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LUMINAL B IS THE MOST COMMON BREAST CANCER SUBTYPE IN PATIENTS OF ALMATY ONCOLOGY CENTER

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Abstract

Introduction: Breast cancer is a heterogenous group of disease that is most prevalent malignant disease of female population of Kazakhstan.

Aim of study: to find most common pathologic type and molecular subtype of breast cancer cases in the Almaty oncology center and evaluate association among molecular subtype with different pathological type, tumor characteristics and Participant's criteria

Materials and methods: A cross sectional–study was conducted at Almaty oncology center, Kazakhstan between January and December 2020. We studied medical records of 818 breast cancer cases and included data of 622 cases in this study. Data about pathologic type, grade, stage, estrogen (ER), progesterone (PR) HER2 overexpression and ki67 were analyzed. Molecular subtype determination in this center was done by using immunohistochemistry and this Criteria ('Luminal A-like' ER/PR +, HER2-, Ki67 low) ('Luminal B-like' ER/PR +, HER2 ± and Ki67 high) ('HER2-positive' HER2+ ER and PR -) (Triple-negative ER and PR absent HER2-). The association were evaluated among molecular subtype with different pathological type, tumor characteristics and Participant's criteria using Chi square test

Results: Most common pathologic type of tumor in this study was NST (85.3%), ILC (3.8%) and DCIS (2.1%) respectively. Most prevalent molecular subtype of tumors: Luminal B (57.6%), luminal A (22.2%), triple negative (12%) and HER/2 enriched (8.3%). There was statistically significant association (p-value <0.05) between Molecular subtype and pathologic type of tumor, grade, stage, size, hormone receptors, HER/2 over expression and mitotic rate.

Conclusion: luminal B was the most prevalent subtype and HER2 positive was the least prevalent and it is better to work more for finding better treatment for luminal B. A significant association among molecular subtype of tumor and pathologic subtype, grade, stage, size, hormone receptors, HER/2 over expression and mitotic rate were found.

Key words: *breast cancer, molecular subtype, immunohistochemistry, Almaty.*

Резюме

LUMINAL B - САМЫЙ РАСПРОСТРАНЕННЫЙ ПОДТИП РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ У ПАЦИЕНТОВ АЛМАТИНСКОГО ОНКОЛОГИЧЕСКОГО ЦЕНТРА

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Введение: Рак груди - разнородная группа заболеваний, которая является наиболее распространенным злокачественным заболеванием женского населения Казахстана.

Цель исследования: найти наиболее распространенный патологический тип и молекулярный подтип случаев рака груди в онкологическом центре Алматы в течение 2020 года и оценить связь между молекулярным подтипом с различным патологическим типом, характеристиками опухоли и критериями участника.

Материалы и методы: это поперечное аналитическое и описательное исследование с января 2020 года по декабрь 2020 года было проведено в онкологическом центре Алматы, Казахстан. Мы изучили медицинские записи о 818 случаях рака груди и включили в это исследование данные о 622 случаях. Были проанализированы данные о патологическом типе, степени, стадии, гиперэкспрессии HER2 эстрогена (ER), прогестерона (PR) и ki67. Определение молекулярного подтипа в этом центре проводилось с использованием иммуногистохимии и следующих критериев («Luminal A-like» ER / PR +, HER2-, Ki67 low) («Luminal B-like» ER / PR +, HER2 ± и Ki67 high) («HER2-

положительный» HER2 + ER и PR -) (тройной отрицательный ER и PR без HER2-). Связь оценивалась среди молекулярных подтипов с различным патологическим типом, характеристиками опухоли и критериями участника с использованием критерия хи-квадрат.

Результаты. Наиболее частым патологическим типом опухоли в этом исследовании был NST (85,3%), ILC (3,8%) и DCIS (2,1%) соответственно. Наиболее распространенный молекулярный подтип опухолей: просвет B (57,6%), просвет A (22,2%), тройной отрицательный (12%) и обогащенный HER / 2 (8,3%). Обнаружена статистически значимая связь (значение p <0,05) между молекулярным подтипом и патологическим типом опухоли, степенью, стадией, размером, рецепторами гормонов, сверхэкспрессией HER / 2 и скоростью митоза.

