemoglobin and hematocrit can be normal or low, and as a result, the lack of plethora can lead to the masking of the clinic. All this can make it difficult to make timely and correct diagnosis of patients. As a result of a number of studies, it has been found that THC are more common in LPV patients than in classic PV (CPV) patients. For this reason, the relationship between JAK2 gene mutation allele burden, thrombocytosis, leukocytosis level and the occurrence of thrombosis during LPV was investigated [13].

It is also considered possible that this situation occurs due to the delay in diagnosis and treatment of patients with LPV [14]. **The aim of the study** is to investigate the laboratory and clinical features of LPV.

Materials and Methods.

An analysis of PV patients registered at the National Center of Hematology and Blood Transfusion was conducted. A retrospective and prospective analysis of patients with PV was performed. Out of them patients with LPV were distinguished. During diagnosis of the disease, general blood analysis, trepanobiopsy and histological examination of bone marrow, molecular genetic examination of peripheral blood and bone marrow were performed. Hemoglobin, erythrocyte, leukocyte, platelet count, hematocrit level was analyzed from hemogram parameters. JAK2 gene mutation was analyzed by RT-PCR method. The diagnostic criteria for LPV were hemogram parameters, namely hemoglobin level < 185 g/l in men and < 165 g/l in women. These parameters were below the diagnostic criteria specified in the 2008 WHO classification. Patients' complaints were analyzed based on the MPN-SAF TSS (myeloproliferative neoplasm symptom assessment form total symptom score) questionnaire; the incidence of thrombotic complications (TC) was investigated. The risk stratification of THC in patients was performed using the Marchioli scale. The low-risk group includes patients aged <60 years and no risk of thrombosis or cardiovascular factors in the anamnesis, the medium risk group includes patients with cardiovascular risk factors, and the high-risk group includes patients over 60 years and/or with a history of thrombosis. All numerical indicators obtained in the course of the research were statistically analyzed taking according to the modern recommendations. Indicators in the groups were arranged in the order of variation, and the average indicator, standard error of this indicator, confidence interval for the 95% confidence level (CI-confidence interval) were calculated for each order. When comparing the groups, the integrity criterion p was taken into account. Calculations were performed using ONE-WAY-ANOVA calculation software.

Results.

It was determined that in 2019-2020, 101 patients with the diagnosis of PV were registered. 47 of them were registered in 2019, and 54 in 2020. The average age of CPV patients was 56.9 ±3.04, of LPV patients was 55.9 ±4.57 (p>0.05). The average age of CPV patients was 55.2 ± 2.99 in men, 57.9 ± 3.04 in women. The average age of LPV patients was 56.2 ± 4.64 in men and 55.2 ± 4.44 in women (p>0.05).

Complaints of LPV and CPV patients were analyzed. Thus, the feeling of fatigue was noted in 30 (83.3%) LPV patients, 55 (84.6) CPV patients; the spread of attention - 21 (58.3%) and 42 (64.6%), respectively, early satiety after food intake - 10 (27.8) and 21(32.3%), apathy-20(55.6%) and 40(61.5%), night sweats-2 (5.6%) and 35(53.8%), itching-1 (2.8%) and 30 (46.2 %), discomfort in the left subcostal area-10 (27.8%) and 21 (32.3%), bone pain -3(8.3%) and 10(15.4%), weight loss-7(19.4%) and 25 (38.5%), high fever was noted in 1(2.8%) and 5(7.7%) patients (Figure 1).

TC noted in patients were investigated. TC were noted in 10 out of 101 PV patients. 6 of them were with LPV, and 4 with CPV. 3 (8.33%) of LPV patients had portal vein thrombosis, 1 (2.77%) - portal and splenic veins thrombosis, 1 (2.77%) - splenic vein thrombosis, 1 (2.77%) - deep vein thrombosis of lower extremities; 2 (3.07%) of CPV patients had acute violation

