Clinical evaluation of the “Caprini” scale for an individual risk prognosis of the postoperative venous thromboembolism in the surgical patients. Fundamental research. 2013; 12-1:11-16. (In Russ).]

5. Кательницкий И.И., Сокиренко И.А., Буриков М.А., Сказкин И.В., Шульгин О.В. Обоснования выбора метода профилактики тромбоэмболических осложнений при лапароскопических операциях на органах брюшной полости и малого таза. Современные проблемы науки и образования. 2016;6. http://www.science-education.ru/ru/article/view?id=25985. [Katelnitsky II, Sokirenko IA, Burikov MA, Skazkin IV, Shoulgin OV. Evidence-based selection of embolism prevention method in laparoscopic abdominal and pelvic surgery. Modern problems of Science and education. 2016.6: URL: http://www.science-education.ru/ru/article/view?id=(In Russ).]

6. Бокерия Л.А., Затевахин И.И., Кириенко А.И. [и др.] Российские клинические рекомендации по диагностике, лечению и профилактике венозных тромбоэмболических осложнений. Флебология. 2015; 4(1):52 [Bokeriya LA, Zatevackhin II, Kirienko AI [et al.]. Russian clinical recommendations by diagnostics, treatment and prophylaxis of the venous thromboembolic complications. Phlebology. 2015; 4(1):52 (In Russ).]

7. Ачинович С.Л., Пригожая Т.И., Бондаренко В.В., Голубев О.А., Надыров Э.А., Туманов Э.В., Нитиш В.Э. Тромбоэмболия легочной артерии при раке прямой кишки по данным аутопсий. Проблемы здоровья и онкологии. 2006; 2(8):38-41. [Achinovich SL., Rrigojaya TI, Bondarenko VV, Golubev OA, Nadyrov EA, Tumanov EV, Nitish VE. Tromboemboly of lung arteries at the cancer of rectum on data autopsy. The problems of the health and oncology. 2006; 2(8):38-41 (In Russ).]

8. Ганцев Ш.Х., Каримов А.И., Огий И.И. Хуснутдинов Ш.М., Ишмуратова Р.Ш., Маматова Г.У., Самышина Е.А., Кзыргалин Ш.Р. Тромбоэмболия легочной артерии: частота, причины и пути профилактики в онкологии. Креативная хирургия и онкология. 2011;4:16-21. [Gantsev ShKh. Karimov AI, Ogiy II, Khusnutdinov ShM., Ishmuratova RSh, Mamatova GU, Samishina EA, Kzirgalin ShR. Thromboembolia of the pulmonary artery in the cancer detection clinic. Creative surgery and oncology. 2011;4:16-21. (In Russ).]

9. Ташкинов Н.В., Кузьмин И.И., Штай-берг К.А., Бабихин А.В. Факторы риска и профилактика тромбоэмболических осложнений при тоталь-ном эндопротезировании тазобедренного сустава. Дальневосточный международный журнал. 2009;2:33-35 [Taschkinov NV, Kuzmin II, Shtaiberg KA, Babihin AV. Risk of and prophylaxis for venous thromboembolism in patients undergoing total hip arthroplasty. Far East medical journal. 2009;2:33-35(In Russ).]

10. Хасанов Р.Ш., Камалов И.А. Профилактика тромбоэмболии легочной артерии у онкологических больных в течение первого года диспансерного наблюдения. Казанский медицинский журнал. 2015; 1(96):13–16 [Khasanov RSh., Kamalov IA. Pulmonary embolism prevention in out-patients with malignancies during the first year of follow-up. Kazan medical journal. 2015;1(96):13–16 (In Russ).]

11. Чарная М.А., Морозов Ю.А. Тромбозы в клинической практике. М.: Гэотар-Медия. 2009:17 [Charnaya MA., Morozov YuA. Thromboses in clinics. M.Geotar-Media.2009:17(In Russ).]

12. Bahl V.A., Hu H.M., Henke P.K. et al. A validation study of a retrospective venous thromboembolism risk scoring method. Ann Surg. 2010; 251(2): 344–350.

