Doctoral School in Medical Sciences

ŞVEŢ Veronica

ONCOLOGICAL MORBIDITY OF BREAST CANCER IN MEDICAL WORKERS IN THE REPUBLIC OF MOLDOVA

321.20. Oncology AND Radiotherapy

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Scientific adviser:

Mereuţă Ion, hab. doc. in med. science, univ. prof., SUMPh "Nicolae Testemitanu"

Members of the guidance commitee:

Grigore Friptuleac, hab.doc. in med. science, univ. prof., SUMPh "Nicolae Testemitanu"
Mihail Ciocanu, hab.doc. in med. science, univ. prof., SUMPh "Nicolae Testemitanu"
Ştefan Gaţcan, doc. in med. science, assoc. prof., SUMPh "Nicolae Testemitanu"

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Sochircă Diana, doc.şt.med., oncologist, Oncological Institute

Official references:

Lapochkina Nina, hab.doc. in med. science, univ. prof.., head of the Oncology department, University of Medicine, Ivanovo, Russia

Friptuleac Grigore, hab.doc. in med. science, univ. prof., SUMPh "Nicolae Testemitanu"

Chilaru Simona, dr. şt.med., Department chief Mammology, Oncological Institute

Author
Şveţ Veronica

Content

CONCEPTUAL REFERENCES OF RESEARCH

Actuality of the subject and the importance of the approached problem. Breast cancer (BC) remains a current problem over time and is the most common form of cancer diagnosed among women worldwide, making it a problem with a global impact on public health. According to statistics from the World Health Organization (WHO) and GLOBOCAN BC is considered the most common form of cancer in women, accounting for 11,6% of all cancers, with up to 2,1 million newly diagnosed cases and 627,000 of deaths (6,6%) annually (WHO, 2018) [146,147,248]. According to the National Cancer Registry data - 2018 in the Republic of Moldova, BC ranks first in the structure of oncological morbidity from malignant tumors in women and is 10.7% of the oncological structure in the female population, annually registering about 1,125 new cases [223, 243].

The exercise of medical activity is one exposed to various risk factors that generate various diseases, including cancer. Analyzing the morbidity rate due to oncological diseases in women's medical staff, the most common remains that of BC [136].

In comparison, the health indices of medical workers (MW) are lower than other professions and differ from the average indicators, so MW being ranked 5th in the structure of morbidity, surpassing even workers in the chemical industry. Medical activity imposes various occupational risks, considered the most vulnerable in terms of health, MSong all intellectuals and is insufficiently studied both internationally and nationally [4,136].

The work of the medical staff is assigned among the heaviest activities and with an enormous responsibility. Medical activity is characterized by the intensity of intellectual work, under certain conditions - obvious physical effort, in situations of patience and responsibility, maximum attention and concentration, activities and prompt decisions in extreme situations [176,177] and various action of risk factors - physical, chemical, biological associated with psychoemotional overload and the development of various lesions to oncological diseases among both physicians (P) and nurses (N) [177].

The purpose of the research: Evaluation of oncological morbidity by mammary gland cancer in medical workers in the Republic of Moldova, of some medical-social and diagnostic aspects, for the modification of the Diagnostic and Monitoring Algorithm in medical workers at risk of developing mammary gland cancer and elaboration of prevention and control measures .

Research objectives:
1. Analysis of breast cancer cases in medical workers in the Republic of Moldova for the period 2010-2018;
2. Comparative evaluation of mamary gland cancer in medical workers according to medical-social and specialized characteristics;
3. Study of comorbidities in respondents medical workers with mamary gland cancer;
4. Characteristics of diagnostic methods and results in medical workers with mMSmary gland cancer with the development of prevention and control measures;
5. Modification of the Algorithm of diagnosis and monitoring (control) in medical workers at risk of developing breast cancer.

The general methodology of the research was elaborated based on the publications of local authors [1,21,33,38,52,53,73,74,78,79,81,95,99,103-115,118,119,129] and abroad [2-15, 17-20,22-24,34-36,42-51,54-63,65-72,84-89,125-128]. For the research and solution of the problems approached in the thesis I used the methods: historical, comparative, mathematical-statistical, standard interview and by telephone, survey-questionnaire. In order to achieve the research goal and objectives, we proposed to perform two studies: 1) descriptive study according to the representative sMSple and 2) selective study, for medical workers - P and N with BC confirmed and reconfirmed cytopathologically / histopathologically in the Scientific Laboratories of Cytology and Morphology within the Oncological Institute of the Republic of Moldova, for the study period 2010-2018.

Scientific novelty and originality. First in the Republic of Moldova was studied and conducted a complex study on BC in MW, a systematic approach was used in evaluating the professional activity of MW with BC, were studied some parameters related to risk factors, the study of medical indicators

depending on the specialty, place of residence, clinical and diagnostic data, tumor stage, etc. of BC at P and N, prevention and control measures were developed, optimization of risk factors of the working environment of MW with modification of the specific diagnostic and monitoring algorithm.

Theoretical importance. Through this research we revealed the importance of studying the phenomenon of BC in medical workers through the increasing number of BC cases, targeting both doctors and nurses, being defined as a valuable medical and social problem with the action of various risk factors, overload obvious psycho-emotional that endangers the health of medical staff. The management of the early diagnosis of the medical workers belonging to the risk group will contribute to the obvious decrease of the number of cases with BC in the medical workers and will allow the increase of the survival of the respondents medical workers with BC in case of early detection.

The applicative value of the theme. The results of the study argued the need to create risk groups of medical workers, determine the most common risk factors in medical activity in order to optimize them and complete the algorithm for diagnosis and monitoring of medical workers with breast cancer, all aimed at early diagnosis of BC to MW.

Implementation of results. The scientific results of the study need to be presented at the level of the Ministry of Health and the Union with the implementation in medical practice at the level of each medical institution with the mandatory annual mammological medical check-up of all medical workers at work or by contract at other medical institutions. mandatory documentation of the results of their investigations through imaging clichés, free and unrestricted access to the respective services and granting a day off for diagnosis with retention of salary, increasing the harm coefficient, optimizing the action of harmful factors at work by providing free special equipment, satisfactory working conditions, provided by the Ministry of Health, Labor and Social Protection or the Compulsory Insurance Company or at the level of the Insured with free access to methods of mammological diagnosis, treatment and medical rehabilitation (including prostheses of the mammary glands), ensuring professional rehabilitation, extension of benefits for temporary or total disability and lifetime disability benefits.

Approval of research results. The study was approved based on the positive opinion of the Research Ethics Committee (minutes no. 36 of 03.05.2016) and of the topic approved by the Scientific Seminar on "Oncology and radiotherapy" (minutes no. 1 of 29.06. 2016) and at the Meeting of the Oncology Department of Nicolae Testemitanu State University of Medicine and Pharmacy of the Republic of Moldova (no. 1 of 28.01.2021).

Scientific research and study materials were presented and discussed at 7 national and international scientific forums (Republic of Moldova, Russia, Poland) at the annual conferences of Nicolae Testemitanu State University of Medicine and Pharmacy collaborators and students Symposium "Oncological surveillance in medical activity, early detection and treatment of tumors ", anniversary edition- 40 years of activity of the Department of Oncology, Hematology and Radiotherapy of Nicolae Testemitanu State University of Medicine and Pharmacy ", the meetings of the Society of Oncologists of IMSP IO during the years 2014-2018; IV National Congress of Oncology of the Republic of Moldova (Chisinau 2015); Mejdunarodna Konferencja Medyczna Polonijnych Organizacji (Polonia, 2014); Всероссийский образовательно- научная конференция студентов и молодых ученых с международным участьем «Медико- биологические, клинические и социальные вопросы здоровья и патологии человека» (Иваново Москва, 2017); Conferinţa Ştiinţifică Internaţională Sănătatea, Medicina şi Bioetica în societatea contemporană. Studii inter şi pluridisciplinare (Chişinău 2018, 2019); The 6-7-8-th International Medical Congress for students and young doctors (Chişinău 2016, 2018, 2020); Miedzinarodna Konferenja Medyczna z okazji Jubileuszu 20 lecia, Stawarzyszenia Polonijnych Organizacji Medycznych w Moldawii weoku obchodow (Chişinău 2018); XXIII Российский онкологический конгресс (Москва, 2019); XI Съезд онкологов и радиологов стран СНГ и Евразии (Казань, 2020); I Congres Naţional de geriartrie şi gerontologie cu participare internaţională în Republica Moldova (Chişinău 2020), Congress dedicated to the 75th anniversary of the founding of USMF "Nicolae Testemitanu" (Chişinău, 2020); IV ежегодная Конференция "Эволюция лекарственной

терапии злокачественных опухолей: гормонотерапии, химиотерапии, таргетной терапии и иммунотерапии" с международным участием (Россия, 2020), V National Congress of Oncology „Prevenția și controlul cancerului- o continuă provocare" cu participare internaţională (Chişinău, 2020).

The thesis materials were reflected in 40 publications, including 24 single authors, 16 co-authors, 32 innovation certificates and 2 patents.

Summary of thesis compartments. The thesis consists of an introduction, 4 chapters, conclusions, practical recommendations and bibliographical references with cited sources. Exposure of the text on 174 pages, illustrated with 15 tables, 30 figures and 38 annexes. The bibliography consists of 251 titles of publications.

In the **Introduction** it was argued the topicality of the topic on breast cancer in the world and especially in medical workers, justifying the approach of the present study and elucidating the purpose and objectives of the study, scientific novelty and originality, new main results and approval.

In Chapter 1 "Breast cancer in the world and selectively in health care workers" was analyzed the classical literature and specialty publications on BC in the world and especially in health care workers. It analyzes the risk factors, the specific conditions related to the workplace, the professional activity of the medical workers, the diagnosis approached in the detection of BC in different countries. The small number of scientific papers regarding BC in the specific group of population and professional-medical workers is argued. The topicality of the research is argued and conclusive data are provided by different authors from different countries on the issue addressed and the need for further studies.

Chapter 2 "Characteristics of the clinical observation material and research methods" includes the characteristics of the material and methods applied in the study: historical method, comparison, standard interview, calculation of sample indices examined by mathematical method, observational and research results according to which questionnaires were developed. This chapter presents the research design and the calculation formula of the sample of the study group, the statistical processing methods, the calculation of the t-Student intensive indicator, the calculation of the standard error, the determination of the statistical conclusion, the statistical data were processed. correlated, descriptive and discriminant, using the following programs: *Info Info 5, SPSS-15.*

Chapter 3 "Cancer morbidity of the mammary gland in medical workers in the Republic of Moldova" contains data on the incidence of BC in medical workers, type of studies, profile, specialty, description of risk factors, work activity - work experience, concomitant diseases , menopausal status, an analysis of the medical and social aspects of the patients in the study, a detailed statistical analysis of clinical and paraclinical parameters and quantification of indices related to the medical and social aspects extracted from the questionnaires and data from observation sheets.

