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Pre-malignant conditions and their early detection

Relevance: Malignant neoplasms belong to socially significant diseases. Pre-malignant conditions that lead to the development of malignant neoplasms and early death. Search for the methods of early detection, and efficient treatment of pre-malignant conditions remain an acute medical problem.

Pre-malignant conditions are associated with a high risk of cancer development.

Purpose of this study was the detection of common nosologies leading to cancer and introduction into the practice of methods of timely detection of malignant neoplasms.

Results: The most common pathologies among the population of Shymkent include diffuse cystic mastopathy (20.2%), cervical dysplasia (19.9%), chronic obstructive pulmonary disease (9.6%), and chronic atrophic gastritis of the gastrointestinal tract (6.6%).

Conclusions: Pre-cancer nosologies shall be registered in special electronic databases (i.e., Integrated Medical Information System) and marked as "pre-malignant conditions" for the outpatient district oncologists and general practitioners. Such monitoring of patients with pre-malignant conditions leads to timely detection of the initial stage of cancer. High-quality organization of prevention and treatment positively affects the survival rate up to 5 years.

Keywords: pre-malignant conditions, early detection, prevention, medical checkup, efficient treatment.

To date, malignant tumors and precancerous conditions are included in the group of socially significant diseases. Precancerous conditions are pathologies with a high risk of their transition to a malignant tumor. For the first time, M. Dubreuil has first introduced the term "precancerous conditions" at the International Congress of Dermatologists in 1896, in London. Now, this term is widely used in oncology.

From the point of risk of transition to cancer pathology (malignization), precancerous conditions can have two forms – obligate or facultative. Obligate precancerous conditions are associated with a high probability of malignization, while in facultative precancerous conditions, the probability of malignization is only 0.1-5%. Precancerous conditions have several types. For example, chronic gastritis can be attributed to a precancerous state of the gastrointestinal tract. According to WHO statistics, 80-90% of the global population have chronic gastritis. 60-70% of people with chronic gastritis are in the working age. Clinical symptoms of stomach ulcers and duodenitis can be observed both in children and adolescents, as well as in 20-30-year-olds. Men suffer from these diseases more often than women. The frequency of such diseases, like metaplasia and gastric dysplasia, is 1.3-50%. Obligate precancerous conditions also include atrophic hyperplastic gastritis (20-75%).

Precancerous pathologies of the liver include chronic hepatitis and cirrhosis.

Precancerous conditions of the breast include mastopathy and chronic diseases developed on the background

of hormonal failure. According to studies, fibrocystic mastopathy often leads to breast cancer (60-65%).

Also, pre-cancerous conditions include such diseases as chronic diseases of the cervix, glandular endometrial hyperplasia, cervical erosion, leukoplakia, and polyps.

Thyroid nodes, metabolic disorders, and the development of degenerative changes are referred to as precancerous conditions of the thyroid gland.

Precancerous skin conditions are radiation damage to the skin tissue under the influence of ultraviolet rays, dermatitis, melanoma, and dangerous nevi.

The literature review results show a very low practical value of the results of studying the distribution of main nosologies leading to malignant neoplasms and their contribution to the formation of cancer diseases. At that, the level of timely detection of malignancies remains doesn't stand up to scrutiny.

Purpose of the study: the development of scientific-sound methods of timely diagnostics of malignant neoplasms caused by the spread of major nosologies leading to cancer, and their implementation into practice.

Methods and Materials: In the course of work on the dissertation (September 1, 2014 to September 1, 2015), transverse (simultaneous) studies were carried out. The permission for scientific research was given by the local ethics committee of Kozha Akhmet Yassawi International Kazakh-Turkish University (protocol No. 9a of 10/29/2015).

In total, 16511 medical cards of outpatients on dispensary file at the outpatient clinics of the city of Shymkent, South Kazakhstan region (clinics №№1-12, except

for №7, the central polyclinic) were analyzed to identify the most common precancer conditions. The search in each clinic was done using the electronic database. Out of all registered patients with precancerous pathologies, we selected those patients who had been treated before and received no treatment in the last 10 years. Patients with unidentified outpatient cards or empty cards, or those who moved to another district or another city, were excluded from the list. We ended up with 15111 outpatient cards for the study. The frequency and percentage ratio were calculated to ensure high-quality processing of data.