13. Goldhaber S.Z., Tapson V.F. A prospective registry of 5,451 patients with ultrasound-confirmed deep vein thrombosis. Am J Cardiol. 2004; 93:259-262

14. O., Trinquart L., Caille V. et al. Prognostic factors for pulmonary embolism: the prep study, a prospective multicenter cohort study. Am. J. Respir. Crit. Care Med. 2010; 181(2): 168–173.

15. Samama Ch.M. Samama M.M. Prevention of venous thromboembolism. Congr. Eur. Soc. Anaestesiol. Amsterdam. 1999: 39-43.

T.N. Aleksandrova, I.I. Mulina, V.N. Yadrikhinskaya,
I.E. Solovieva, L.D. Terekhova, N.I. Pavlova, Kh.A. Kurtanov

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF CHRONIC MYELOPROLIFERATIVE DISEASES IN THE REPUBLIC SAKHA (YAKUTIA)

DOI 10.25789/YMJ.2019.67.10

Republican Hospital No. 1 - National Centre of Medicine (Yakutsk, Russia): **ALEKSANDROVA Tuiara Nikonovna** – hematologist, junior researcher of the laboratory of heritable pathology alexandrova_tuyara@mail.ru; **MULINA Inna Ivanovna** – Head of the Department of hematology; **SOLOVIEVA Irina Eremeevna** – hematologist; **TEREKHOVA Lena Dmitrievna** – hematologist; **YADRIKHINSKAYA Vera Nikolaevna** – candidate of medical sciences, associate professor of department «Hospital therapy, professional diseases, clinical pharmacology» Medical Institute of North-Eastern Federal University; Yakut science Centre of the complex medical problems: **PAVLOVA Nadezhda Ivanovna** – PhD, temporary acting chief scientific officer - head of the laboratory of heritable pathology E-mail: solnishko_84@inbox.ru; **KURTANOV Khariton Alekseevich** – PhD, Chief Scientific Officer - Head of the Department of Molecular Genetics. Tel.: +7 (914) 106 00 30. E-mail: hariton_kurtanov@mail.ru.

Chronic myeloproliferative diseases are characterized by excessive proliferation of myeloid cell lines and a high risk of thrombotic complications. The **purpose** of the research was to analyze the clinical features and epidemiology of chronic myeloproliferative diseases in the Republic Sakha (Yakutia). We carried out a retrospective analysis of medical records of patients followed-up by hematologists of Yakutsk from 1995 to 2018. The study included 104 patients, 39 of them were diagnosed with ET (27 women and 12 men), 40 had PV (21 women and 19 men), and 25 had PMF (11 women and 14 men). The diagnosis was established based on the current diagnostic criteria of the World Health Society (WHO).

The results of study demonstrated an increase of disease incidence in 2015-2016, prevalence of thrombotic complications among people younger than 60 years and the prevalence of the latent onset of the disease. The average time from thrombosis onset to disease diagnosis was 1 year. Arterial thrombosis such as acute disorders of cerebral circulation and myocardial infarction occurred more often.

It is necessary to carry out a molecular genetic study to identify driver mutations. During follow up 19.4% of patients have developed re-thrombosis.

Keywords: chronic myeloproliferative diseases, thrombosis, cardiovascular risk.

Introductio. Chronic myeloproliferative diseases (CMPD) result from malignant transformation of pluripotent stem cell followed by clonal proliferation of one or more myeloid cell lines (erythroid, myeloid, megakaryocytic) that differentiate into mature forms. Mutations of genes *JAK2*, *MPL* and *CALR,* leading to hyperactivation of the JAK-STAT signaling pathway, play a key role in developing CMPD [11, 13]. Polycythemia vera (PV) is characterized by proliferation of three myeloid cell lines, while in essential thrombocythemia (ET) hyperplasia of the megakaryocytic line with thrombocytosis are mainly observed. In case of primary myelofibrosis (PMF) abnormal megakaryocytes produce cytokines leading to the development of bone marrow fibrosis and extramedullary hematopoiesis [7].

The main clinical problem of patients with CMPD, leading to disablement and death, is thrombotic complications [5]. In large international studies, it was shown that thrombosis is observed in 23.4% of patients with PV and 12% of patients with ET [12]. Arterial thrombosis, especially in cerebrovascular system, is more common than venous one. Mortality of patients with CMPD because of cerebrovascular diseases is 1.5 times higher than in general population [4]. Venous thrombosis is less common, but affects patient survival and development of microcirculatory disorders causing decrease in quality of life. Thrombotic complications are less common in patients with PMF, which can be explained by transformation into secondary acute myeloid leukemia and lower survival rates [7].