The results presented in Chapter 4 "Diagnosis of breast cancer in medical workers" relate some features of BC diagnosis in medical workers, highlighting multiple aspects of diagnosis - diagnosis range, tumor topography, clinical forms of BC, growth forms, various methods diagnostic tests performed and their specificity, morphological and immunohistochemical confirmation, the degree of differentiation, detection by TNM and stages, analysis of reproductive health in women, etc. An important role is played by the scientific argumentation of completing the BC Diagnostic Algorithm in medical workers.

The synthesis of the obtained results is a compartment of analysis and reasoned conclusions on the results of own research and comparative analysis, of opinions of the specialists cited in the bibliographic analysis of the thesis regarding the problems approached in research.

The thesis concludes with general conclusions and methodical recommendations, where the results of the research and directives formulated in order to optimize the diagnosis and control of BC in medical workers are exposed. The bibliography consists of 251 titles.

The Annex compartment consists of 38 annexes with tabular material, questionnaire, copies of the Invention Patents and of the Innovator Certificates, of the Implementation Acts.

Keywords: mammary gland cancer ● medical workers ● concomitant diseases ● Diagnostic algorithm ● morbidity ● prevention and control measures ● risk factors.

1. BREAST CANCER WORLDWIDE AND SELECTIVELY IN MEDICAL WORKERS. LITERATURE REVIEW

1.1. Breast cancer in the world - current clinical and medico-social problem

For more than 20 years BC has been the most common form of cancer, it is placed in the top of the most common oncological diseases among women, representing a clinical and medico-social problem current and important in the health system around the world. Of all cancer sites in women, BC makes up 24.2%, which means that 1 in 4 new cases diagnosed in the world make BC [223, 231,232,243,251]. According to the National Cancer Registry data -2018 in the Republic of Moldova BC ranks first in the structure of morbidity from malignant tumors in women -10.7% of the oncological structure in the female population, annually registering about 1,125 new cases [223, 243]. BC remains a critical issue from both a clinical and medico-social point of view, keeping its relevance in all countries for several decades.

The medico-social importance of this pathology is determined by the polymorphism of oncological pathology, by the mechanisms of primary tumor development, metastases, high morbidity and its growth tendencies, high mortality, primary disability. This disease also affects other components of patients' lives and quality of life [217,218,219].

1.2. The characteristic of cancer morbidity of the mamary gland in medical workers

Medical activity has been recognized as one of the oldest professions, with exposure to a variety of risk factors and hazardous work environment, which can develop various diseases, including cancer. Oncological morbidity in PMW is one of the emerging health problems of this decade, continuing to grow globally, resulting in many obvious social and economic problems [12].

In the specialized literature there are few scientific papers that would elucidate the incidence through BC in MW-doctors and nurses, being a specific social and professional group. Likewise, there are few conclusive data on BC in doctors according to different specialties, which would highlight some peculiarities of BC in female medical staff. Daily exposure at work to various risk factors - dangerous physical, chemical and biological, psychological lead to the appearance and development of several pathologies, including cancer. The results of extensive studies conducted in different countries since the 80s revealed a higher risk of cancer in doctors and nurses compared to the general population, and the most common type of cancer in female health workers was breast cancer, of the brain [177].

The results of research in several hospitals conducted in different countries on oncological morbidity and medical mortality, show that the interaction of multiple occupational risk factors the most affected group of MW is the female-doctors and nurses, where gland pathology predominates[177]. In recent decades, various scientific papers have been conducted on the role of the work environment, risk factors and their influence on the development of cancer in doctors in various specialties. These studies have been conducted in countries such as the USA, Denmark, Thailand, Taiwan, Finland, Sweden, Italy, Russia, Romania, Norway, emphasizing the role of occupational or work-related risk factors in the development of different types of cancer in different countries, medical specialities. Initial studies on medical personnel conducted in the USA, Finland (1989-2001) noted the role of ionizing radiation as a primary risk factor in the development of various types of cancer, including breast cancer. Studies conducted in Taiwan (2001) showed a higher incidence of BC in physicians than in the general population, and the most common oncological disease was BC in female MW and accounted for 5,8% *vs* the general population with 2,6 cases and according to the medical specialties, it was found that the most affected doctors from those included in the study were internists with 3,57% of cases, pediatricians 12,5%, obstetricians-gynecologists 2,63%, family doctors 5,36%, radiologists 14.29%, other categories made up a total of 10,71%. Other studies conducted in Taiwan (2000-2010) conducted on nurses found an increased incidence of BC of 6.8% *vs* the general population 3,1% times. Another study conducted in Russia (1961-2005) marked a maximum incidence in MW women compared to male MW, and the share by BC accounted for 17% of all oncological diseases in women. The results of research conducted in Norway, USA (1988-1998), Boston, Germany and Romania (2000-2010), on work in night shifts or 24-hour shifts, showed that the number of guards performed during professional activity increases the risk,

development of both BC and other cancers and is closely correlated with work experience [158,163,168,170,177].

1.3 Characteristics of methods for diagnosing mamary gland cancer in medical workers

Rimpelä and collaborators in the studies on medical staff - P and N analyzed that this group of patients have easier access to health services, sufficient financial resources and the practice of healthy habits. Some authors state that doctors participate in cancer screening more often [132], are more careful about their health, are diagnosed more often and earlier, and have lower mortality rates. Other studies have found that physicians consult a specialist later than others for a variety of reasons, such as self-treatment, phobia of the disease, and awareness of the negative consequences that may occur during treatment or the failure to treat an advanced disease [157].

It is also given that the annual examinations of women doctors/nurses do not include USG, mammography, CT or MRI, often being paid individually by medical staff, other times these methods are even avoided financially, which increases the risk of a late diagnosis of BC. Likewise, the medical staff frequently avoids the control of the mammary glands by the specialist, based on their own experience, knowledge or embarrassment to do this control at the colleague. It is said that many treatments are often performed on the breast at the appearance of signs in the mammary gland without consulting a mammologist.

We did not find scientific data regarding the very new methods of performing the diagnosis of BC in MW, but there are peculiarities in this direction and as an explanation of the high share of BC in MW such as late addressability, neglect of annual medical check-up, mammological screening, practicing self-treatment, neglecting the first signs or symptoms against the background of a better computerization regarding the oncological disease of BC, of the existence in the occupational risk group (or from other risk groups), the action of the risk factors specific to the workplace. It is also known about the evolution of a treatment of respondents medical workers (RMW) with BC, especially doctors, which is more difficult, often with complications, frequently asked questions and recommendations during treatment, the involvement of several colleagues or administration that strains the activity work of the specialist. The situation is even more special from a psycho-emotional point of view and the evolution of the disease in this case. This to the end and explains the peculiarities of the diagnosis of BC in MW, with incidence of BC more frequently in the early stages, lower mortality, high disability [85,87].

A key role in improving treatment outcomes and BC prognosis is early diagnosis which is the basic screening program. The strategic goal in making a correct diagnosis is to detect the early stages of BC as early as possible, with obvious results in treatment and increased effectiveness, of course, and the reduction of the spread of the disease and recurrences. Early diagnosis strategies focus on ensuring timely access to cancer treatment by reducing barriers to care and / or improving access to effective diagnostic services.

BC in MW has been insufficiently studied in the world, and never in the Republic of Moldova, with a higher incidence than the general population, where many authors highlight the diversity of risk factors that lead directly to various diseases of the mammary gland even BC. According to the data of different authors, the most informative methods for early detection of BC are population screening and mammographic oncological screening. Additionally, CT, MRI, PETCT can be used. Confirmation methods are cytological by aspiration or fingerprinting, and biopsy with subsequent histological and immunohistochemical exMSination.

2. CHARACTERISTICS OF CLINICAL OBSERVATION MATERIAL AND RESEARCH METHODS

The scientific research is a cross-sectional-descriptive study, conducted within the Department of Oncology of the USMP "Nicolae Testemitanu" and the study unit were patients -MW with BC confirmed / reconfirmed cyto / histopathologically in the Cytological or Morphopathological Laboratory of within Oncological Institute, data from the National Cancer Registry, medical records, outpatient cards, informed consent to the study for the period 2010-2018. For the real estimation of the incidence of BC in

medical workers, of the epidemiological peculiarities and of the medico-social risk factors, of the diagnostic methods of BC the results obtained from the survey were used and additionally from the forms of the Bureau of Statistics, the data were analyzed with the help of the Department of Public Health and by the National Center for Health Management.

In order to achieve the purpose and objectives of the research, two studies were planned: 1.the descriptive study, according to the volume of the representative sample and 2. the selective study. The representative sample was calculated in the Epi-INFO ProgrMS 7.2.2.6, "Stat Gade Sample Size and Power" section for cross-sectional study based on the following parameters: population-number of female medical workers in the Republic of Moldova, 2018-21.563; frequency - 2 to 100; allowed error- ES = 1.0%; design effect- 1.5; result 99.9%, CI n = 177, with 10.0% non-response, n = 195. Proportional stratification of the sample P 73 (37.0%) and N 123 (63.0%). The inclusion of RMW in the study was performed according to the inclusion and exclusion criteria.

The research was conducted based on historical, comparative, mathematical-statistical methods, standard interview and by telephone, surveys that were used in the literature review, in order to obtain the proposed results and to formulate conclusions. In conducting the research, the ethical and moral requirements of the patients were observed and it did not include elements of human experimentation. The presence in the study of indices with several nominal and scalar variables allowed the separate processing of statistical data. The data obtained were processed by computerized by methods of variational, correlational and discriminant analysis.

Statistical research was conducted using modern mathematical methods and the generally-accepted statistical processing software "Statistical Package for the Social Sciences" SPSS 17 for Windows 10.0.5 (SPSS, Chicago, IL, USA) and "GraphPad PRISM® 5.0 for Windows 5.0 (GraphPad Software, Inc.).

3. BREAST CANCER MORBIDITY IN MEDICAL WORKERS IN THE REPUBLIC OF MOLDOVA

3.1. Breast cancer morbidity and their medical and social characteristics in medical workers in the Republic of Moldova (2010-2018)

The results of our research showed that for the 2010-2018 study period, BC in MW accounted for 196(17.9%) of the total number of oncological diseases in women by various locations. Respectively, the study sample was represented by 73(37%) P and 123(63%) N (figure 1, 2).
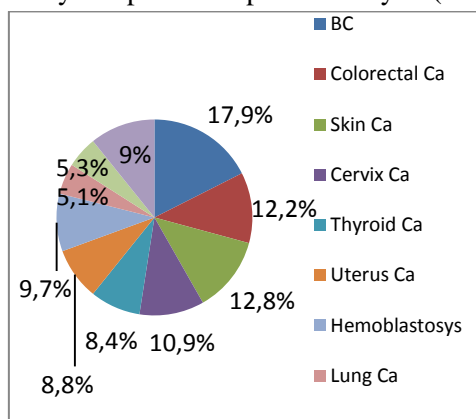
Figure 1. **The share of cancer by various localizations to MW in women Republic of Moldova years 2010-2018,%**
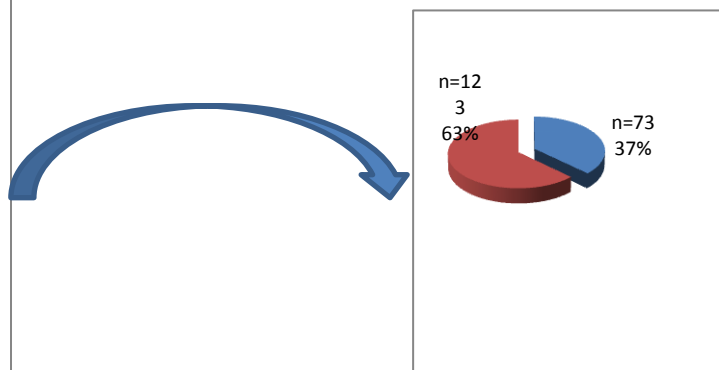
Figure 2. **Distribution of RMW with BC depending on studies, %**

The distribution of respondents of age-dependent medical workers demonstrated a continuous increase in values through BC during the study years, with a maximum incidence at the age of 65-69 years, making a total of 39 (19,8%) of which 14 (19,2%) P and 25 (20,3%) N and which is closely correlated with the increase of the work period with the maximum incidence at 35 years of work corresponding to the age of 65-69 years common to both P as well as N (figure 3.4).