Заключение: просвет B был наиболее распространенным подтипом, а HER2-положительный - наименее распространенным. Была обнаружена значимая связь между молекулярным подтипом опухоли и патологическим подтипом, степенью, стадией, размером, рецепторами гормонов, сверхэкспрессией HER 2 и скоростью митоза.

Ключевые слова: *рак груди, молекулярный подтип, иммуногистохимия, Алматы.*

Түйіндеме

LUMINAL B - АЛМАТЫ ОНКОЛОГИЯЛЫҚ ОРТАЛЫҒЫНЫҢ ПАЦИЕНТТЕРІНДЕ СҮТ БЕЗІ ОБЫРЫНЫҢ ЕҢ КӨП ТАРАЛҒАН КІШІ ТҮРІ

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Кіріспе: Сүт безінің қатерлі ісігі-бұл Қазақстан әйелдерінің ең көп таралған қатерлі ауруы болып табылатын аурулардың түрлі тобы.

Зерттеу мақсаты: 2020 жылы Алматы қаласының Онкологиялық орталығында сүт безі обырының ең көп таралған патологиялық түрін және молекулярлық кіші түрін табу және молекулярлық кіші түрі мен түрлі патологиялық типтің, ісік сипаттамаларының және қатысушы өлшемдерінің арасындағы байланысты бағалау.

Материалдар мен әдістер: бұл көлденең аналитикалық және сипаттамалық зерттеу 2020 жылдың қаңтарынан 2020 жылдың желтоқсанына дейін Қазақстан, Алматы онкологиялық орталығында жүргізілді. Біз сүт безі қатерлі ісігінің 818 жағдайы туралы медициналық жазбаларды зерттедік және осы зерттеуге 622 жағдай туралы мәліметтерді енгіздік. HER2 эстрогеннің (ER), прогестеронның (PR) және ki67 патологиялық түрі, дәрежесі, сатысы, гиперэкспрессиясы туралы деректер талданды. Бұл орталықтағы молекулалық кіші түрді анықтау иммуногистохимия және келесі критерийлер бойынша жүргізілді («Luminal A-like» ER / PR +, HER2-, Ki67 low) («Luminal B-like» ER / PR +, HER2 ± и Ki67 high) ("HER 2-оң" HER2 + ER және PR -) (HER2-жоқ үштік теріс ER және PR). Байланыс молекулалық кіші түрлер арасында әр түрлі патологиялық типтермен, ісік сипаттамасымен және қатысушы критерийлерімен хи-квадрат критерийін қолдана отырып бағаланды.

Нәтижелері. Бұл зерттеуде ісіктің жиі кездесетін патологиялық түрі сәйкесінше NST (85,3%), ILC (3,8%) және DCIS (2,1%) болды. Ісіктердің ең көп таралған молекулалық кіші түрі: в люмені (57,6%), а люмені (22,2%), үштік теріс (12%) және HER / 2 (8,3%) байытылған. Молекулалық кіші тип пен ісіктің патологиялық түрі, дәрежесі, сатысы, мөлшері, гормон рецепторлары, HER / 2 шамадан тыс экспрессиясы және митоз жылдамдығы арасындағы статистикалық маңызды байланыс (p <0,05 мәні) табылды.

Қорытынды: в люмені ең көп таралған кіші тип болды, ал HER2 оң - ең аз таралған. Ісіктің молекулалық кіші түрі мен патологиялық кіші түрі, дәрежесі, сатысы, мөлшері, гормон рецепторлары, HER / 2 суперэкспрессиясы және митоз жылдамдығы арасында маңызды байланыс табылды.