The calculations were made on a PC using the MS Excel program. We also used the SPSS data (SPSS Inc 17, Chicago, IL, USA) and made a statistical analysis.

Results: The nosologies which become the main cause of malignant tumors are very common among residents of the South Kazakhstan region. Among these dangerous diseases, the precancerous state of the mammary glands has a special place. In our epidemiological studies, we detected 3,065 cases of diffuse cystic mastopathy, and the frequency of its malignization was 46.2%. It is worth mentioning that the level of timely detection of the disease after its malignization was not high. Thus, 26.9% of malignant neoplasms were detected at stage I, 29.3% – at stage II, and 47.2% – at stages III and IV. Untimely diagnostics of diffuse cystic mastopathy affected the 5-year survival rates of cancer patients. Only 65.8% of patients have lived for 5 years with a malignant tumor, while the rest has died in the initial stages of the disease.

Table 1 – The level of the malignization of precancerous conditions over the past decade (% , 95% CI)

Organs	Those on file at the dispensary (N = 15111)	The share of cured (% , 95% CI)	The share of malignization (% , 95% CI)	Cancer stages			
				I	II	III	IV
1	2	3	4	5			
Esophagus	1232	55.5 (CI: 25.7-58.2)	44.5% (CI: 41.7-47.2)	11.2	29.0	55,4	4.3
Stomach	2145	47.8% (CI: 45.7-49.9)	52.2% (CI: 50.0-54.2)	10.0	30.8	45.6	13,4
Liver	649	54.7% (CI: 50.8-58.4)	45.3% (CI: 41.5-49.0)	6.8	44.5	32.3	16.3
Respiratory system	1450	60.4% (CI: 57.8-62.9)	39.5% (CI: 37.1-42.1)	27.1	31,0	34.1	7.6
Skin covering	1321	50.7% (CI: 48.0-53.5)	49.2% (CI: 46.5-51.9)	26,4	20,4	49.3	3.8
Kidneys, urinary system	962	69.5 (CI: 66.6-72.4)	30.3% (CI: 27.5-33.3)	35.9	47.6	12.6	3,7
Milk glands	3065	53.7% (CI: 52.0-55.5)	46.2% (CI: 44.4-48.0)	22.9	29.3	30.6	17.0
Cervix	3214	65.4% (CI: 63.7-67.0)	34.6% (CI: 32.9-36.2)	29.9	26.2	35.5	8.2
Rectum	921	61.3% (CI: 58.1-64.4)	38.6% (CI: 35.5-41.8)	6.7	35.6	42.9	14.6
Total	15111	8748 (57.8)	6363 (42.2)	6.7	35.6	42.9	14.6

Common background nosologies with a high probability of malignization include reflux esophagitis of the esophagus (probability of transition into a malignant tumor – 65.9%), chronic atrophic gastritis (54.8%), melanoma-like nevus (77.3%), and chronic hepatitis (58.2%). The nosologies with a medium probability of malignization include dysplasia of the cervix (38,4%), atrophic esophagus esophagitis (30.4%), polyp of the stomach (43.6%), gastric ulcer (41,4%), polyp rectum (38.6%), chronic obstructive pneumonia (39.5%), cirrhosis (42%), kidney cyst (39.2%), chronic pyelonephritis (28.1%), and kidney stones (28%). The diseases with a low probability of malignization are esophageal polyp (13%) and skin scars (13%). It is worth noting that such diseases as the esophagus polyp (79.1%), chronic pyelonephritis (90.3%), kidney cyst (89.1%), and chronic obstructive inflammation of lungs (58.1%) often are detected at stages I and II of malignization. Chronic atrophic gastritis (33.3%) rarely leads to the formation of neoplasms leading to cancer.

The highest 5 - year survival after diagnosis was detected in diseases such as gastric ulcer (75.5%), fibrosis (73.6%), melanoma - like nevus (83.9%), and neck polyp uterus (75%), cervical dysplasia (65.9%), chronic pneumonia (59.6%), kidney cyst (58.1%), kidney stones (58.5%), and chronic hepatitis (48, 9%).