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Figure 3. **Distribution of RMW with BC by age ,%**

Figure 4. **Characteristic RMW with BC depending on the work activity,%**

According to the geographical area, the most affected proved to be the northern area 61 (31,1%) RMW corresponding to 28 (38,3%) P and 33 (26,8%) N, and the least cases were registered in the Eastern area with 34 (17,3%) RMW with the pr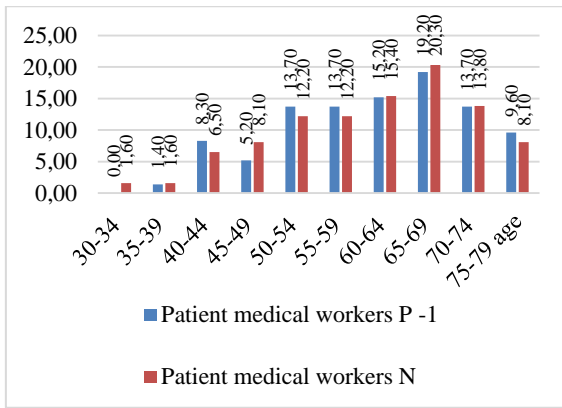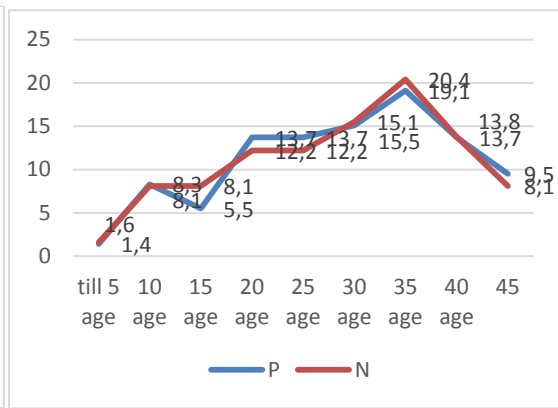edominance of P 26 (21,1%) and N 8 (11%) cases. According to the place of residence, the majority of RMW 109 (55,6%) were from urban areas, where the number of MS 69 (56,1%) cases predominated and P accounted for 40 (54,8%) cases. For the rural environment, 87 (44,4%) cases of BC were registered in which N 54 (43,9%) predominated and P with 33 (45,2%) cases cases, (p = 0,0001) (figure 5).
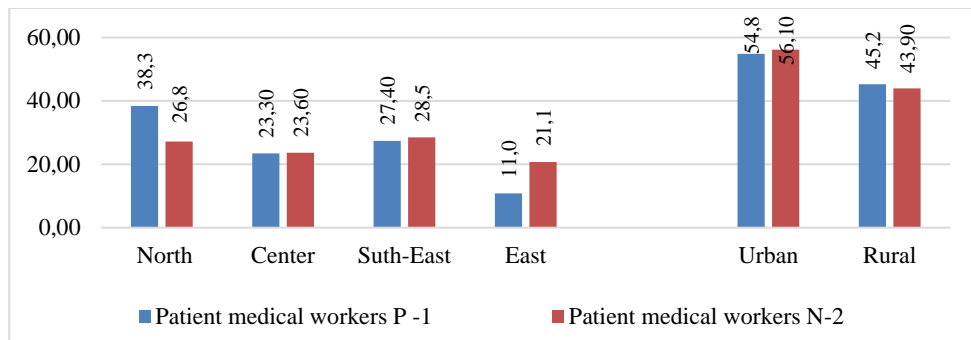
Figure 5. **General characteristic of RMW with BC depending on the geographical area and the environment of origin,%**

The assessment of the working conditions depending on the place of medical activity of RMW was important, because it appreciated in 100% cases good conditions only with activity in private medical institutions and private medical offices, such as pharmacies and dentists, and no case of conditions unsatisfactory work. While MW from state institutions argued that they worked in unsatisfactory conditions, especially with activity in hospitals districts 44 (33,1%), medical offices 35 (26,3%) cases (figure 6).
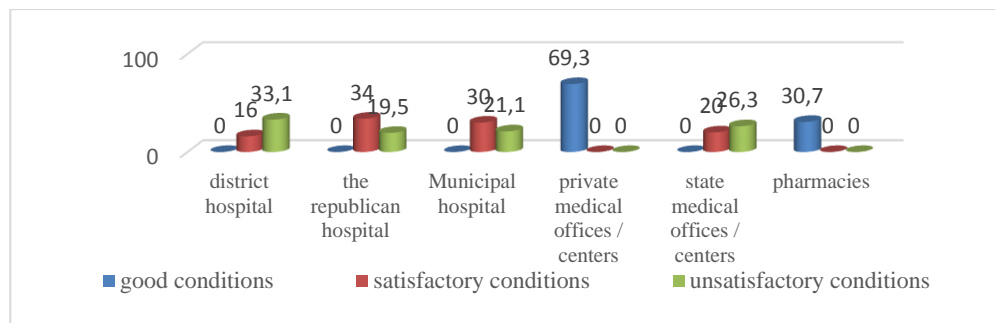
Figure 6. **The share of BC to MW depending on the place and working conditions in the Republic of Moldova, years 2010-2018,%**

According to the level of studies of RMW with BC we obtained that 123 (63%) were represented by MA with secondary medical education, and 73 (37%) of the respondents were represented by P, of which with the scientific title of doctor habilitat in sciences medical made up 1 (1,4%) case, doctors of medical science were 2 (2,8%) cases, computer doctors 70 (95,8%) cases, $\chi2=1,124,(p = 0,1317)$. The characteristic of RMW according to the activity profile we established that from the total number of RMW with BC the medical staff from the therapeutic profile predominated with 102 (52,1%), of which P made up 52 (71,3%) and N 50 (40,6 %) cases, and from the surgical profile from the total number of 90 (45,9%) RMW predominated N with 71 (57,8%) and P 19 (26%) cases. The least RMW with BC were among managers 4 (2%) from both P 2 (2,7%) and N 2 (2,62%) cases, $\chi2 = 1,041$; (p=0,1121)(figure7).
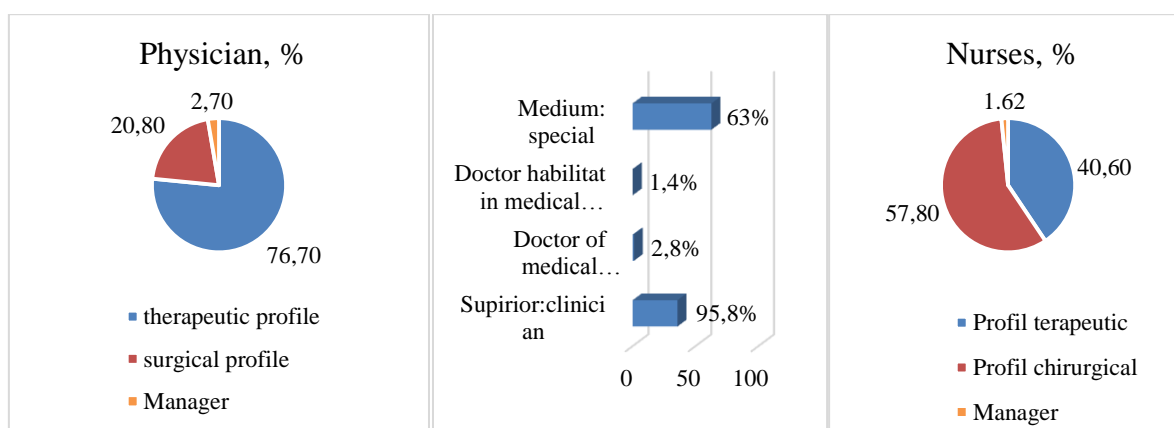
Figure 7. **RMW characteristic with BC, depending on profile and medical studies,%**

The study on the specialties in which doctors work, we obtained that most were active in the therapeutic field making up 56 (76,7%) cases, of which 18 (24,7%) interns (cardiologists, pulmonologists, gastrologists, hepatologists, pediatricians, endocrinologists), surgeons with 13 (17,9%) (surgeons-generalists, obstetricians-gynecologists), family doctors 8 (10,9%), radiologists 9 (12,3%), oncologists 7 (9,6%) (oncologists surgeons, oncologists chemotherapists, oncologists radiotherapists), emergency physicians 5 (6,9%), anesthesiologists-resuscitators 6 (8,2%) cases, physicians-pharmacists 3 (4,1%) cases, dentists and physicians psychiatrists in 2 (2,7%) cases, $\chi2 = 0,101$, (p = 0,0216) (figure 8).
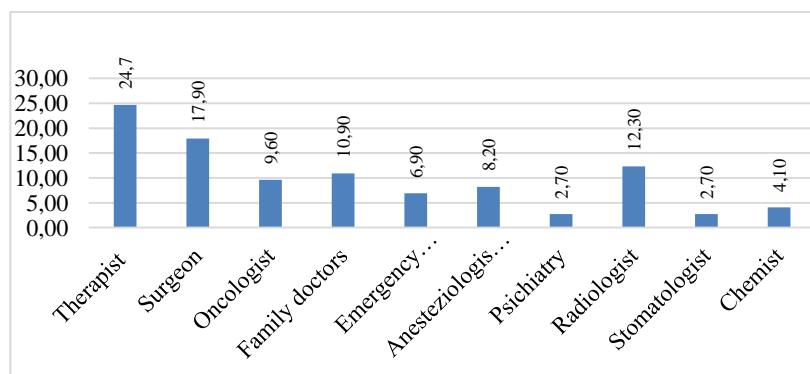
Figure 8. **Distribution of RMW with BC by specialty,%**