Түйінді сөздер: *сүт безінің қатерлі ісігі, молекулалық кіші түрі, иммуногистохимия, Алматы.*

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Introduction

Breast cancer is the most prevalent cause of cancer death in women [1] and the second cause of cancer death in both sexes after Lung cancer in Asia [2] For several years, cancer has been the third cause of death in Kazakhstan [3, 4] BC is the most common malignant disease among the female population of this country [4]. It has had highest incidence of malignant disease in both sexes since 2004. During last years, breast cancer incidence in Kazakhstan increase, although mortality tended to decrease [5, 6]

Breast cancer is a heterogenous group of disease with different risk factors, natural history and response to treatment. The most common classification for breast cancer are pathologic classification and molecular sub typing based on gene expression pattern. Molecular classification has prognostic value in addition to determining treatment plan. There is a simplified classification for molecular subtyping based on IHC marker according to the 2015 St Gallen Consensus Conference. This classification divides breast carcinoma into luminal A, luminal B, HER2+, and triple-negative sub types based on expression of ER, PgR, HER2, and Ki-67.

Gold standard in breast lesions diagnosis is histologic classification [7] and Most common types of invasive breast cancer is carcinoma of non-specific type (NST) (70% - 75%) and Invasive lobular carcinomas (ILC) (5% - 15%) [8] and other types are less common.

In the present study, we aimed to research on the prevalence of breast cancer subtypes in patients referred to Almaty oncology center and finding association between molecular subtype of BC with different criteria of breast cancer, and characteristics of patients in Almaty city.

Material and methods

Type of study and Participants: A cross sectional study was done on breast cancer cases of female that referred to Almaty oncology center during the year 2020 (from first of January to end of December 2020).

Inclusion criteria: female with breast cancer referred to Almaty oncology center during the year 2020 with recorded results of pathologic and immunohistochemical test in Almaty oncology center.

Exclusion criteria: male patients and patients with incomplete recorded results of pathologic and immunohistochemical test in Almaty oncology center and patients referred before or after year 2020

Ethical consideration: This research was conducted with prior approval from Al-Farabi Kazakh national university ethical committee (IRB-286/08.04.2021)

Data source: Information about breast cancer case was requested from department of statistics of Almaty oncology center then Information about histopathologic examination and IHC result were added to previous data from records in IHC laboratory. Cases without pathologic diagnosis and IHC test results were omitted.

Specimen preparation: The specimens of Almaty oncology center, were taken from patients in Almaty oncology center via core needle biopsy or resected tumor via surgery in Pathological Bureau during year 2020 (from first of January to end of December).

Histological preparation of slides was done in Pathological Bureau and immunohistochemical preparation and study was done in IHC laboratory of Almaty oncology center. For identification of tumor type and histologic grade based on WHO classification [9] hematoxylin and eosin stains were used. Immunohistochemical staining was done by VENTANA automatic machine and all regents used in staining are products of this company. Tumors with ≥ 1% positively nuclear-stained cells were considered positive for both ER and PgR expression [10]. Allred scoring system used for evaluation of ER and PR expression. Besides, HER2 positive was scored if the staining occurred for > 10% of tumor cells [11] ki 67 marker was product of VENTANA company and used based on manufacturer instruction. Tumors with ≥ 20% nuclear positivity in staining considered high-rate proliferation and tumors with <20% positivity considered low proliferation rate.

SISH test: The entire procedure was carried out on an automated staining system (VENTANA bench mark ULTRA Staining System) according to the manufacturer's instructions. Positive and negative controls were used for each staining run.

Statistical analysis: Statistical analysis was done by IBM SPSS statistic (version 26). Mean ± standard deviation was used for continuous variables and frequencies & percentages for categorical variables. Pearson chi square test and Fisher exact test were run for evaluating association between different categorical factors. In cases that frequency of each cell in contingency table was less than five in more than 20% of cells, fisher exact test was used instead of Pearson chi square test.