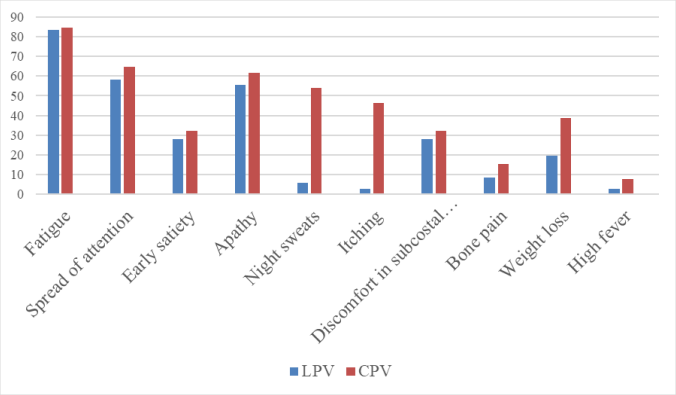

Figure 1. *Frequency of complaints in LPV and CPV patients.*

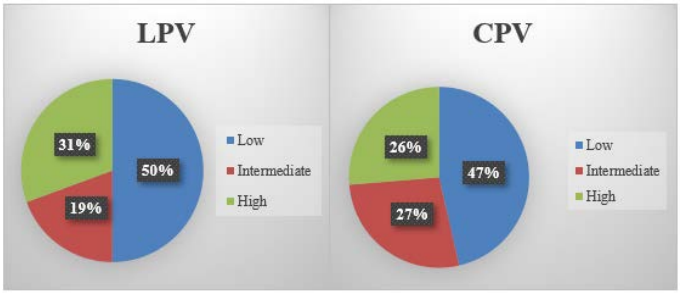

Figure 2. *Risk groups of CPV and LPV patients.*

Table 1. *Characteristics of thrombosis in LPV and CPV patients.*

Characteristics of thrombosis	LPV (number of patients) N=36 (100%)	CPV (number of patients) N=65(100%)
Acute violation of cerebral blood circulation, stroke	0	2(3.1)
Portal vein	3(8.3)	1(1.5)
Portal and splenic veins	1(2.8)	0
Splenic vein	1(2.8)	0
Deep veins thrombosis of lower extremities	1(2.8)	1(1.5)

of cerebral blood circulation, stroke, 1 (1.53%) - portal vein, 1 (1.53%) - deep veins thrombosis of lower extremities (Table 1).

The frequency of splenomegaly in patients was investigated. Out of 65 CPV patients 30(46.2%) and out of 36 LPV patients 12 (33.3%) had an increased spleen size (>4 cm).

Patients were divided according to thrombohemorrhagic risk groups. Out of 65 CPV patients 17 (26.15%) were in high, 18 in medium (27.7%), 30 (46.15%) in low-risk group; out of 36 LPV patients 11 were in high (30.6%), 7 in medium (19.4 %), and 18 (50%) in low-risk group (Figure 2).

Hemogram indicators of 36 LPV (men/women-23/13) and 65 CPV (25/40) patients were analyzed. Thus, patients with LPV compared to patients with CPV and respectively the average level of hemoglobin was 163.5 ±4.51 g/l and 194 ±3.89 g/l (p<0.001), the average number of erythrocytes was 6.8 ±0.43 $x10^{12}$/l and 8.1 ±0.32 $x10^{12}$/l (p<0.001), the average number of leukocytes-15.3 ±2.65 $x10^{9}$/l and 14.3 ±2.33 $x10^{9}$/l (p>0.05), the average number of platelets-752.1 ±100.61 $x10^{9}$/l and 579

Table 2. *Laboratory parameters of patients with LPV and CPV.*

Parameter	LPV	CPV	p
Man/woman, number of patients (%)	23/13(63.9/36.1)	25/40 (38.5/61.5)	
Age, year	**55.9 ±4.573**	**56.9 ±3.039**	>0.05
Hemoglobin, q/l	**163.5 ±4.508**	**194 ±3.890**	<0.001
Erythrocyte, $x10^{12}$/l	**6.8 ±0.425**	**8.1 ±0.316**	<0.001
Hematocrit,%	**52.7 ±2.777**	**60.8 ±1.288**	<0.001
Trombocyte, $x10^{9}$/l	**752.1 ±100.611**	**579 ±70.257**	<0.05
Leucocyte, $x10^{9}$/l	**15.3 ±2.646**	**14.3 ±2.334**	>0.05
JAK2V617F gene allel burden,%	**44.5 ±9.016**	**51.1 ±4.546**	>0.05