When evaluating the risk factors, we obtained that in 100% of RMW cases they argued a psycho-emotional tension and obvious physical intensity, related to continuous stress, related to both medical activity and collegial relations and administration, and between 80-90% RMW argued contact with chemicals - drugs, reagents, disinfectants, etc. and an unbalanced diet. Other risk factors analyzed included smoking, alcohol, mammary gland trauma, and 22-79% radiation (figure 9).
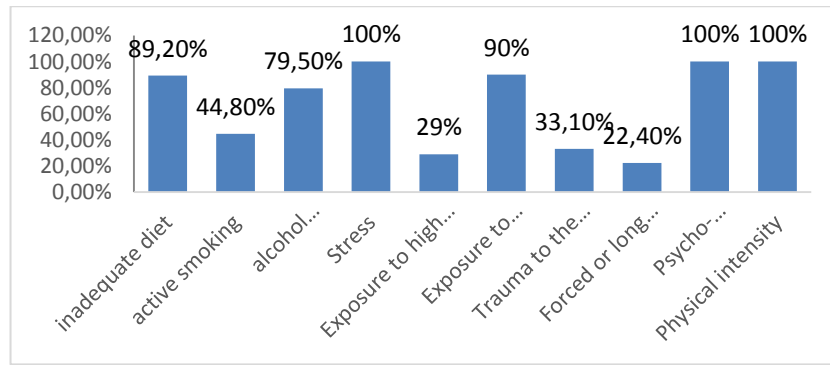
Figure 9. **Frequency of risk factors in MW medical activity with BC,%**

RMW with aggravated hereditary collateral anamnesis were 14 (7,1%) cases, of which on the mother line 9 (64,2%) with the predominance of BC 4 (45%) cases, Uterine cancer 2 (22%), Cervical cancer, gastric cancer and colorectal cancer 1 (11%) case. From the aggravated hereditary-collateral anamnesis on the father's line were 5 (35,8%) RMW, of which with Lung Cancer and Gastric Cancer was found in 2 (40%) cases and Esophageal Cancer in 1 (20%) case (p= 0,0115) (figure 10).
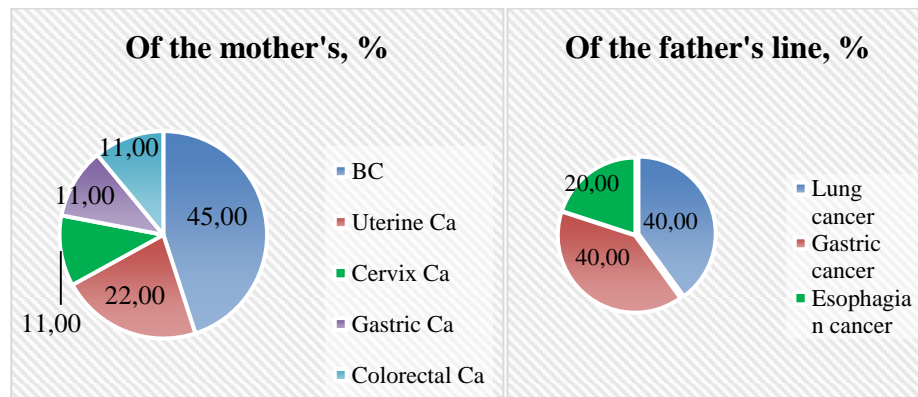
Figure 10. **Hereditary-collateral aspects on the line of mother and father of RMW,%**

The majority of respondents in study 180 (92%) had concomitant diseases, of which 178 (90,8%) RMW had one or more comorbidities. The most common comorbidities were cardiovascular 170 (86,7%) cases, endocrine and metabolic diseases 85 (47,7%), DM 76 (42,6%), obesity 115 (64,6%), gastrointestinal diseases. intestinal 99 (55,6%) cases and osteoarticular 110 (61,7%), gynecological diseases 68 (34,7%) cases, $\chi2 = 0,214$, (p = 0.3127) (figure11).
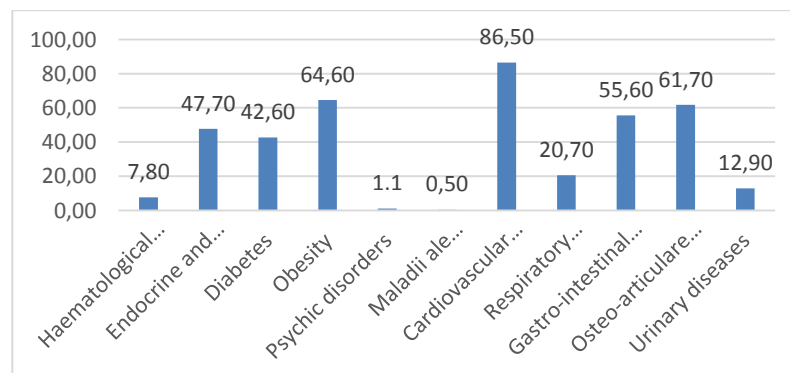
Figure 11. **Characteristic of RMW with BC depending on the presence of concomitant diseases,%**

The least comorbidities were mental and neurological in a total of 3 cases. Other oncological diseases in this group of respondents both from the anamnesis of life and during the study were not present.

3.2. Analysis and comparative evaluation of cases of breast cancer and reproductive health in medical workers during the years 2010-2018

Gynecological diseases were detected in 68 (34,7%), where inflamatory diseases of the uterus and appendages 32 (47,1%), uterine fibroids 13 (19,1%), metrorrhagia 7 (10,2%) predominated, erosions and ovarian cysts up to 3 (5,9%). RMW with BC who suffered 2 and more gynecological diseases made up 52 (26,5%) cases, to a practically equal extent in P and N, $\chi2 = 0,091$, (p = 1,1027) (figure 12).
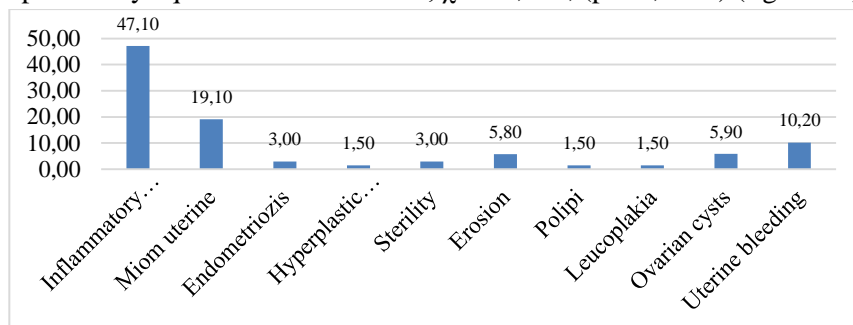
Figure 12. **Gynecological diseases to the RMW with BC,%**

According to the data obtained with early menarche (up to 11 years) it was established in 42 (21,4%) respondents with BC and late menarche (over 15 years) was detected in 22 (11,3%) RMW. Depending on the type of menstruation 95 (48,5%) RMW argued various pathological types of menstruation from which predominated algomenorrhea 32 (33,7%) and hypermenorrhea 30 (31,6%), polymenorrhea 25 (26,3%), opsomenorrhea 8 (8,4%). According to the type of premenstrual syndrome 68 (34,6%) RMW presented under various accusations and cephalic forms 45 (66,1%), $\chi2 = 2,892$, (p = 0,5272), mixed 12 (17,7%), $\chi2 = 0,913$, (p = 0,9671) and less neuropsychic 9 (13,2%), $\chi2 = 0,267$, (p = 0,0182) and edematous 2 (3%), $\chi2 = 0,593$, (p = 0,4247) (Table 1).

Table 1. Clinical forms of PMS to the RMW with BC,%

Clinical form in PMS	Respondents MW with PMS		χ^2, gl=1, p
	c.a.	%	
Cephalic	45	66,1	χ2=2,892, p=0,5272
Edematouse	9	13,2	χ2=0,593, p=0,4247
Neuropsychic	2	3	χ2=0,267, p=0,0182
Mixt	12	17,7	χ2=0,913, p=0,9671

According to the number of pregnancies of RMW with BC, it was found that 2 (1,0%) RMW had no pregnancy, represented only by P. Most respondents had 2 births (52%) to a practically equal extent in P and N. Medical abortions were stipulated at 93 (47,4%) in which 2 abortions predominated - 39 (41,9%). The mean age at first birth for P was 28,52 ± 0,18 years, and in N 22,42 ± 0,27 years (95% CI; 39,45 – 45,61) (figure 13).
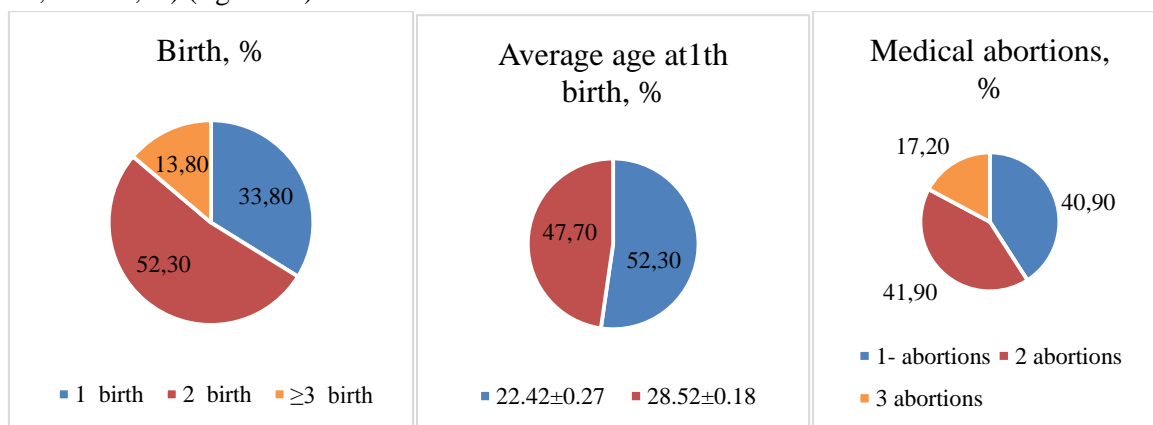
Figure 13. **Distribution of RMW with BC depending on the number of births, average age of first birth and medical abortions,%**

The total number of RMWs that gave birth was 194 (98.9%), of which 21 (10.8%) did not breastfeed at all, and up to 6 months was recorded at 114 (65.8%) RMW more frequently found at MW M, $\chi2 = 1.152$, (p = 0.4128).

The majority of RMW with BC in the study were in the postmenopausal period 137 (69.9%), (p = 1.0371) cases, followed by the premenopausal period 28 (14.3%), (p = 0.3901), menopause 24 (12.3%), (p = 0.1471) cases and the least 7 (3.5%), (p = 0.1109) of the fertile period (table 2). In menopause-induced up to 47 years was found in 5 (20.8%) patients as a result of uterine fibroids complicated by metrorrhagia followed by surgery in the volume of total hysterectomy with appendages.

Table 2. Distribution of MW with BC depending on menopausal status,%

| Menopausal status	Respondents medical workers		χ^2, gl=1,p
	c.a.	%	
Fertile	7	3,5	χ2=0,326, p=0,1109
Premenopausal	28	14,3	χ2=1,375, p=0,3901
Menopausal	24	12,3	χ2=1,104, p=0,1471
Postmenopausal	137	69,9	χ2=8,311, p=1,0371

Evaluation of BC stage *vs* menopausal status we found that most RMW were in stage II of the disease with 103 (52.6%) cases in the postmenopausal period 80 (77.7%) cases and the least in the fertile period 7 (12.5%) cases. With stage I there were 56 (28.6%) RMW, stage III disease 28 (14.2%) and the fewest cases in stage IV 9 (4.6%) cases (Table 3).