Result

The total number of patients that recourse to Almaty oncology center during the year 2020 was 818, 622 cases with available IHC test results were included in the study. Patients with incomplete tests result or medical records were excluded from this research.

Included women were from 23 different ethnicities with mean age of participants was 57.4± 13.10 range from (24-93). grade II was more common (51.2%) than other grades and 60% were in stage II. 61% of tumors in this study had (2-5 cm) size in greater dimension. 94% of them did not have metastasis. More information about these criteria is presented in table number one. Carcinoma of non-specific type (NST) composed 85.3% of all tumors. More detail about percentage of different type of tumor is presented in figure 1. High percentage of tumors were ER/PgR positive (79.7%) and HER2 negative (79%) with high proliferation rate (75.6%). Details of immunohistochemical test results is presented in table 2. Most common intrinsic subtype of tumor was luminal B. percentage of each molecular subtype is presented in figure 2

Luminal A subtype has smaller size tumors in comparison to triple negative and HER/2 positive tumors

Because of important role of molecular sub types of breast cancer in determining plane of treatment and prognosis of disease, a chi square test was conducted for finding association of molecular subtypes with different clinical and immunohistochemical factors. P-value <0.05 considered significant. Pearson chi square test or fisher exact test was significant for association among molecular sub type of tumor and pathologic type of tumor, grade, stage, size, hormone receptors, HER/2 over expression and mitotic rate. Details are presented in table 3.

Table 1.

Social Characteristics of Patients and criteria of tumors (n= 622)

Characteristics		Count	Percentage
Ages(years)	Mean ± SD	57.4± 13.10	
	Min – Max	24-93	
	<50	195	31.4
	≥50	427	68.6
Ethnicity	Kazakh	269	46.2
	Russian	192	33
	other	121	20.8
Histologic grade	1	49	8.4
	2	298	51.2
	3	235	40.4
Tumor stage	0	17	3
	1	116	20.7
	2	337	60.1
	3	60	10.7
	4	31	5.5
Tumor size	T0	20	3.5
	T1	128	22.6
	T2	345	61
	T3	19	3.4
	T4	54	9.5
Lymph node status	N0	65	10.5
	N1	88	14.1
	N2	25	4.0
	N3	8	1.3
	NX	436	70.1
Metastasis	M0	531	94.0
	M1	34	6.0