Disease manifestation can have a long-term latent course without obvious signs of myeloproliferation, which complicates early disease diagnosis and increases the risk of complications.

Objective: to analyze the clinical and epidemiological features of CMPD in the Republic Sakha (Yakutia).

Materials and methods. We carried out a retrospective analysis of medical records of patients followed-up by hematologists of Yakutsk from 1995 to 2018. The study included 104 patients, 39 of them were diagnosed with ET (27 women and 12 men), 40 had PV (21 women and 19 men), and 25 had PMF (11 women and 14 men). The diagnosis was established based on the current diagnostic criteria of the World Health Society (WHO) [14]. The epidemiological, clinical, laboratory, therapy data obtained during outpatient consultation. Primary incidence was calculated as ratio of newly diagnosed patients` number to average region population number per 100 thousand populations. Complete blood cells (hemoglobin, platelet, leukocyte counts and number of blast cells) and spleen size were recorded at the time of diagnosis. Analysis of correlation of risk factors with incidence of thrombosis was performed using a four-field contingency table (table 1) and a χ-square test with Yeats correction ($p_{\chi 2}$). Results were considered significant at $p < 0.05$.

χ-square test with Yeats correction

$$\chi^2 = \sum_{i=1}^{r}\sum_{j=1}^{c}\frac{(|O_{ij} - E_{ij}| - 0,5)^2}{E_{ij}}$$

calculated by formula:

where Oij is the actual number of observations ij, Eij is the expected number of observations.

Results and discussion. According to literature review CMPD are mainly found in the elderly. The median age of patients at the moment of disease manifestation in our study was 50 years in ET (from 38 to 77 years), PV – 56 years (from 21 to 80 years) and PFM – 60 years (from 28 to 80 years). The median time of follow-up was 48 months (from 2 months to 23 years). In Republic of Sakha (Yakutia), the primary incidence of ET in different years ranged from 0 to 0,83, PV – from 0 to 0,73, and PMF – from 0 to 0,52 per 100 thousand population per year (fig. 1). The primary incidence of CMPD reached its maximum in 2015-2016 years, which is most likely due improvement of diagnosis with molecular genetic testing. According to foreign researchers' data, the primary incidence of ET is 0,38-1,7, PV – 0,68-2,6, and PMF – 0,1-1 per 100 thousand population per year [8], in Russian Federation there are no large epidemiological studies.

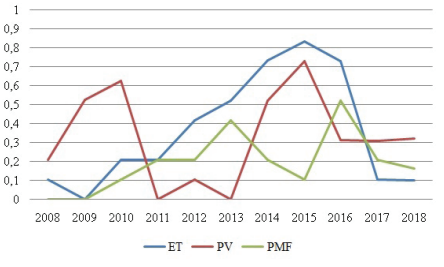
At the moment of diagnosis in patients with ET isolated thrombocytosis was the most common sign. Patients with PV demonstrated the signs of three-lineage hyperplasia and in PMF patients – leukocytosis with thrombocytosis. Splenomegaly was more common in patients with PMF (table 2).

Table 1

Four-field contingency table

	Patients with thrombosis	Patients without thrombosis	Total
Presence of risk factor	A	B	A + B
Absence of risk factor	C	D	C + D
Total	A + C	B + D	A + B + C + D

Thrombotic complications were recorded in 42,5% of patients with PV (17/40), 30,8% of patients with ET (12/39) and 28,0% (7/25) with PMF (table 3). According to the literature, thrombosis is more common among patients with PV [6, 15], which is associated with an extreme increase in the number of blood cells, hematocrit, and increased blood viscosity. In 58,3% (21/36) cases thrombosis was the first clinical symptom of disease. On average, the time from thrombosis to diagnosis of disease was 1 year. CMPD often has a latent manifestation. Polycythemia or thrombocytosis can be masked by increased plasma volume and/or hypersplenism, which causes difficulties in interpreting laboratory data, and