Discussion: We collected data on preventive measures taken to reduce nosologies leading to malignant neoplasms, as well as those associated with a high risk of malignization. The main reason was the improper assessment of the risk of malignization.

The situation could be improved by a proper organization of screening on major nosologies leading to malignant tumors. Especially in outpatient clinics, where these diseases are often detected, one should take control of educational and methodological procedures aimed at general practitioners and introduce strict sanitary-hygienic monitoring of their daily work. Every patient with a disease that leads to malignancy should undergo complete clin-

ical and laboratory tests, receive an oncologist consultation. The patients with the first signs of malignancy shall receive psychological assistance and undergo a full examination at the oncology center and be referred to treatment. Only properly organized the screening and clinical examinations will help identify malignant tumors at their first manifestation and increase the 5-year survival rates.

In the observational study conducted by a group of authors in 2017, mammary gland hyperplasia turned out to be the most common malignant neoplasm. In 2017 by several authors, premalignant conditions were identified in 6271 women with low indices, 1132 (18.0%) with very indices, and 2921 (46.6%) with fuzzy data. The statistical significance of cancer development has been established. In 2017, in China, several authors revealed a frequent malignization of precancerous conditions of the stomach. Diseases such as erosion of the stomach, polyps, and stomach ulcers were also often mentioned.

Conclusion:

1. By pathologies, which often lead to the development of malignant tumors, include "diffusely cystic breast disease" 20.2 (95% CI:19,6-20,9%), "cervical dysplasia" 19.9 (95% CI:16.3-17.5%), "chronic obstructive pneumonia" 9.6 (95% CI:9.1-10.0%) and "chronic atrophic gastritis of the stomach" 6.6 (95% CI:6.2-7.0%).

2. Due to timely detection, the 5-year survival was 36.1% with the malignization of reflux esophagitis and 28.4% with the malignization of atrophic gastritis. According to the data obtained, the level of diagnosis and early diagnosis of diseases is very low, so the level of dispensary care remains low.

3. Most of the patients suffering from malignant pathologies were in the retirement age (56.9%). Still, the share of working-age cancer patients was 42.8%, indicating the high socio-economic significance of cancer.

4. Registration of malignancies with a mark "Precancerous disease" in a specialized electronic database (e.g., CMIS (complex medical information system) database) used by general doctors and oncologists, careful observation and treatment of patients with malignant tumors, timely detection of initial stages of cancer, high-quality organizational and prevention measures have a positive influence on 5-year survival rates.

Suggestions:

Register cancer-related diseases in the special electronic registers, mandatory supervision of doctors - oncologists, patients with precancerous pathologies to control the dynamics of the disease, which will reveal cancer at early stages.

Advantages and disadvantages of the study:

Benefits:

In this study, the obtained outpatient records and medical cards, as well as the materials registered in the last decade, were fully explored to identify precancerous conditions.

Disadvantages:

The study was conducted in the city of Shymkent, South Kazakhstan region. The data collected taking into consideration the particularities of each region of the Republic of Kazakhstan could contain errors.

References:

1. Kotelevets S.M. Populyatsionnyye osobennosti v rasprostranennosti infektsii *Helicobacter pylori* (Population characteristics in the prevalence of *Helicobacter pylori* infection) // *Dnevnik Kazanskoy meditsinskoy shkoly (Diary of Kazan Medical School)*. – Kazan', 2016. – № 1. – P. 14–16, [in Russian];
2. Tazhibayeva K.N., Janabaev N.S., Kerimov R.A., Buleshov M.A. *Onıtústik Qazaqstan oblysynda turǵyndar arasyndaǵy onkologialyq aıyrylardyń skrinıń tásilimen anyqalǵynyń kázirgi tańdaǵy jaǵdaiy (The current state of cancer detection among residents of the South Kazakhstan region by the screening method)* // *Vestnik KazNMU (Bulletin of Kazakh National Medical University)*. – Almaty, 2015. – №4. – P. 137–139, [in Russian];
3. Tazhibayeva K.N. *Onıtústik Qazaqstan oblysy Shymkent qalasy eńbekke qabletti turǵndar arasynda onkoskrinıń tehnologialarynyń eńgizý tiimdiligini baǵalay (Evaluation of the effectiveness of the implementation of cancer screening among the working population of the city of Shymkent, SKO)* // *Astana medisina jýrnaly (Astana Medical Journal)*. – 2016. – № 2(88). – P. 136–140, [in Russian];
4. Buleshov M.A., Tazhibayeva K.N., Sultanbekov K.A., Nesipbaeva Z.ZH. *Territorial'nyye i ekologicheskiye osobennosti rasprostraneniya onkologicheskikh patologii v Yuzhno-Kazakhstanskoy oblasti (Territorial and environmental features of the spread of cancer pathology in the South Kazakhstan region)* // *Vestnik KazNMU (Bulletin of Kazakh National Medical University)*. – 2015. – № 4 (73). – P. 29–32, [in Russian];
5. Grzhibovskiy A.M., Ivanov S.V. *Poperechnyye (odnomomentnyye) issledovaniya v zdravookhraneniya (Cross-sectional (simultaneous) research in healthcare)* // *Nauka i Zdravookhraneniye (Science and Healthcare)*. – 2015. – №2. – P. 5–18, [in Russian];
6. Order of the Minister of Health of the Republic of Kazakhstan "On amendments and additions to the order of the acting Minister of Health and Social Development of the Republic of Kazakhstan dated July 28, 2015 No. 626 "On approval of the Rules for the provision of consultative and diagnostic assistance": approved on March 30, 2019, No. ҚР ДСМ-17;
7. Order of the Minister of Health and Social Development of the Republic of Kazakhstan "On the approval of the Rules for the provision of primary health care and the Rules for the attachment to organizations of primary health care": approved on April 28, 2015, No. 281;
8. Kotelevets S.M. *Vozrastnaya dinamika infitsirovannosti Helicobacter pylori u starshikh vozrastnykh grupp (Age dynamics of Helicobacter pylori infection in elderly groups)* // *Dnevnik Kazanskoy meditsinskoy shkoly (Diary of Kazan Medical School)*. – 2015. – № 2. – P. 11–12, [in Russian];
9. Tazhibayeva K.N., Buleshov M.A., Buleshova A.M., Grzhibovskiy A.M., Zhanabayev N.S. *Prichiny otkaza patsiyentov s podozreniyem na zlokachestvennyye novoobrazovaniya ot dal'neyshego meditsinskogo obsledovaniya, po mneniyu (Reasons for the refusal of patients with suspected malignant neoplasms from further medical examination, according to district doctors of the South Kazakhstan region)* // *Nauka i Zdravookhraneniye (Science and Healthcare)*. – 2016. – №5. – P. 90–100, [in Russian];
10. Tazhibayeva K.N., Buleshov M.A., Buleshova A.M., Grzhibovsky A.M. *Qazaqstanda jáne Shetelde eńbek etý jasyndaǵy turǵyndar arasynda uıymdastyrylatyn onkologialyq skrinıń tiimdiligini baǵalay nátiжелeri júeli ábeıttik sholý (Systematic literary reviews of the effectiveness of oncoscreenings among*

the able-bodied population in Kazakhstan and abroad). // *Nauka i Zdravookhraneniye (Science and Healthcare)*. – 2016. – № 6. – P. 123–145, [in Kazakh];

11. Tazhibbaeva K.N., Zhanabaev N.S., Beisembaeva Z.I. Oñtústik Qazaqstan oblysy shymkent qalasynda erbekke qabletti turýndardyń medisinalyq-áleymettik ómir súry deńgein baǵalaý jáne onkologialyq kómehti uymdastyry kórsetkishteri (Assessment of medical and social well-being of the working population and the organization of cancer care in the city of Shymkent, SKO) // *As-tana medisina jýrnaly (Astana Medical Journal)*. – 2016. – №3. – P. 121–126, [in Kazakh];

12. Tazhibbaeva K.N., Nesipbaeva Z.Zh., Aldekeeva A.T., Yusupova A.B. Oñtústik qazaqstan oblysynda qaterli jańa túzilister boiynsha turýndar densaýlyǵyn baǵalaý (Health assessment of the city of Shymkent SKO, by the criteria of precancerous pathologies) // Oñtústik Qazaqstan Memlekettik Farmasevtika Akademiasy Habarshy (South Kazakhstan State Pharmaceutical Academy). – 2015. – № 4 (73). – P. 6–9, [in Kazakh];