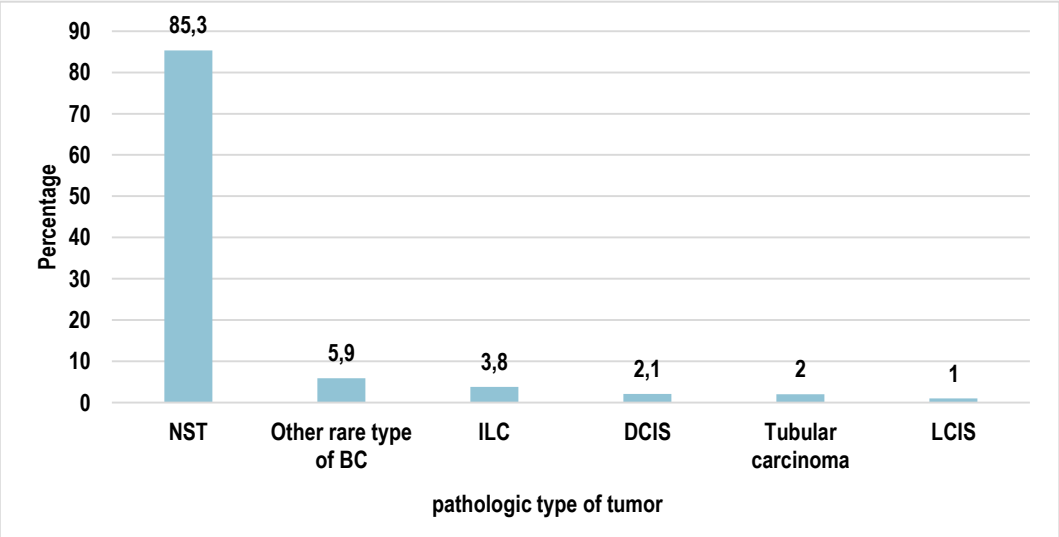

Figure 1 - pathologic types of tumors in 6 groups

Table 2.. **Immunohistochemical test results (n=622).**

Characteristics		Count	Percentage
ER (in Allred scoring system)	Negative (0 and 2)	154	25.1
	Low (3 and 4)	41	31.8
	Intermediate (5 and 6)	27	36.2
	High (7 and 8)	391	63.8
PgR (in Allred scoring system)	Negative (0 and 2)	218	36.3
	Low (3 and 4)	72	12
	Intermediate (5 and 6)	92	15.3
	High (7 and 8)	218	36.3
HER2	Positive	121	21.0
	Negative	455	79.0
Ki67	Low (<20%)	150	24.4
	High (≥20%)	465	75.6

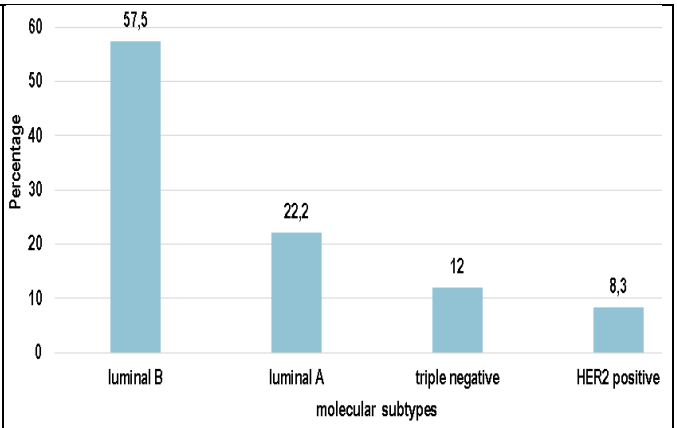

Figure 2. Percentage of each molecular subtype.

Table 3. **Association between Clinical and Immunohistochemical Factors with Intrinsic Molecular Subtypes.**