Table 3. RMW characteristic with BC depending on stages v / s menopausal status,%

Menopausal status	TNM stage							
	I		II		III		IV	
	c.a.	%	c.a.	%	c.a.	%	c.a.	%
Fertile	7	12,5	0	0	0	0	0	0
Premenopausal	9	16,1	9	8,8	8	28,6	2	22,2
Menopausal	5	8,9	14	13,5	3	10,7	2	22,2
Postmenopausal	35	62,5	80	77,7	17	60,7	5	55,6
χ^2, gl=1, p	χ2=12,131,p=0,004		χ2=14,241,p=0,0002		χ2=10,011,p=0,005		χ2=6,214,p=0,001	

The evaluation of body mass vs. menopausal status at RMW determined that in most cases the pre/ postmenopause and menopause periods were weighted. Therefore, with a body mass of 71-80 kg -92 (47%), (p = 0.0005) cases, which argue an excess body mass, from the postmenopausal period made up 58 (42.3%) RMW and in the period premenopausal - 19 (67.8%) respondents, in the menopausal period 14 (58.3%) cases and 1 case (14.2%) in the fertile period. For body mass of 61-70 kg were recorded a total of 65 (33.2%), (p = 0.0228) RMW, with the predominance of RMW in the postmenopausal period 54 (39.4%) cases, in the premenopausal period 6 (21.4%) cases, in the menopausal period 4 (16.7%) and only one case in the fertile period 14.2% cases. Weights over 80 kg and more were recorded in a total of 9 respondents (4.6%), (p = 0.0002) cases, of which 5 (3.7%) are in the postmenopausal period, 3 (12 , 5%) during menopause and one case (3.6%) during premenopause (Table 4).

Table 4. RMW characteristic with BC depending on body mass v / s menopausal status,%

Body mass (kg)	Fertile		Premenopausal		Menopausal		Postmenopausal		χ^2, gl=1, p
	c.a.	%	c.a	%	c.a.	%	c.a.	%	
≤ 40	0	0	0	0	0	0	0	0	χ2=0, p=1,000
41-50	3	60	23	10.7	0	0	0	0	χ2=1,981, p=0,0475
51-60	1	20	4	14.3	2	8	31	22.5	χ2=1,596, p=0,0271
61-70	1	20	18	64.3	20	80	102	73.9	χ2=3,951, p=0,0228

71-80	0	0	2	7.1	3	12	3	2.2	χ^2=0,127, p=0,0005
>80 kg	0	0	1	3.6	0	0	2	1.4	χ^2=0,104, p=0,0002

The results obtained in the study demonstrated once again that obesity plays a significant role in the development of BC, especially in the premenopausal and postmenopausal period, these results being described in the literature. This ratio decreases with lifestyle changes such as healthy eating, sufficient fluid intake, playing sports.

4. CHARACTERISTICS OF METHODS OF DIAGNOSIS OF BREAST GLAND CANCER IN MEDICAL WORKERS

4.1. Evaluation of methods for diagnosing breast gland cancer in medical workers during the study period (2010-2018)

According to the studies performed regarding the diagnosis of BC in MW, we detected that only 21 (10.7%) of the total respondents in the study participated in breast screening and 171 (87.2%) respondents went for breast control at the onset of breast cancer. Signs or symptoms and only 4 (2.1%) were occasionally detected by other specialists - gynecologists, surgeons, traumatologists. According to the diagnosis interval, the most frequent was 2-4 weeks at 92 (46.9%), and the least cases in> 6 months - 6 (3.2%), (p = 0.0001) . The diagnosis at hospitalization of BC was confirmed in 109 (55.6%) RMW, in 17 (8.7%) RMW -FM localized, with CAP 8 (4.1%) cases and with Suspicion of cancer 62 (31, 6%) cases (figure 14).
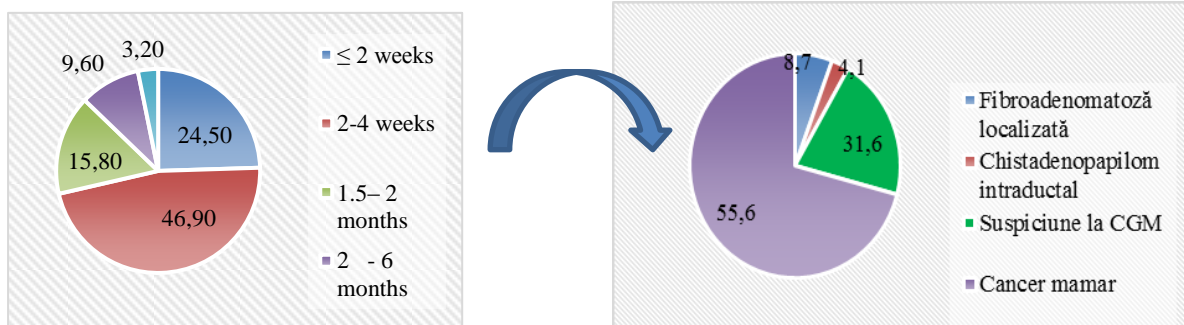
Figure 14. **The interval of establishing the diagnosis of BC and the diagnosis at hospitalization at RMW with BC,%**

The annual medical check-up was not performed by all RMWs and they argued the lack of a mammologist at work, the lack of time for consultation or overwork at work, and others neglected medical check-up and mammology screening. MW with basic didactic activity at the State University of Medicine and Pharmacy "Nicolae Testemitanu" did not have the medical examination performed, nor did they have an annual medical check-up medical card.

According to the study we determined that RBG was the most affected 104 (53.1%), followed by LBG with 81 (41.3%) respondents and bilateral damage made up 11 (5.6%), $\chi 2 = 1.113$, (p = 1411). Mostly the tumor was located in the lateral superior quadrant 117 (59.5%), respectively in the inferior lateral quadrant 30 (15.4%), the central one 24 (12.3%), superior - medial 21 (10.8%) and lower medial 4 (2.0%). In the accessory lobes, the tumor was not detected in any respondent in the study. Calculated value: $\chi 2 = 1.155$, (p = 0.1182) (figure 15).
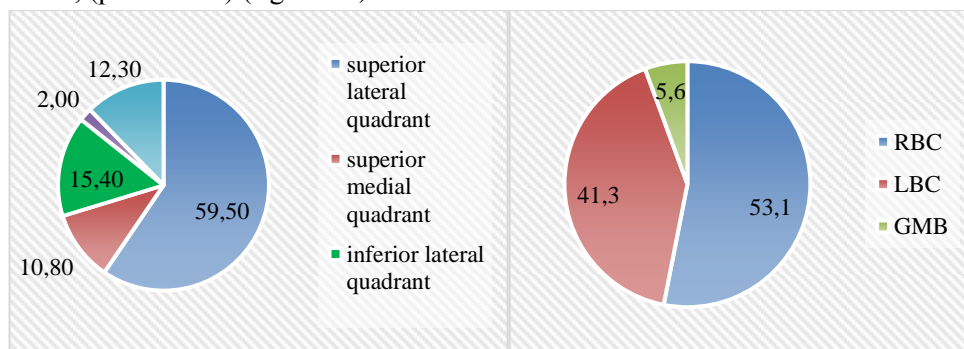
Figure 15. **BC study in MW depending on tumor location and tumor site,%**

The nodular clinical form was the most common of BC 173 (88.2%), Paget's disease 9 (4.6%), and the total diffuse forms accounted for 14 cases (7.2%). Skin signs of mammary gland skin damage were recorded in 13 (6.6%) RMWs with BC- various such as umbilical cord, edema, nipple retraction, discoloration, "orange peel" sign, bloody nipple removal. It is conclusive and significant that in 140 (71.4%) of the respondents medical workers with BC presented axillary lympho-adenopathy, $\chi 2 = 1.091$, (p = 1.0117).

From the laboratory methods partially performed by some respondents, we evaluated the tumor marker CA 153 at only 7 (3.5%) RMW, of which at 5 (71.4%) R was higher than 25 U / ml, and at 2 (28.6%) were appreciated within the norm. Hormone levels of Estrogen, Progesterone and Prolactin, T3, T4, TSH, antiTPO, antiTG were assessed at 8 (4%) RMW, in all cases with indices within the norm. Hormone levels in the blood were chosen by respondents with thyroid gland pathology and respondents who passed gynecological examination.

The ultrasonographic (USG) and mammographic method was performed at 196 (100%) RMW. A special research was the study of the inormativity / non-informativeness of the diagnostic methods performed in BC by RMW with BC. Non-informativeness of USG investigations proved to be 4.5% cases, $\chi 2 = 0.101$, (p = 0.1020), mammography 2%, $\chi 2 = 0.025$, (p = 0.1521), thermography 15%, 1% MRI and CT 2% of cases, $\chi 2 = 0.913$, (p = 0.2001) (Table 5).

Table 5. Methods of examination of the mammary gland at RMW with BC and the degree of informativeness / non-informativeness of the result,%

Metode	Nr.		Informativity		χ^2, gl=1, p
	c.a.	%	Informative	Neinformative	
Ultrasonography	196	100	95,5	4,5	χ^2=13,214, p=0,001
Termography	12	6,1	85	15	χ^2=18,211, p=0,008
mammography	196	100	98	2	χ^2=0, p=1,000
RMN	15	7,6	99	1	χ2=0, p=1,000
TC	8	4	98	2	χ2=0, p=1,000
PET	1	0,5	99	1	χ2=0, p=1,000

The cytological method of confirming BC was performed in 196 (100%) RMW, of which in 33 (16.8%) cases it was uninformative. Tumor trepanobiopsy was performed in 76 (38.7%) RMW and in 87 (44.4%) of RMW, the sectorial resection was performed with urgent histology / after paraffin (figure 16).
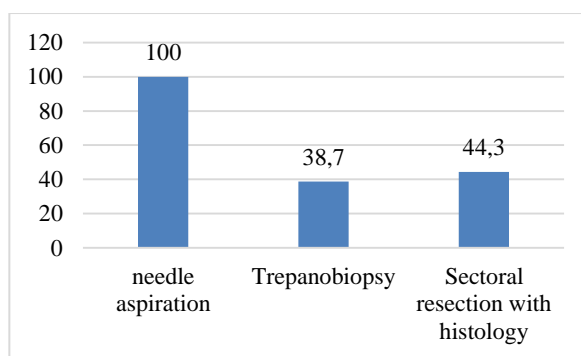
Figure 16. **Methods of confirming BC to MW,%**

The staging of BC at MW showed that in stage I according to the international TNM classification there were 62 (31.6%) cases, in stage II 103 (52.6%) cases, in stage III 22 (11.3%) cases and in stage IV 9 (4.6%) of cases. The evaluated ratio between the stage of the tumor and the years included in the study we realized that they have unstable values of growth and decrease. The in situ carcinoma, respectively stage 0, was not detected in any respondent in the study, which explains the importance of performing annual mammological control and breast screening.