Morbidity of CMPD in Republic of Sakha (Yakutia) 2008-2018 years

Table 2

Clinical characteristics of patients at diagnosis

	ET	PV	PMF
Men, % (abs.)	30.8 (12)	47.5 (19)	56 (14)
Women, % (abs.)	69.2 (27)	52.5 (21)	44 (11)
Median age (from min to max)	50 лет (от 38 до 77 лет)	56 лет (от 21 до 80 лет)	60 лет (от 28 до 80 лет)
Average erythrocytes count, $M \pm m_м$*	4.7±0.9	6.6±1.4	5.1±1.4
Average hemoglobin count, $M \pm m_м$	135±19.6	171±25.2	127±30.5
Average hematocrit, $M \pm m_м$	46.5±4.6	51.3±7.7	41.7±42.6
Average leukocytes count, $M \pm m_м$	9.4±2.7	14.1±13.3	31.4±9.0
Average thrombocytes count, $M \pm m_м$	1113±442.2	711.8±445.3	881.5±615.2
Splenomegaly, % (абс.)	38.5 (15)	47.5 (19)	60 (15)

*$M \pm m_м$ – mean value ± standard deviation

Table 3

Prevalence of thrombotic complications in patients with CMPD, % (abs.)

Localization	ET (n=39)	PV (n=40)	PMF (n=25)
Arterial, total	25.6 (10)	30.0 (12)	16.0 (4)
Cerebral blood flow acute disturbances	12.8 (5)	22.5 (9)	12.0 (3)
Myocardial infarction	12.8 (5)	7.5 (3)	4.0 (1)
Venous, total	6.0 (2)	12.5 (5)	12.0 (3)
Deep vein thrombosis	6.0 (2)	10.0 (4)	4.0 (1)
Splanchnic vein thrombosis	-	2.5 (1)	8 (2)

the clinical picture is represented only by thrombosis [6].

Arterial thrombosis (30,0 and 25,6%) prevailed among thrombotic complications in patients with PV and ET — acute disorders of cerebral circulation and myocardial infarction, less frequently seen venous thrombosis (12,5 and 6%). In patients with PMF, arterial thrombosis was observed in 16% of cases, and venous in 12%. The median time between the diagnosis of the disease and the development of thrombosis was 3 years (from 0 to 30 years). Recurrent thrombotic complications were observed in 19,4% (7/36). The predominance of arterial thrombosis over venous thrombosis is explained by the direct participation in the pathogenesis of clot formation of the vascular endothelium. Damage to the vascular wall caused by hyperviscosity syndrome and the production of proteolytic enzymes by activated neutrophils, morphological and functional changes of blood cells and procoagulant state of plasma represent a multicomponent mechanism of clot formation. A number of publications report a higher thrombogenic potential of platelets in patients with *JAK2*V617F mutation [9].

The analysis of risk factors for thrombotic complications included both major factors (age over 60 years, history of cardiovascular risks) and additional (thrombocytosis more than $1000*10^9$/l and leukocytosis more than $11*10^9$/l) [3]. The contribution of different factors to pathogenesis of thrombosis is widely discussed in literature, and a number of scales have been proposed for risk stratification. Most authors agree that statistically significant risk factors for thrombotic complications are age over 60 years and history of thrombosis [2]. Among additional risk factors, some authors pay special attention to leukocytosis. It was demonstrated that activated leukocytes synthesize prothrombotic substances that cause functional changes in the endothelium, stimulate platelet activity, and they contribute to generation of thrombin and development of thrombosis [15].

Statistically significant differences in the group of patients with thrombosis and without thrombosis were revealed only by the presence of cardiovascular risk factors ($p < 0.05$) (table 4). There were no statistically significant differences in incidence of thrombosis in groups of people older than 60 years and younger. Thrombotic complications in people of working age have a high social significance, since they can lead to disability and a decrease in quality of life.

During follow-up molecular genetic testing was performed in 20,2% of patients (21/104), of which in 15,4% of patients (16/104) mutation of *JAK2* gene was fond and in 3,8% (4/104) mutation of *CALR* gene. Among patients with *JAK2*V617F mutation, thrombotic complications were observed in 62,5% of cases.