Characteristics		Luminal A	Luminal B	Triple negative	HER2+	All cases	Chi square	P value
		n (%)	n (%)	n (%)	n (%)	n (%)		
Age (years)	<50	32 (24.2)	113 (32.8)	22 (30.0)	18(36.0)	185 (30.9)	3.909	0.271
	≥50	100 (75.8)	232 (67.2)	50 (69.4)	32 (64.0)	414 (69.1)		
Ethnicity	Kazakh	58(47.2)	150(46.4)	26(37.7)	23(50.0)	257(45.8)	5.105	0.530
	Russian	44(35.8)	103 (31.9)	29(42.0)	12 (26.1)	188(35.5)		
	Other	21(17.1)	70 (21.7)	14(20.3)	11(23.9)	116(20.7)		
Grade	1	33 (27.0)	13 (3.9)	1 (1.4)	0 (0.0)	47 (8.2)	120.9	<0.001
	2	73 (59.8)	185 (55.2)	24 (34.3)	14 (30.4)	296 (51.7)		
	3	16 (13.1)	137 (40.9)	45 (64.3)	32 (69.6)	230 (40.1)		
Tumor size	T0	5(4.3)	4 (1.3)	2 (2.9)	2(4.5)	13(2.4)	38.09	<0.001
	T1	47 (40.2)	62 (19.5)	13 (18.8)	4(9.1)	126 (23.0)		
	T2	58 (49.6)	206 (64.8)	46 (66.7)	28 (63.6)	338 (61.7)		
	T3	2 (1.7)	11 (3.5)	3 (4.3)	2 (4.5)	18 (3.3)		
	T4	5 (4.3)	35 (11.0)	5 (7.2)	8 (18.2)	53 (9.7)		
N	N0	13 (9.8)	33 (9.6)	14 (19.4)	5 (10.0)	65 (10.9)	12.2	0.43
	N1	15(11.4)	52 (15.1)	9 (12.5)	9 (18.0)	85 (14.2)		
	N2	5 (3.8)	15 (4.3)	3 (4.2)	2 (4.0)	25 (4.2)		
	N3	1 (0.8)	5 (1.4)	0 (0.0)	2 (4.0)	8 (1.3)		
	NX	98(74.2)	240 (69.6)	46 (63.9)	32 (64.0)	416 (69.4)		
M	M0	113 (96.6)	297 (93.7)	66 (95.7)	38 (86.4)	515 (93.8)	6.28	0.09
	M1	4 (3.1)	20 (6.6)	3 (4.3)	6 (13.6)	33 (6.0)		
Stage	0	5 (4.3)	4(1.3)	0 (0.0)	2 (4.5)	11 (2.0)	52.235	<0.001
	1	47 (40.2)	55 (17.4)	10 (15.2)	2 (4.5)	114 (20.9)		
	2	57 (48.7)	202 (63.7)	45 (68.2)	27 (61.4)	331 (60.8)		
	3	4 (3.4)	38 (12.0)	8 (12.1)	8 (18.2)	58 (10.7)		
	4	4 (3.4)	18 (5.7)	3 (4.5)	5 (11.4)	30 (5.5)		
Pathologic sub type	NST	102 (70.8)	305 (93.6)	68 (94.4)	42 (85.7)	517 (87.5)	46.97	<0.001
	ILC	12 (8.3)	9 (2.8)	0 (0.0)	2 (4.1)	23 (3.9)		
	Other	30 (20.8)	12 (3.7)	4 (5.6)	5 (10.2)	51 (8.6)		

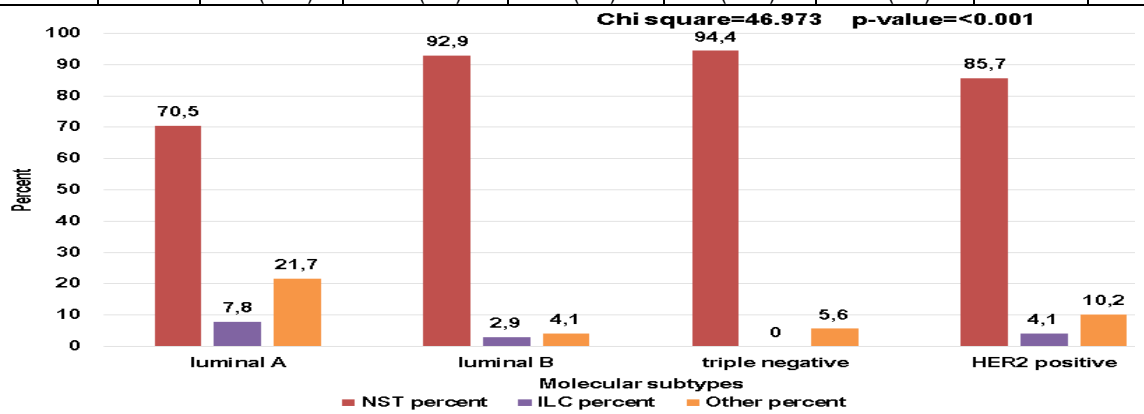

Figure 3. Association of molecular subtype of tumor with pathologic type.

Discussion

Taking account to heterogenous nature of breast cancer, determining most common and less common BC types and associated factors are important for improving preventing programs . identification of most common and less common BC types help health care provider to guide investment in treatment researches. There is no study that evaluate most common cancer type in Almaty city and investigate association of different clinicopathological criteria with molecular subtype of tumors. Molecular subtype of tumor determine treatment plane. For example luminal cancers are treated by hormone therapy, HER2 positive tumors by targeted therapy and Based on available data BC is very common in Almaty city, there for study about cancer types is a must. For this reason we studied all female breast cancer cases referred to Almaty oncology center (main center for diagnosis of cancer for citizen of Almaty city) since first of January to end of December 2020 to determine pathologic and molecular subtype of tumors and find associated factors to molecular subtypes.