Table 6. **Evaluation of BC in MW according to years and disease stage,%**

Years	st.I TNM		st.II TNM		st.III TNM		st.IV TNM		χ^2, gl=1, p
	c.a	%	c.a	%	c.a	%	c.a	%	
2010	5	8,0	19	18,4	2	9,1	1	11,1	χ^2 =0 p =1,000
2011	7	11,3	14	13,6	1	4,5	2	22,2	χ^2 =0,071 p =0,4109
2012	3	4,9	23	22,4	4	18,2	3	33,3	χ^2 =0,0522 p =0,3101
2013	9	14,5	10	9,7	3	13,6	0	0	χ^2 =0,078 p =0,4931
2014	8	12,9	8	7,8	4	18,2	2	22,2	χ^2 =0,927 p =0,0899
2015	6	9,7	12	11,7	2	9,1	0	0	χ^2 =0,989 p =0,1081
2016	7	11,3	5	4,8	2	9,1	0	0	χ^2 =0 p =1,000
2017	7	11,3	10	9,7	1	4,5	1	11,1	χ^2 =0,061 p =0,0362
2018	10	16,1	2	1,9	3	13,6	0	0	χ^2 =0,0633 p =0,0241
Total	62	31,6	103	52,5	22	11,3	9	4,6	χ^2 =0,0131 p =0,0221

And according to the study year, the most vulnerable proved to be 2012 with 33 (16.8%) registered cases, and due to the stage was stage II 103 (52.6%) cases, χ2 = 0.112, (p = 0, 8727) (Table 6).

4.2 Morphological and immunohistochemical features of mammary gland cancer in medical workers

The most common histological form developed in RMW with BC was invasive ductal carcinoma 111 (56.7%) cases, χ2 = 2,300, (p = 0.4109), of which P 40 (54.8%) cases and 71 (57.8%) N. Lobular carcinoma was identified in 26 (13.3%) RMW, χ2 = 0.102, (p = 0.3109), of which P 9 (12.3%) and in N 17 (13.8%) cases. The medullary form was established in 6 (3.1%) RMW, χ2 = 0.071, (p = 0.1043) cases, of which P 3 (4.1%) and 3 (2.4%) N. Papillary carcinoma increased by 15 (7.6%) cases, of which P 10 (13.7%) and 5 (5.4%) N. The mucin type was recorded at 18 (9.1%), χ2 = 0.832, (p = 0.3818) of which 4 (5.5%) at P and 10 (8.1%) at N. The tubular shape had a frequency of 11 (5.6%), χ2 = 0.401, (p = 0.1010) cases, of which at P 7 (9.6%) RMW and 4 (3.2%) cases . Paget's disease of the breast made up a total of 9 (4.6%), χ2 = 0.552, (p = 0.1041), of which 3 (4.1%) in P and N 6 (4.9%), (Table 7).

Table 7. **RMW characteristic with BC depending on histological form,%**

Forma histologică	P n=73		N n=123		χ^2, gl=1, p
	c.a.	%	c.a.	%	
Lobular	9	12,3	7	13,8	χ^2 =0,102, p =0,3109
Medular	3	4,1	3	2,4	χ^2 =0,071, p =0,1043
Ductal	40	54,8	71	57,8	χ^2 =2,300, p =0,4109
Papilar	10	13,7	5	5,4	χ^2 =0,421, p =0,1018
Mucinous	4	5,5	10	8,1	χ^2 =0,832, p =0,3818
Tubular	7	9,6	4	3,2	χ^2 =0,401, p =0,1010
Paget Ca	3	4,1	6	4,9	χ^2 =0,552, p =0,1041

According to the types of tumor growth, the solid form was determined at 123 (62.8%) RMW, of which in P 48 (65.8%) cases and 75 (61.0%) in N. Squamous growth was identified in 53 (27.1%) RMW, of which P 17 (23.3%) and 36 (29.3%) N (figure 17).
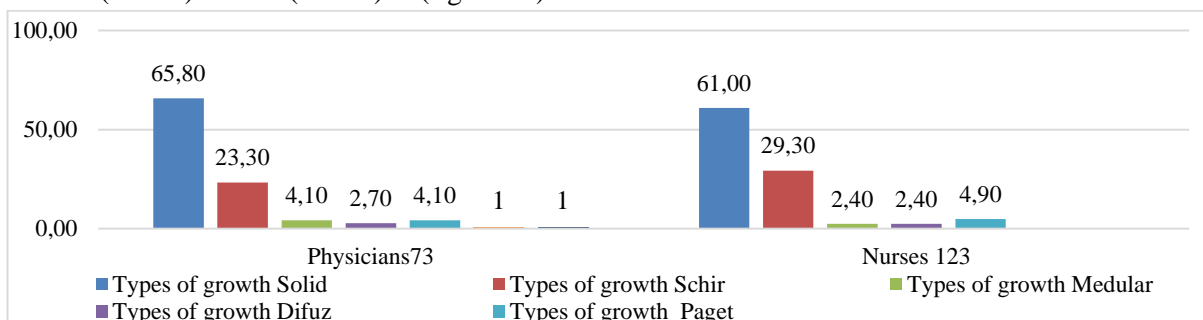

Figure 17. **RMW characteristic with BC depending on the form of tumor growth,%**

The form of spinal cord growth was found in 6 (3.0%) RMW, of which 3 (4.1%) cases and 3 (2.4%) N were recorded in P. The diffuse form of cancer had a higher frequency of 5 (2.5%) cases, of which 2 (2.7%) described in P and 3 (2.4%) in N. The Paget type had an index of 9 (4.6%) cases, of which in P it was detected in 3 (4.1%) cases and 6 (4.9%) in N, the average value: $\chi 2 = 1{,}072$, (p = 0.1077).

Examination of hormone receptor status and Her2 / neu expression was identified only at 98 (50%) MWR performed in the Morphological Laboratory within IMSPIO as well as in other private laboratories, including abroad. Thus, out of the total number of MWR with immunohistochemical results, 53 (54.1%) cases were recorded in P and 45 (45.9%) were determined in N, $\chi 2 = 1.124$, (p = 1.0127) (figure 18).
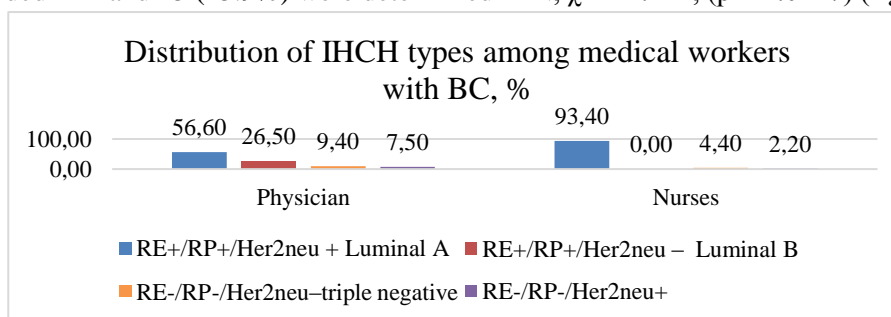
Figure 18. **Distribution of IHCH types among medical workers with BC,%**

When studying hormone receptors, the most common immunocystochemical type recorded was Luminal A type attested at 72 (73.5%) of which 30 (56.6%) at P and 42 (93.4%) N. Luminal type B was found in 14 (14.2%) RMW, of which 14 (26.5%) in M and no case in MS. Triple negative carcinoma was identified in 7 (7.1%) RMW, of which 5 (9.4%) in P and 2 (4.4%) in N. Her2neu-positive immunohistochemical type was determined at 5 (5.2%) RMW, of which 4 (7.5%) at P and 1 (2.2%) at N.

The degree of tumor differentiation (G) was identified only in 114 (58.2%) RMW, of which in P 66 (90.4%), $\chi 2 = 0.012$, (p = 0.0813) cases and 48 (39 %), $\chi 2 = 0.061$, (p = 0.1025) at N (Table 8).

Table 8. **RMW ratio with BC depending on the degree of differentiation,%**

Differentiation of degree	Physician n=73		Nurses n=123		χ^2, gl=1, p
	c.a.	%	c.a.	%	
G_1	50	75,8	12	25	$\chi^2 =0{,}870, p =0{,}1041$
G_2	7	10,6	8	16,7	$\chi^2 =0{,}319, p =0{,}1121$
G_3	0	0	4	8,3	$\chi^2 =0{,}116, p =0{,}1004$
G4	9	13,6	24	50	$\chi^2 =0{,}538, p =0{,}1352$

The high degree of G1 cell differentiation was at 62 (54.4%), $\chi 2 = 0.870$, (p = 0.1041) RMW, of which M 50 (75.8%) cases and MS 12 (25%) cases. The average degree of differentiation G2 was 15

(13.2%), χ2 = 0.319, (p = 0.1121) cases, of which in P 7 (10.6%) cases and N 8 (16.7%) cases . The low degree of differentiation of G3 tumor was determined only at MS 4 (3.5%), χ2 = 0.116, (p = 0.1004) RMW. G4 undifferentiated tumor was identified in 33 (28.9%), χ2 = 0.538, (p = 0.1352) RMW of which in M 9 (13.6%) cases and 24 (50%) in MS.

Of the total number of RMW with stage IV BC there were 9 (4.6%), χ2 = 1.011, (p = 0.2124) cases, with the spread of the tumor process: in bones 4 (44.4%) cases, in liver and lungs 2 (22.2%) cases and with metastasis in bones and lungs 3 (33.3%) cases (figure 19).

Figure 19. **Spread of tumor stage in stage IVa BC to RMW,%**

The total number of respondents with regional lymph node involvement was 140 (71.4%), χ2 = 1.071, (p = 1.1327) cases, from which the study on the ratio of tumor size vs. lymph node involvement we obtained that at 10 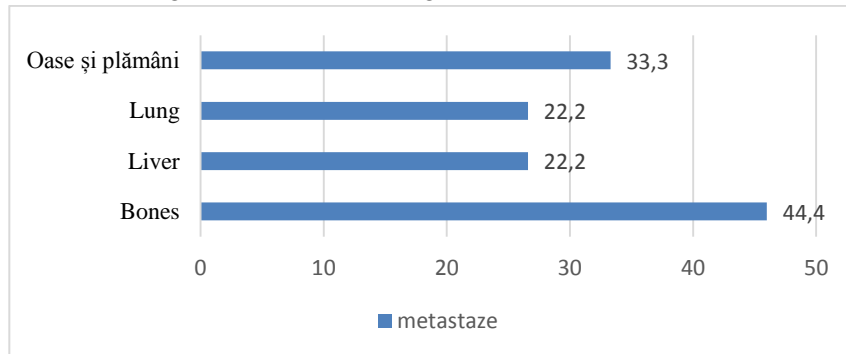(7, 2%) the diameter of the tumor was up to 1 cm, in 12 (8.6%) cases the size of the tumor 1-2 cm, with the size of the tumor from 2-3 cm 44 (31.4%) cases, and with the size over 3 cm 74 (52.9%) cases (figure 19).