First-line therapy with interferon was prescribed to 42,5% of patients (17/40) with PV, 51,3% (20/39) with ET and 24% (6/25) with PMF. Hydroxyurea was administered to 30% (12/40) of patients with PV, 23,1% (9/39) with ET, and 44% (11/25) with PMV. In other cases, patients receive antiplatelet and vascular therapy. 6 patients are currently receiving targeted therapy with Ruxolitinib with positive effect. During therapy with Ruxolitinib, thrombotic complications were not observed in patients.

Conclusion. In the Republic Sakha (Yakutia) for the research period (1995-2018) the primary incidence of ET per 100 thousand population per year was 0 – 0.83, PV – 0 - 0.73, and PMF – 0 – 0.52, reaching maximum values in 2015-2016. Thrombotic complications, which are a serious clinical problem, are observed in patients with CMPD in 28-42.5% of cases. In a half of the cases, thrombosis was a first clinical symptom of myeloproliferative disease. A statistically significant risk factor for thrombosis is the presence of cardiovascular risks, which determines the need for a comprehensive approach to the treatment of this group of patients.

Table 4

Prevalence of thrombosis risk factors in patients with and without thrombosis, % (n)

Risk factor	Patients with chronic myeloproliferative diseases	
	without thrombosis (n=68)	with thrombosis (n=36)
Age 60 and older	51.5 (35)	47.2 (17)
Cardiovascular risk factors	19.1 (13)	38.6 (15)
Thrombocytosis>$1000*10^9$/l	30.9 (21)	19.4 (7)
Leukocytosis >$11*10^9$/l	27.9 (19)	33.3 (12)

* $p_{\chi 2}$ – χ-square test with Yeats correction

References

1. Шихбабаева Д.И., Полушкина Л.Б., Шуваев В.А., Мартынкевич И.С., Капустин С.И., Замотина Т.Б., Фоминых М.С., Удальева В.Ю., Зотова И.И., Шмелева В.М., Смирнова О.А., Волошин С.В., Бессмельцев С.С., Чечеткин А.В., Абдулкадыров К.М. Генетические маркеры наследственной тромбофилии и риск тромботических осложнений у больных с истинной полицитемией. Клиническая онкогематология. 2017;10(1):85-92. [Genetic markers of hereditary thrombophilia and risk of thrombotic complications in patients with polycythemia vera. Shikhbabaeva DI, Polushkina LB, Shuvaev VA, Martynkevich IS, Kapustin SI, Zamotina TB, Fominykh MS, Udal'eva VU, Zotova II, Shmeleva VM, Smirnova OA, Voloshin SV, Bessmel'tsev SS, Chechetkin AV, Abdulkadyrov KM. Klinicheskaja onkogematologija. 2017;10(1):85-92. (In Russ.).] DOI: 10.21320/2500-2139-2017-10-1-85-92

2. Меликян А.Л, Суборцева И.Н. Биология миелопролиферативных заболеваний. Клиническая онкогематология. 2016;4(3):314-325. [Melikyan AL, Subortseva IN. Biology of myeloid malignancies. Klinicheskaja onkogematologija. 2016;4(3):314-325. (In Russ.).] DOI: 10.21320/2500-2139-2016-9-3-314-325

3. Танашян М.М., Кузнецова П.И., Лагода О.В., Шабалина А.А., Суборцева И.Н., Меликян А.Л. Миелопролиферативные заболевания и ишемические инсульты. Анналы клинической и экспериментальной неврологии. 2014;8(2):41-45. [Tanashyan MM, Kuznetsova PI, Lagoda OV, Shabalina AA, Subortseva IN, Melikyan AL. Myeloproliferative diseases and ischemic stroke. Annaly klinicheskoj i eksperimental'noj nevrologii. 2014;8(2):41-45.(In Russ.)]

4. Танашян М.М., Кузнецова П.И., Раскура-

жев А.А., Лагода О.В. Некоторые аспекты профилактики нарушений мозгового кровообращения у пациентов с миелопролиферативными заболеваниями. Неврология. 2017;4(1):40-43. [Tanashyan MM, Kuznetsova PI, Raskurajev AA, Lagoda OV. Certain aspects of stroke prevention in patients with myeloproliferative diseases. Nevrologija. 2017;(4)1:40-43. (In Russ.)]