Pathologic type of tumors:

In gathered data there were 21 types of cancer. For better presentation we classified types that composed less than one percent of all cases, in a single group and called it other rare type. NST with 523 cases was most prevalent type of cancer in this study that composed 85.3% of all cases. ILC and DCIS with 23(3.7%) and 13 (2.1%) cases have second and third position.

In previous studies, NST is most frequent type and ILC is second one, for example study of Abiltayeva and colleagues in North East of Kazakhstan [12], Al-thoubaity in Saudi Arabia [13], Caldarella and colleagues in Italy [14], Badowska-Kozakiewicz and teammates in Poland [15].

Molecular subtype of tumors:

In this study we found luminal B, most prevalent type (57.5%) of tumors. There is similar finding (56.5%) in study of Thang et al in Vietnam [16] and Mandaliya and colleagues in Australia (51%) [17]. Some authors like Fatemi et al [18], San et al [19] and Paramita and colleagues [20] found luminal B more prevalent than other types.

A study that was conducted in Semey and Pavlodar cities and include 253 cases from 10 years, reported luminal A is most prevalent. Difference in results may be due to different study setting or different ethnicity of participants. In our study 33% of participants are Russian while in their study this percentage is 58.1

APPENDIX A

Variable coding

Table A.1. Variable coding used for SPSS.

No	Variable	Code
1	Age	<50 =1, >50 =2
2	Ethnicity	Kazakh =1, Russian =2, other =3
3	Tumor size	T0 =1, T1 =2, T2 =3, T3=4, T4=5
4	Lymph node invasion	N0 =1, N1 =2, N2=3, N3=4, NX =0
5	Metastasis	M0 =1, M1=2
6	Pathologic type of tumor	NST =1, ILC =2, DCIS=3, Other=4
7	Histologic grade	G1 =1, G2=2, G3=3
8	Stage	I =1, II =2, III =3
9	Estrogen receptor status	Negative =1, Positive =2
10	Estrogen expression level	Negative =1, low =2, intermediate =3, high =4
11	Estrogen expression score	Non =0, 2 = 2score, 3 = 3score, 4=4 score, 5 =5 score, 6 =6 score, 7= 7score, 8 = 8 score
12	Progesterone receptor status	Negative =1, Positive =2
13	Progesterone expression level	Negative =1, low =2, intermediate =3, high =4
14	Progesterone expression score	Non =0, 2 = 2score, 3 = 3score, 4=4 score, 5 =5 score, 6 =6 score, 7= 7score, 8 = 8 score
15	HER2 over expression	Negative =1, Positive =2
16	Ki67 level	<20% =1 ≥20% =2
17	SISH result	Negative =1, Positive =2
18	Molecular subtype	Luminal A =1, Luminal B =2, Triple negative =3, HER2 positive = 4

Association among clinical and immunohistochemical factors and molecular subtypes

In our finding, tumor size, grade, stage and pathologic type of tumor have statistically significant association with molecular subtype of tumors. In next lines similar results in previous studies are presented.

Grade of tumor: Statistical analysis showed that molecular subtype of tumor is associated with grade of tumor with p-value <0.001. In our study luminal A tumors have mostly grade I and II, while grade III is seen predominantly in luminal B, triple negative and HER/2 positive sub types. These results is similar finding of San and teammate in Myanmar [19], Paramita et al [20] and Setyawati and colleagues [21] in Indonesia, Li and his group in China [22]. In the study of El Fatemi et al in Morocco [18], study in Kazakhstan [12] and study of Hashmi and colleagues in Pakistan [23], there is a small difference, in their samples, more than half of HER/2 positive cases are in grade II, while in our study are in grade III. This differences maybe related to different study setting, screening program situation and ethnicity.