Table 3. *Stratification of the risk of TC in PV.*

Risk qroup	**Age >60 and/or history of thrombosis**	**Cardiovascular risk factors**
Low	-	-
Intermediate	-	+
High	+	+/-

±70.26 $x10^{9}$/l ($p<0.05$), the average hematocrit-52.7 ±2.78 % and 60.8 ±1.29 % ($p<0.001$), JAK2 gene allele burden - 44.5 ±9.016 % and 51.1 ±4.55 % ($p>0.05$) (table 2).

Discussion.

According to the results of a study among 101 patients with PV diagnosed in 2019-2020, 36 patients (35.6%) with LPV were identified. The obtained results do not contradict previous studies. In our previous study, among 193 patients diagnosed in 2014-2018, 66 patients (34.2%) with LPV were identified [15,16]. In previous foreign studies a high frequency of arterial thrombosis was found in LPV patients compared to CPV patients, and no difference was noted in comparison with venous thrombosis. According to other data, venous thrombosis was more common in PV patients than arterial thrombosis. Patients with LPV have a higher frequency of thromboses than CPV [14]. According to our results, TC was found in 6 (16.7%) out of 36 LPV patients, and only in 4 (6.2%) out of 65 CPV patients. Although the level of Hb and Ht is lower during LPV, TC is more common. What can be associated with this? Most likely, this can be associated with thrombocytosis and leukocytosis in the hemogram of patients. Perhaps these patients have additional hereditary disorders of hemostasis or other mutations with a bad prognosis. Due to results of our study a count of thrombocytes in LPV was higher than in CPV, no significant difference was found in leukocyte count. As a result of the ECLAP study, which included 1638 patients, scientists concluded that age >60, along with thrombosis, cardiovascular factors can act as risk factors for the formation of TC (table 3) [17-19]. In our study we stratified patients into 3 risk groups of TC and the frequency of patients in a high-risk group in LPV was higher than in CPV. The risk factors of thrombosis in patients have been determined. Investigation the factors affecting the frequency of thrombosis in patients with PV allows more effective treatment and prevents TC in these patients. The indicators obtained as a result of the present study will be used during the creation of the register of patients with PV.

Conclusion.

Thus, as a result of our research, no statistically significant difference was established between the average age of CPV and LPV patients. No statistically significant difference was established between the average age of men and women in CPV and LPV patient groups. The complaints of CPV patients were more intense, the increase in the size of the spleen was more registered. More patients were in a high-risk group of THC during LPV compared to CPV. TC were more marked in LPV patients. Hemoglobin, hematocrit level and erythrocyte count were higher in CPV patients compared to LPV patients, no statistically significant difference was recorded in leukocyte count and JAK2V617F gene allele loading, and platelet count was lower.

According to the obtained results, it can be concluded that timely and correct diagnosis of the latent form of PV is of great importance. Despite the fact that the disease passes in a latent, masked form, THC are more likely to occur. This can be attributed to the high platelet count in the blood and the lack of timely treatment of the underlying disease.

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РЕЗЮМЕ

Клиническая и лабораторная характеристика латентной формы истинной полицитемии.

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Высокий уровень гемоглобина и гематокрита один из наиболее важных показателей истинной полицитемии (ИП). Однако в некоторых случаях эти показатели могут быть нормальными или ниже нормы. Эта форма болезни называется латентной или маскированной ИП (ЛИП). Было установлено, что тромбогеморрагические осложнения (ТГО) наиболее часто встречаются при ЛИП, чем при классической ИП (КИП). В некоторых исследованиях была проанализирована связь между аллельной нагрузкой генетической мутации JAK2, уровнем тробоцитоза, лейкоцитоза и частотой встречаемости тромбоза при ЛИП. Результаты некоторых из них противоречивы. Возможно, что эта ситуация возникает в связи с несвоевременной диагностикой и лечением больных ЛИП.