5. Жернякова А.А., Мартынкевич И.С., Шуваев В.А., Полушкина Л.Б., Фоминых М.С., Удальева В.Ю., Зотова И.И., Шихбабаева Д.И., Волошин С.В., Бессмельцев С.С., Чечеткин А.В., Абдулкадыров К.М. Факторы риска развития тромботических и геморрагических осложнений при эссенциальной тромбоцитемии. Онкогематология. 2017;12(2):30-38. [Zhernyakova AA, Martynkevich IS, Shuvaev VA, Polushkina LB, Fominykh MS, Udal'eva VU, Zotova II, Shichbabaeva DI, Voloshin SV, Bessmeltcev SS, Chechetkin AV, Abdulkadyrov KM. Thrombotic and bleeding risk factors in essential thrombocytemia. Klinicheskaja onkogematologija. 2017;(10)3:402-408. (In Russ.).] DOI: 10.17650/1818-8346-2017-12-2-30-38

6. Абдулкадыров К.М., Шуваев В.А., Мартынкевич И.С. Что нам известно об истинной полицитемии (обзор литературы и собственные данные). Онкогематология. 2015;10(3):28-42. [Abdulkadyrov KM, Shuvaev VA, Martynkevich IS. All we know about polycythemia vera: literature review and own experience. Onkogematologija. 2015;10(3):28-42. (In Russ.).] DOI: 10.17650/1818-8346-2015-10-3-28-42.

7. Duangnapasatit B, Rattarittamrong E, Rattanathammethee T, Hantrakool S, Chai-Adisaksopha C, Tantiworawit A, Norasetthada L. Clinical Manifestations and Risk Factors for Complications of Philadelphia Chromosome-Negative Myeloproliferative Neoplasms. Asian Pac J Cancer Prev. 2015;(16)12:5013-5018. DOI: 10.7314/APJCP.2015.16.12.5013.

8. Moulard O, Mehta J, Fryzek J, Olivares R, Iqbal U, Mesa RA. Epidemiology of myelofibrosis, essential thrombocythemia, and polycythemia vera in the European Union. O Moulard, J Mehta, J Fryzek [et al.]. Eur J Haematol. 2014; 92(4):289-297. DOI: 10.1111/ejh.12256. DOI: 10.1111/ejh.12256.

9. Arellano-Rodrigo E, Alvarez-Larrán A, Reverter JC, Villamor N, Colomer D, Cervantes F. Increased platelet and leukocyte activation as contributing mechanisms for thrombosis in essential thrombocythemia and correlation with the JAK2 mutational status. Haematologica. 2006;91(2):169-175.

10. Sazawal S, Rathi S, Chikkara S, Chaubey R, Seth T, Saraya A, Das J, Mahapatra M, Saxena R. JAK2V617F mutation in patients with splanchnic vein thrombosis. Dig Dis Sci. 2010;55(6):1770-1777.

11. Vainchenker W, Delhommeau F, Constantinescu SN, Bernard OA. New mutations and pathogenesis of myeloproliferative neoplasms. Blood. 2011; 118(7):1723–1735.DOI:10.1182/blood-2011-02-292102.

12. Tefferi A, Rumi E, Finazzi G, Gisslinger H, Vannucchi AM, Rodeghiero F, Randi ML, Vaidya R, Cazzola M, Rambaldi A, Gisslinger B, Pieri L, Ruggeri M, Bertozzi I, Sulai NH, Casetti I, Carobbio A, Jeryczynski G, Larson DR, Müllauer L, Pardanani A, Thiele J, Passamonti F, Barbui T. Survival and prognosis among 1545 patients with contemporary polycythemia vera: an international study. Leukemia. 2013;27:1874-1881. DOI: 10.1038/leu.2013.163

13. Tefferi A, Vannucchi AM. Genetic risk assessment in myeloproliferative neoplasms. Mayo Clinic proceedings. 2017;92(8):1283-1290. DOI: 10.1016/j.mayocp.2017.06.002

14. Barbui T, Thiele J, Gisslinger H, Kvasnicka HM, Vannucchi AM, Guglielmelli P, Orazi A, Tefferi A. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion. Blood cancer J. 2018; 8(2):15. DOI: 10.1038%2Fs41408-018-0054-y

15. Casini A, Fontana P, Lecompte TP. Thrombotic complications of myeloproliferative neoplasms: risk assessment and risk-guided management. J ThrombHaemost. 2013; 11(7):1215-1227. DOI: 10.1111/jth.12265.