Ki67: In our study tumors with high proliferation rate are mostly in triple negative and HER/2 positive groups. This finding is in accordance with result of previously mentioned study in Indonesia. In Myanmar and Pakistan studies, mean of ki67 in triple negative and HER/2 positive is higher than luminal subtypes that is proving our findings.

Tumor size: small size tumors **(**<2cm) composed around 90% of luminal A cases and frequency of tumors (>5cm or extended to chest wall) in HER/2 and triple negative sub type is more. T2 (2-5 cm) is most frequent size in all groups. It means that luminal A has smaller size tumors in comparison to triple negative and HER/2 positive tumors.

This finding is similar to results of Liu et al study in China [24],study of Zavyalova and teammate in Russia [25], Study of El Fatemi and colleagues in Morocco in north Africa with P=0,0003 for association of tumor size and molecular subtype [18]. In El Fatemi study also T2 is most prevalent and highest percentage of T3 and T4 is in HER/2 positive and triple negative subtypes. San and colleagues in Myanmar found that tumors larger than 2 cm were more in HER2 and triple negative subtype [19]. Caldarella et al in Italy, concluded there is significant association for tumor size and luminal B HER/2 negative, triple negative and HER/2 positive subtypes [14].

Stage of tumor: Most of tumors in our study were in stage II, and in all sub type the highest percentage belongs to this stage. Stage III and IV are most frequent in non-luminal A subtypes while stage I and II composed 88% of luminal A tumors.

Same distribution of stage in different molecular groups was found in study of Zavyalova and teammate in Russia. In this research 87% of luminal A are in stage I and II, and triple negative and HER/2 positives tumor have more stage III than other subtypes [25]. In the study of Mehdi and colleagues in Oman, patients with HER/2 sub type and basal cell like (BCL) tumors had higher stage while early stages were observed in luminal types tumors [26] Study of Caldarella et al in Italy found a significant association between molecular sub types and tumor stage [14] In participants of research in China that was conducted by Li et al, stage 0,I and II composed around 90% of all luminal A cases and stage III is most prevalent in HER/2 positive and BCL tumors [22]. Study in Myanmar showed BCL tumors and HER2, are diagnosed with more advanced stages (stage II, III and IV) [19]. All of this finding are similar to our findings.

Pathologic type of tumor: In our finding percentage of NST in luminal A subtype is less than other three groups and in luminal B is more than other group and most of ILC are in luminal A, and other rare histologic type of tumor has higher percentage in luminal A group. (as presented in figure 3)

In study of Al-thoubaity [13] and Alnegheimish et al [27] in Saudi Arabia similar to these results were found. NST is more frequent in non- luminal A and ILC tumors mostly are luminal A. In Italy, similar to our study ILC and tubular carcinoma are more frequent in luminal A group [14] El Fatemi and colleagues found that there is a significant association between molecular and histologic types of tumor (p<0.00001).in their study similar to our results, ILC percentage in luminal A subtype is higher than other sub types [18]

Study strengths and limitations: One of the strengths of this study is that it is believed to be the first study in Almaty that investigated breast cancer subtypes and the association of determining factors with each other by completing electronic data base information from paper-based data.

Limitations: First of all, the study was done by using medical records and some important information about patients' medical history like menopausal status and obstetric and gynecologic data was not available. Second, data recorded in the electronic data base did not include IHC test results and researcher had to investigate paper based medical records for them. This method tend to omitting around 200 cases from study (in the cases of unsuccessful search) and having a low amount of information about lymph node invasion and distant metastasis of tumor. Third: having no control group

Conclusion

Most common Pathologic type of tumor in this study was NST, ILC and DCIS respectively. Most prevalent molecular subtype of tumors: Luminal B, luminal A, triple negative, HER/2. There was statistically significant association (p-value <0.05) between Molecular subtype and pathologic type of tumor, grade, stage, size and mitotic rate

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