4.3. Algorithm for diagnosing breast cancer in nursing workers and creating risk groups for responding nursing workers with breast cancer

The multitude of risk factors that affect the health of medical workers, including mental, stressful, chemical, physical factors, etc., and the need to develop groups at risk of developing BC in MW and modify the algorithm for diagnosis and monitoring of MW according to these groups. now it is missing, we initiated the argumentation of the study and its elaboration. In order to determine the risk groups of medical workers for BG diseases, it is necessary to determine by Order, the head of the Medical and District Institutions. We determined a classification of medical workers depending on concomitant diseases, aggravated anamnesis and increased risk of developing BC:

I. Medical workers - women - low risk - represented by healthy MW who do not have both gynecological and BG pathology, but with an aggravated hereditary-collateral anamnesis, use of long-term oral contraceptives, active smokers.

II. Medical workers - women at medium risk - did not have pregnancies, did not breastfeed, with traumas of the mammary gland, with pathologies of the genitals, thyroid gland, liver, mMSmary gland, with dystrophic lesions of the mammary gland - fibrocystic mastopathy, solitary cyst, obesity, D, pituitary / hypothaMWSic tumors, respondents with an internship over 20 years.

III. Medical workers - women at high risk with proliferative lesions such as epithelial hyperplasia, radial scarring, sclerosing adenosis, ductal ectasia, fatty necrosis or lipogranuloma and precancerous conditions - intracanalicular papilloma, nipple adenoma, mastitis, adenoma benign effects of GM, over 30 years of work experience(figure 20).

Modification of the Algorithm for diagnosis and monitoring of medical workers

Patient Physician/nurses		Monthly self-monitoring

```
┌─────────────────────┐                              ┌──────────────┐
│   Family doctor     │              ←               →│              │
└─────────────────────┘                              └──────────────┘
┌─────────────────────┐  ╭──────────╮ ╭──────────╮ ╭──────────╮  ┌─────────────────┐
│  Prophylactic       │  │ I-th     │ │ 2-nd     │ │ 3rd      │  │ Another medical │
│  control            │← │ clinical │ │ clinical │ │ clinical │  │ institution     │
│ (population         │  │ group    │ │ group    │ │ group    │  │ that has a      │
│  screening)         │  ╰──────────╯ ╰──────────╯ ╰──────────╯  │ oncologist-     │
└─────────────────────┘                                          │ mamologist or   │
                                                                 │ oncogynecologist│
                        ┌──────────────────────────────────────┐ └─────────────────┘
                        │ Medical annual mammological and       │
                        │ gynecological examination at work     │←→
                        └──────────────────────────────────────┘
```

Family doctor

Prophylactic control (population screening)

I-th clinical group

2-nd clinical group

3rd clinical group

Another medical institution that has a oncologist-mamologist or oncogynecologist

Medical annual mammological and gynecological examination at work

Specialized oncology care

Oncological Polyclinic Oncologist - mammologist

Physical examination, if necessary USG and mammography. Consultation of the gynecologist. Mandatory annual monitoring

Physical examination, mandatory documented by USG and mammography, gynecological examination

Cytological examination

Biopsy Morphological examination.

CT, MRI, PET free

Case diagnosed

Council 3 specialists

Specialized treatment

Surgical treatment

Combine treatment

PCHT, hormonal treatment

Complex treatment
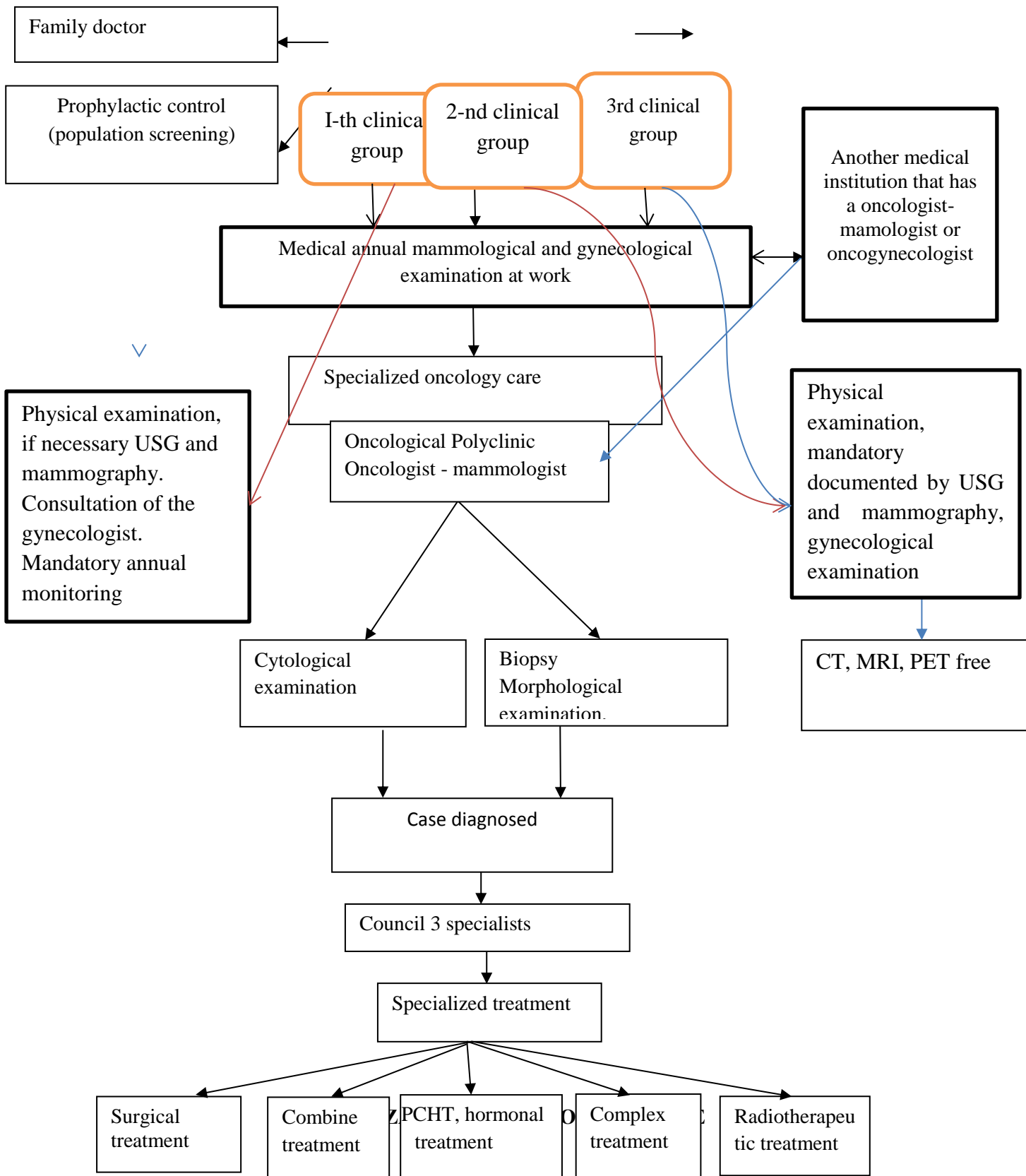
Radiotherapeutic treatment

Fugure 20. **Modification of the Algorithm for diagnosis and monitoring of medical workers**

SYNTHESIS OF THE RESULTS OBTAINED

      A fairly current and important issue for public health is the early diagnosis of BC, especially MSong MW, which according to multiple epidemiological, clinical, diagnostic, treatment and

rehabilitation studies is constantly increasing in terms of incidence, mortality and and disability worldwide. The socio-economic changes that took place in the country at the beginning of the XX and XXI centuries, as well as the high stress had a decisive influence on the health indicators of MW in extremely unfavorable conditions for existence [179,183].

BC is a common global health problem due to the complexity and constellation of various risk factors of various origins, which promotes the development of BC in women and is the leading cause of cancer-related death. Every year 220 thousand MW temporarily lose their work capacity, 76% of them have chronic diseases and only 40% are registered at the dispensary. Over 10% of all diagnosed diseases are present in MW women [209].

In this paper we proposed a complex research of studying the diagnosis of BC in MW from an epidemiological, clinical-paraclinical point of view and of some medico-social aspects in order to diagnose BC early and develop prevention and control measures for this specific group of respondent.

The study was conducted based on the proposed objectives: analysis of cases of breast cancer in medical workers in the Republic of Moldova during the years 2010-2018; comparative evaluation of BC in MW according to the medico-social and specialized characteristics; studying comorbidities in RMW with BC; highlighting the diagnostic methods and results at MW with BC with the elaboration of prevention and control measures; modification of the Diagnostic and Monitoring (Control) Algorithm for MW with risk of developing BC.

The results obtained in the study emphasize the important role in studying the particularities of risk factors at work, the specificity of medical activity, the increased number of cases of BC in MW, late addressability and high disability, significant and early job loss for both the medical system as well as for the country's economy [178].

According to the studies of the scientist Vasyukova G. et al. the incidence of occupational diseases at MW in 2004 in the SMSara region exceeded similar indicators of workers in the petrochemical industry 5 times, in the electricity industry - 13.2 times, in chemical production 2 times, in the production and distribution of electricity, gas and water 1.7 times [180]. A scientific cohort study conducted in Taiwan (2013), on a group of 14,889 physicians, studied the incidence of cancer of health care workers (women and men) vs. the general population, showing that the incidence rate of cancer in M is much larger than in the comparison group. Thus, of all the types of cancer analyzed, the share by BC was 5.8% in female doctors vs. 2.6% in the comparative group of the general population [170,177]. In our research, this figure accounted for 196 (17.9%) of the total number of oncological diseases in women through various locations for the period 2010-2018, of which 73 (37%) P and 123 (63%) N.

Due to the specificity of the work activity, the medical staff is frequently exposed to unfavorable working conditions, especially being determined in the state institutions [181]. These studies also correspond to the results of our research, which showed that in 100% of cases good working conditions were assessed only in private medical institutions 13 (6.7%) and unsatisfactory working conditions assessed only MW in state medical institutions -133 (67.8%) especially from District Hospitals 44 (33.1%) respondents, Republican Hospital 26 (19.5%) cases, Municipal Hospital 28 (21.1%) cases, State Cabinets 35 (26 , 3%) cases, (p = 0.0001).

According to studies by SchernhMSmer E. et.al. conducted on a batch of 116,671 medical workers from 1989-1999, Women's Hospital and Harvard Medical School, Institute for Applied Cancer Research and KFJ-Hospital (Boston), studied the relationship between medical activity in night shifts and 24 hours and BC in MW M and MS, and determined the following results that melatonin has potential oncostatic activity and is acutely suppressed by light exposure. This study shows the association between night work and the risk of BC, possibly through melatonin. Thus, it was determined that MW P and N who reported more than 20 years of night guards have a 3.2 higher risk compared to MW women who did not report any guard (RR multivariate 1.79; IC 95% 1.06 –3.01) [170.177].