13. Kholmatova K.K., Gorbatova M.A., Khar'kova O.A., Grzhibovskiy A.M. Poperechnyye issledovaniya: planirovaniye, razmer vyborki, analiz dannykh (Cross-sectional studies: planning, sample size, data analysis) // *Ekologiya cheloveka (Human Ecology)*. – 2016. – №2. – P. 49–56, [in Russian];

14. Kholmatova K.K., Kharkov O.A., Grzhibovsky A.M. Osobennosti primeneniya kogortnykh issledovaniy v meditsine i obshchestvennom zdravookhraneni (Features of the application of cohort studies in medicine and public healthcare) // *Ekologiya cheloveka (Human Ecology)*. – 2016. – № 4. – P. 56–64, [in Russian];

15. Kholmatova K.K., Grzhibovskiy A.M. Primeneniye issledovaniy «sluchay-kontrol'» v meditsine i obshchestvennom zdravookhraneni (Application of case-control studies in medicine and public healthcare) // *Ekologiya cheloveka (Human Ecology)*. – 2016. – № 8. – C. 53–60, [in Russian];

16. Kholmatova K. K., Grzhibovskiy A. M. Panel'nyye issledovaniya i issledovaniya trenda v meditsine i obshchestvennom zdravookhraneni (Panel studies and trend studies in medicine

and public healthcare) // *Ekologiya cheloveka (Human Ecology)*. – 2016. – № 10. – C. 57–64, [in Russian];

17. Kholmatova K.K., Khar'kova O.A., Grzhibovskiy A.M. Eksperimental'nyye issledovaniya v meditsine i zdravookhraneni: planirovaniye, obrabotka dannykh, interpretatsiya rezul'tatov (Experimental research in medicine and healthcare: planning, data processing, interpretation of results) // *Ekologiya cheloveka (Human Ecology)*. – 2016. – № 11. – C. 50–58, [in Russian];

18. Agreus L., Kuipers E.J., Kupcinskas L., Malfertheiner P., et al. Rationale in diagnosis and screening of atrophic gastritis with stomach-specific plasma biomarkers // *Scand J Gastroenterol.* – 2012. – Vol. 47(2). – P.136–147;

19. International Agency for Research on Cancer, World Health Organization. Schistosomiasis, liver flukes and Helicobacter pylori. IARC working group on the evaluation of carcinogenic risks to human // *Monogr Eval Carcinog Risks Hum.* – 1994. – Vol. 61. – P. 218–220;

20. Boecker W., Stenman G., Schroeder T., Schumacher U., Loening T., Stahnke L., Löhnert C., Siering R.M., Kuper A., Samoilova V., Tiemann M., Korsching, Buchwalow I. EMulticolor immunofluorescence reveals that p63- and/or K5-positive progenitor cells contribute to normal breast epithelium and usual ductal hyperplasia but not to low-grade intraepithelial neoplasia of the breast // *Virchows Archiv.* – 2017. – Vol. 5. – P. 493–504;

21. Vierkant R.A., Degnim A.C., Radisky D.C., Visscher D.W., Heinzen E.P., Frank R.D., Winham S.J., Frost M.H., Scott C.G., Jensen M.R., Ghosh K., Manduca A., Brandt K.R., Whaley D.H., Hartmann L.C., Vachon C.M. Mammographic breast density and risk of breast cancer in women with atypical hyperplasia: an observational cohort study from the Mayo Clinic Benign Breast Disease (BBD) cohort // *BMC Cancer.* – 2017. – Vol. 17(1). – P. 84;

22. Zhou L., Li J.L., Zhou Y., Liu J.B., Zhuang K., Gao J.F., Liu S., Sang M., Wu J.G., Ho W.Z. Induction of interferon-λ contributes to TLR3 and RIG-I activation-mediated inhibition of herpes simplex virus type 2 replication in human cervical epithelial cells // *Mol Hum Reprod.* – 2015. – Vol. 21(12). – P. 917–929.