Цель работы: Изучение лабораторных и клинических особенностей ЛИП. **Материалы и методы:** Был проведен анализ больных ИП зарегистрированных в 2019-2020 гг. Среди них были выявлены больные с ЛИП. Во время диагностики заболевания были изучены общий анализ крови, трепанобиопсия и гистологическое исследование костного мозга, молекулярно-генетическое исследование периферической крови и костного мозга. Все числовые показатели, полученные в ходе исследования, были статистически проанализированы с учетом современных рекомендаций. Показатели в группах были выстроены в вариационные ряды и для каждого ряда рассчитывались средний показатель, стандартное отклонение , доверительный интервал для 95% уровня достоверности (ДИ-доверительный интервал). При сравнении групп учитывался критерий значимости p. Расчеты проводились с использованием программного обеспечения ONE-WAY-ANOVA.

Результаты: Был проведен анализ 101 больного. Из них у 36 пациентов была выявлена ЛИП. Был проведен сравнительный анализ клинических и лабораторных параметров больных с ЛИП и КИП. При ЛИП жалобы больных были менне интенсивны; размеры селезенки меньше; тромботические осложнения встречались чаще; показатели гемоглобина, гематокрита, количества эритроцитов были ниже; количество тромбоцитов было выше; количество лейкоцитов и аллельная нагрузка гена JAK2V617F статистически не отличались. Большая часть больных с ЛИП в сравнении с КИП была в высокой группе риска ТГО.

Заключение: Основываясь на полученные результаты, можно прийти к выводу, что своевременная и точная диагностика ЛИП очень важна. Несмотря на то, что болезнь проходит в латентной, маскированной форме, ТГО при этом встречаются чаще. Это можно связать с высоким количеством тромбоцитов и несвоевременным лечением заболевания.

Key words: истинная полицитемия, латентная полицитемия, JAK2V617F.

SUMMARY

MEDICAL AND STATISTICAL INDICATORS OF PATIENTS WITH POLYCYTHEMIA VERA.

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A high level of hemoglobin and hematocrit is one of the most important laboratory indicators of polycythemia vera (PV). Nevertheless, in some cases, these indicators may be normal or below the norm. This form of the disease is called latent or masked PV (LPV). It has been found that thrombohemorrhagic complications (THC) are more common in LPV patients than in classic PV (CPV) patients. The relationship between JAK2 gene mutation allele burden, thrombocytosis, leukocytosis level and the occurrence of thrombosis during LPV was analysed in different studies. The results some of them were conflicted. It is also possible that this situation occurs due to the delay in diagnosis and treatment of patients with LPV.

Aim: investigate the laboratory and clinical features of the latent form of PV.

Materials and methods: An analysis of PV patients registered in 2019-2020 was conducted. Out of them patients with LPV were distinguished. During diagnosis of the disease, general blood analysis, trepanobiopsy and histological examination of bone marrow, molecular genetic examination of peripheral blood and bone marrow were performed. All numerical indicators obtained in the course of the research were statistically analyzed taking according to the modern recommendations. Indicators

in the groups were arranged in the order of variation, and the average indicator, standard error of this indicator, confidence interval for the 95% confidence level (CI-confidence interval) were calculated for each order. For comparing the groups, the integrity criterion p was taken into account. Calculations were performed using ONE-WAY-ANOVA calculation software.

Results: We study 101 patients. Out of them 36 patients with latent polycythemia were identified. The clinical and laboratory parameters of patients with LPV and CPV were compared. In latent PV the complaints of patients were less intense; the size of the spleen was smaller; thrombotic complications were more often; hemoglobin, hematocrit, erythrocytes count was lower; the number of platelets was higher; leukocytes count and JAK2M617F gene allel burden were not statistically different. The most part of LPV patients, in contrast to CPV patients, was in a high-risk group of THC.

Conclusion: According to the obtained results, it can be concluded that timely and correct diagnosis of LPV is very important. Despite the fact that disease passes in a latent, masked form, THC are more likely to occur. This can be attributed to the high platelet count in the blood and the lack of timely treatment of the disease.

Key words: polycythemia vera, latent polycythemia vera, JAK2V617F.