Another important retrospective study conducted in Thailand (1995-2008), on a batch of 2,331 MW from the National Cancer Institute and 7 other regional cancer centers in the given country, showed

that the incidence of BC in MW MS was evident. compared to the general population, explaining this phenomenon by the action of specific work environment factors, especially those in hospitals, as well as the variety of activities and work complexity of a doctor and nurse, exposure to physical, chemical and biological factors , including shift work, continuous stress, etc. The study specified that most MWs were exposed to a variety of specific carcinogens during their daily activity, including radiation from diagnostic and therapeutic clinics [130], ethylene oxide [148], and exposure to antineoplastic drugs. during their preparation and administration, working with formaldehyde or other carcinogenic chemicals for laboratory work, etc. [164]. All these dangerous substances, specifically hospital, are classified by the IARC as carcinogenic to humans (class I) [24, 152, 157,164]. Comparatively, in our study RMW marked the contact with chemicals (antibiotics, narcotics, cytostatics, disinfectants, etc.), and an unbalanced diet (fast food, buns, breadcrumbs, saMWSi, low fluid and fruit) in 80-90% of RMW. Our studies on the period of the menstrual cycle, the character of the menstrual cycle we obtained that with early menarche up to 11 years was established in 42 (21.4%) respondents MW, late menarche over 15 years was detected in 22 (11.3 %) respondents, which correspond to the results of the research of other scientists.

Of particular importance were the scientific studies that studied the number of births vs. the age of MW, which differ greatly from the general population, respectively MW women who gave birth to their first child after 30 years were 2-5 times higher risk of BC compared to RMW <25 years of age [181,185]. In our studies, the sMSe phenomenon was determined that at the age of over 30 years from the first birth made up a total of 19 (9.8%) RMW, of which 18 (25.3%) M and 1 case (0.8%) MS, (p = 0.0001). The average age at first birth for M was 28.52 ± 0.18 years, and in MS 22.42 ± 0.27 years (95% CI; 39.45 - 45 , 61). According to our studies, we determined that 2 (1.0%) of RMWs did not have a pregnancy, being represented only by doctors, and most RMWs had 2 births 100 (52%) to a practically equal extent in both doctors and nurses. Out of the total number of respondents who gave birth 194 (98.9%) did not breastfeed 21 (10.8%), for various reasons. Breastfeeding up to 6 months was recorded at 114 (65.8%).

According to data from studies conducted by Krechkovsky E. et al. (1984) established that MSong the physical factors in medical activity an important place is presented by ionizing and non-ionizing radiation, ultrasound generated by diagnostic and surgical equipment. The obvious risk of developing malignant neoplasms of the breast, uterus, ovaries, lungs and brain is associated with exposure of medical personnel to ionizing radiation [183]. From some data of the literature we detected that the specialties with high risk of developing neoplasms are surgeons, obstetricians-gynecologists, midwives, nurses with activity in the surgical profile and less in the therapeutic one. The highest number of incapacity for work was characteristic of MW in the therapeutic, radiological, physiotherapy, surgical, functional diagnostic departments. Doctors get sick more often and for a longer period of time than nurses [185]. In comparison, in our studies we determined an increased rate of MW M with BC with higher activity in the therapeutic profile 102 (52.1%) RMW, of which M 52 (71.3%) and MS 50 (47.9%) RMW, and in the surgical profile activated 90 (45.9%) RMW where MS predominated with 71 (78.8%) and M 19 (21.2%) cases. The least MW with BC were MSong managers 4 (2%), respectively M 2 (2.7%) and N 2 (2.62%) cases, $\chi2 = 1,041$, p = 0.1121.

A major US study conducted within the Nurses Health Study: NHS and NHS II project on 12,701 MS on the influence of known carcinogenic risk factors and the development of BC found that 8,562 highlighted contact with risk factors, which was confirmed. subsequently to 2,441 cases of BC. A special role in the development of BC was age in correlation with the work experience over 30 years and more of MS [168, 177]. Our studies determined that most RMWs with BC 39 (19.9%) were presented at the age of 65-69 years, of which M made up 14 (19.2%) and MS 25 (20.3%).).

According to the research of the scientist Bektasova M. et al. who studied MW morbidity in the Primorsk region, found that the incidence of cardiovascular disease MSong MW was low (55 per 100 workers), while the number of disability days was increased by 1118 per 100 employees. . From diseases of the musculoskeletal system (31.6 ± 1.15) and the nervous system (14.7 ± 0.8) were significantly more

common and diseases of allergic and infectious etiology (53.0% and 37.4 %) [179,185]. In our studies we determined that 178 (90.8%) RMW had one or more comorbidities, the most common being cardiovascular 154 (86.5%), endocrine and metabolic diseases 85 (47.7%), D 76 (42.6%), Obesity 115 (64.6%), gastrointestinal diseases 99 (55.6%), osteoarticular 110 (61.7%), gynecological diseases 68 (34.7%) cases, $\chi 2 = 0.214$, p = 0.3127.

According to studies conducted by Professor Izmerova N. and Sivociavolaia O. on gynecological diseases in MW estimated a very high risk of their development compared to the general population, including menstrual and menstrual disorders 22.7 ± 1.9 , prolapse and prolapse of female genitals 13.8 ± 0.7. In particular, these disorders were determined in MW women surgeons, obstetricians-gynecologists, midwives and nurses with a surgical profile, especially with the work experience of 10-14 years, which expressively increases the risk of developing gynecological diseases including cancer of the reproductive organs [188,192]. The results of our research showed that 18 (9.1%) MW had a disordered menstrual cycle, of which with accusations at menstruation were 95 (48.5%) MW with the predominance of algomenorrhea 32 (33.7%) and hypermenorrhea 30 (31.6%), followed by polymenorrhea 25 (26.3%). Premenstrual syndrome was present in 68 (34.6%) RMW with forms - cephalic 45 (66.1%), mixed 12 (17.7%) and less neuropsychic 9 (13.2%) and edematous 2 (3 %), $\chi 2 = 0.109$, p = 0.8211. Of the gynecological comorbidities in RMW were recorded in 68 (34.7%) RMW, where infMWSmatory diseases of the uterus and appendages 32 (47.1%), uterine myoma 13 (19.1%), metrorrhagia 7 (10, 2%), erosions and ovarian cysts up to 3 (5.9%). RMW with BC who suffered 2 and more gynecological diseases made up 52 (26.5%) cases, in practically equal measures in P and N, $\chi 2 = 0.091$, p = 1.1027.

Important studies were conducted in Nurses Health Study II 1989-1999 which detected that premenopausal MA who reported ≥20 years of work in night shifts showed a significant increase in the risk of BC (relative risk = 1.22) compared who never worked night shifts [150, 151]. In our studies we established that the majority of RMW with BC included in the research were in the postmenopausal period 137 (69.9%) cases, followed by the premenopausal period 28 (14.3%), menopause 24 (12.3%) and the less 7 (3.5%) in the fertile period.

In the literature data we did not find studies related to the diagnostic methods used, methods of confirmation and their informativeness, histological type, forms of BC growth in MW. However, according to studies conducted in various countries that have studied the oncological morbidity of MW, they found that having knowledge in the field, he goes to the specialist or colleague later after a medical check-up, neglects the annual medical check-up and uses self-treatment more frequently than other groups. [168,184].

In the future, it is necessary to create a unified database of information or register, which will include all the information on MW comorbidities in the Republic of Moldova and the creation of a program for the prevention of major occupational diseases in MW. When preparing and conducting regular medical examinations, special attention should be paid to the risk groups of women with reproductive organ pathology and for the formation of risk groups, "Methodological recommendations for occupational risk assessment based on data from periodic medical examinations" should be applied.

GENERAL CONCLUSIONS

1. The share of malignant tumors by various locations in female MW for the study period was 1090 cases with a predominance of BC- 196 (17.9%) cases being composed of 73 (37%) P and 123 (63%) N.

2. According to the medical-social and specialized characteristics, we determined that the northern area was the most affected - 61 (31.1%) and the majority being from rural areas 109 (55.6%). The most vulnerable age was 65-69 years, making up 39 (19.9%) cases, being closely correlated with the age of the work period with a maximum peak of 35 years.

3. According to the activity profile MW P were the majority of the therapeutic profile made up of 52 (71.3%) which included specialties: therapists 18 (24.7%), surgeons 13 (17.9%), radiologists 9 (12 , 3%), oncologists 7 (9.6%), family doctors 8 (10.9%), and in N predominated the surgical profile 71 (57.8%) cases.

4. The most common risk factors were stress and physical intensity 100%, improper nutrition and the action of chemicals 80-90%, hereditary-collateral history was aggravated at 9, menstrual disorders showed 18 (9.1%) MW, with early menarche up to 11 years 42 (21.4%) cases and late menarche 22 (11.3%) cases, with premenstrual syndrome were 68 (34.6%) RMW, with predominance of the cephalic form 45 (66.1%) cases, menstruation with algomenorrhea accounted for 32 (33.7%) cases. The mean age at first birth in P was 28.52 ± 18 years and in N 22.42 ± 0.27 years.

5. According to menopausal status 137 (69.9%) RMW were in the postmenopausal period, and the least in the fertile period 7 (3.5%). From the concomitant diseases predominated CV 154 (86.5%), obesity 115 (64.6%), pathologies of Bone 110 (61.7%), GI tract 99 (55.6%), D 76 (42, 6%), and from the gynecological organs 68 (34.7%) cases, the most common: inflammatory diseases of the uterus and appendages 32 (47.1%), uterine fibroids 13 (19.1%) and metrorrhagia 7 (10, 2%) cases.

6. The late diagnosis was due to the delayed addressability of the mammologist and the practice of self-treatment. 21 (17.1%) LMs participated in breast screening, all of which were represented by N. The diagnosis of BC was established in 109 (55.6%) cases most frequently performed at the interval up to 4 weeks 92 (46.9%). The majority of respondents were diagnosed in stage II - 103 (56.6%) with RBC involvement with 104 (53.1%) cases located in the upper lateral quadrant 117 (59.5%) cases.

7. The diagnostic methods were the basic ones of the physical examination, USG, mammography and cytological confirmation method in 100% of cases, also all RMW opted for histological confirmation methods by trepanobiopsy 76 (38.7%) and at 87 (44.3%) by sectorial resections of the mammary gland with urgent histology / after paraffin.

8. Creation of an automated MW testing system for the formation of high risk groups of BC, with the assessment of risk factors specific to the profile and specialty of work and completion of the Monitoring and Control Algorithm that will optimize MW monitoring, early diagnosis of BC and comorbidities , both nurses and doctors.

PRACTICAL RECOMMENDATIONS

1. For the purpose of early detection of BC in health care workers, the importance of breast gland self-monitoring in health care workers, especially MW patients at high risk of BC (aggravated hereditary history, cancer history, breast glands trauma, endocrine diseases, mammary gland pathologies, etc.) with a consultation with a specialist oncologist - mammologist in public and private medical institutions.

2. To organize breast screening for medical workers at work or other institutions made by contract.

3. To be appointed responsible, for the monitoring and control of patients with BC-medical workers, an oncologist-mammologist within the CCD of Oncological Institute.

4. For the early diagnosis to be implemented the diagnostic Algorithm of BC in medical workers.

5. Elaboration of the annual medical control sheet of the doctors from the State University of Medicine and Pharmacy "Nicolae Testemitanu".

Research directions for the future:

1. Research in the field of molecular - genetic aspects of BC in medical workers.

2. Research of occupational risk factors selective for each profile and medical specialty.

3. Assessment of risk factors for reproductive health, especially during pregnancy, toxic substances, biological and chemical agents in MW activity.

4. Elaboration of "Methodological recommendations for occupational risk assessment based on the data of periodic medical examinations".

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