16. Survival and prognosis among 1545 patients with contemporary polycythemia vera: an international study / A. Tefferi, E. Rumi, G. Finazzi [et al.] // Leukemia, 2013, V.27, P.1874-1881. DOI: 10.1038/leu.2013.163

17. Tefferi A. Genetic risk assessment in myeloproliferative neoplasms. Mayo Clinic proceedings. 2017, V.92, №8, p.1283-1290. DOI: 10.1016/j.mayocp.2017.06.002

18. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion / T.Barbui, J. Thiele, H. Gisslinger [et al.] // Blood cancer J, 2018, Vol.8, №2, P.15. DOI: 10.1038%2Fs41408-018-0054-y

19. Thrombotic complications of myeloproliferative neoplasms: risk assessment and risk-guided management / A Casini, P Fontana, TP Lecompte // J ThrombHaemost. 2013, V.11, №7, P.1215-1227. DOI: 10.1111/jth.12265.

M. P. Kirillina, V. I. Kononova, S. I. Sofronova, A. K. Ivanova, E. L. Lushnikova

THE INCIDENCE OF DYSPLASTIC CHANGES IN CERVIX UTERI AMONG WOMEN OF DIFFERENT AGE GROUPS

DOI 10.25789/YMJ.2019.67.11

Yakutsk, Republic Sakha (Yakutia), Russia: **KIRILLINA Maria Petrovna –** Candidate of Biological Sciences, Senior Research Scientist, Head of Yakut Science Centre of Complex Medical Problems Laboratory, Head of NEFU Medical Institute Clinic Laboratory,kirillinamp@mail.ru,89142716881, **KONONOVA Irina Vasilievna** – Candidate of Medical Science, Research Worker of Yakut Science Centre of Complex Medical Problems Laboratory, irinakon.07@mail.ru 89243683673, **SOFRONOVA Sargylana Ivanovna** – Candidate of Medicine, Senior Research Associate, Head of Scientific and Organizational Department of Yakut Science Centre of Complex Medical Problems Laboratory, sara2208@mail.ru 89841094825, **IVANOVA Anna Konstantinovna -** Clinical Pathologist of NEFU Medical Institute Clinic, ivanova.ak11@gmail.com, 89248647588, **LUSHNIKOVA Elena Leonidovna**- Doctor of Biological Science, professor, the head of FSBIS Institute of Molecular Pathology and Pathomorphology "Federal Research Center of Fundamental and Translational Medicine" 630117,Novosibirsk,Timakova st.,2, pathol@inbox.ru8(383)334-80-03.

The article presents an analysis of the incidence of dysplasia degrees and cervical cancer (CC) in women of different age groups based on cytological studies from 2016 to 2018 inclusive. The frequency of incidence of CIN 1, CIN 2, CIN 3 and CC was determined, which is inversely dependent on the dysplasia degree in all age groups of women. While the incidence of CIN 2, CIN 3 and CC was decreasing, CIN 1 increased between 2016 and 2018. Women 26-35 years had the highest incidence of CIN 1, CIN 2 and CIN 3; also CIN 2 was detected in women 36-45 years, as in the first group; women of 46-55 years had a sharp rise in CC - it is 2.5 times higher than in previous two groups. The peak incidence of CC was in patients aged 56 years and older.

Keywords: screening, oncocytology, diagnosis, dysplasia, cervical cancer.

Relevance. According to various authors, cervical pathology makes up from 10 to 15% of all gynecological diseases [3]. Occurrence and development of the causes and mechanisms of cervix uteri pathological processes are rather complex and understudied process [2]. As is known, dysplastic changes in the cervix uteri epithelium are considered as precancerous states [6], there is evidence that one of the main conditions for the development of dysplasia and CC is the persistence of the human papillomavirus (HPV) [8,9].The state of local immunity, as a regeneration process control agent [1], has great importance in the development of dysplastic processes in the cervix uteri, as well as a hormonal state, since cell developing and differentiation in the stratified squamous epithelium of the cervix uteri is hormone-dependent. Because of the hormonal status in women depends on age, it determines the usefulness of studying the features of dysplastic changes in cervix uteri in different age groups, irrespective of the