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Article

Comparison of the immunohistochemical profile between women with breast cancer over 40 and under 40 years old

*Comparação do perfil imunohistoquímico entre mulheres com câncer de mama maiores de 40 e menores de 40 anos**

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ABSTRACT: Objective: To compare immunohistochemical profiles, such as surrogate molecular classifications of breast carcinomas and histological findings, among women under and over 40 years of age. Methods: This was an observational, quantitative, and retrospective study based on data from the Instituto de Patologia de Araçatuba (IPAT), located in the countryside of the state of São Paulo, Brazil. Pathology reports from biopsy or surgical excision recorded between January 1, 2017, and June 30, 2020 (42 months) were reviewed. Only ductal and lobular carcinomas were histologically analyzed. Age, histological subtype, and immunohistochemical data of estrogen receptor, progesterone receptor, Her-2 and Ki-67 (< 20% x ≥ 20%) were analyzed. Specimens were categorized into two groups based on patient age at diagnosis (≤ 40 years vs. > 40 years). Results: There was no significant difference between the two age groups regarding hormone receptor, Her-2 evaluation, or histological classification (ductal vs. lobular). Nevertheless, breast cancer in younger women was associated with a higher Ki-67 index (p = 0.015). In the group aged 40 years and younger, half of the cases were classified as Luminal B-like, Her-2 negative, and 19% were triple-negative. For women over 40 years old, 57% were classified as luminal B-like, Her-2 negative, 9% were luminal A-like, and only 13% were triple-negative. Conclusion: The frequency of breast among young woman is substantial, and they tend to exhibit higher Ki-67 indexes.

KEY WORDS: Breast Carcinoma; Mammary Ductal Carcinoma; Lobular Carcinoma; Mass Screening.

RESUMO: Objetivo: Comparar os perfis imunohistoquímicos, incluindo marcadores substitutos da classificação molecular e descobertas histológicas de carcinomas mamários, de mulheres com menos e mais de 40 anos de idade. Métodos: Este foi um estudo observacional, quantitativo e retrospectivo baseado em dados do Instituto de Patologia de Araçatuba (IPAT), localizado no interior do estado de São Paulo, Brasil. Foram revisados os relatórios de patologia obtidos por biópsia ou excisão cirúrgica entre 1º de janeiro de 2017 e 30 de junho de 2020 (42 meses). Apenas carcinomas ductais e lobulares foram analisados histologicamente. Idade, subtipo molecular e dados imunohistoquímicos do receptor de estrogénio, receptor de progesterona, Her-2 e Ki-67 (< 20% x ≥ 20%) foram avaliados. Os espécimes foram divididos em dois grupos de acordo com a idade da paciente no momento do diagnóstico (≤40 anos x >40 anos). Resultados: Não houve diferença significativa entre os dois grupos etários em relação ao receptor hormonal, avaliação do HER-2, ou classificação histológica (ductal x lobular). No entanto, houve uma associação entre o grupo de mulheres mais jovens e um índice de Ki-67 mais elevado (p = 0,015). No grupo de mulheres com 40 anos de idade ou menos, metade dos casos foram classificados como Luminal B, HER-2 negativo, e 19% foram triplamente negativos. No grupo de mulheres com mais de 40 anos, 45% eram Luminal B, HER-2 negativo, 21% eram Luminal A, e apenas 13% eram triplo-negativos. Conclusão: A frequência do câncer da mama entre as mulheres jovens não é pequena e essa população tende a apresentar índices de Ki-67 mais elevados.

PALAVRAS-CHAVE: Neoplasias da mama; Carcinoma Ductal de mama; Carcinoma Lobular; Programas de Rastreamento.

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INTRODUCTION

Breast cancer is a heterogeneous and multifocal disease. According to GLOBOCAN 2020 data, female breast cancer emerges as the most commonly diagnosed cancer, representing 11.7% of all cases. Its incidence, for both genders and across all ages, reaches 2.3 million cases. In terms of mortality, it ranks fifth among all cancers, accounting for 6.9% of deaths, which equates to approximately 685 thousand deaths[1]. Women residing in developing nations exhibit a 17% higher mortality rate compared to those in developed nations (15.0 and 12.8 per 100,000, respectively)[1]. According to the Brazilian National Cancer Institute, more than 66,000 new cases of breast cancer were recorded in Brazil in 2020, representing an adjusted incidence rate of 43.74 cases per 100,000 women[2]. Traditionally, breast cancer is a rare disease among young women (under 40 years of age), with most cases occurring after the age of 50[2].

According to the fifth edition of the World Health Organization *(*WHO*)* Classification of Tumours, there are four primary molecular types of breast carcinoma: Luminal A, Luminal B (Her-2-negative or Her-2-positive), human epidermal growth factor receptor-type (Her-2)-positive, and triple-negative[3]. The WHO recommends employing an immunohistochemistry panel for surrogate definitions of early invasive breast carcinoma subtypes, as adopted by the 13th St. Gallen International Breast Cancer Conference (2013) Expert Panel. This panel is based on the expression of ER, PR, ERBB2 (HER-2), and Ki-67, with in situ hybridization confirmation when appropriate[3]. Luminal A is the most common subtype, accounting for approximately 50%–60% of cases[3-5]. It demonstrates high survival and recurrence rates[3-5]. Luminal B constitutes 10%–20% of cases and presents a more aggressive pattern, higher histological grade, increased proliferation, and worse outcomes compared to Luminal A, as well as high recurrence rate and metastases primarily to bone and liver[3-5]. The Her-2 subtype comprises 15% of all breast carcinomas and is morphologically characterized by high proliferation, with 75% demonstrating a high histological grade and 40% exhibiting a somatic mutation in the p53 gene[3,4]. Triple-negative breast cancer is more prevalent among young women and is associated with poorer outcomes compared to other subtypes[3,6].

In Brazil, the Ministry of Health guidelines recommend screening mammography for women aged 50 to 69 every two years[7]. The rationale is that mammograms may cause more harm than good in younger women[7]. The risk of death associated with screening in this age group equals the potential benefit. Between ages 50 and 59, the balance of risks and benefits of screening is uncertain, but likely favorable. Between ages 60 and 69, the benefits are probably higher and the best among these age groups[7]. However, the Brazilian College of Radiology, along with the Brazilian Society of Mastology and the Brazilian Federation of Gynecology and Obstetrics Associations, advocate for screening mammography starting at age 40 to enable early diagnosis and reduce mortality[8]. The American Society of Oncology recommends annual screening mammography beginning at age 45 to 54 years and transitioning to biennially at age 55 years[9]. European guidelines advise screening mammography between ages 50 and 69[10]. In South Korea, biennial screening mammography is recommended for women aged 40 to 69, and according to individual risk and preference for women over 70 years of age[11]. Japanese guidelines recommend mammography screening without clinical breast examination for women aged 40 to 74[12]. There are no recommendations for screening women under 40.

Although younger women are typically not included in screening programs, in 2008, the American Cancer Society reported that 182,460 women in the United States were diagnosed with breast cancer. Among them, 40% were in their 40s, 20% were in their 30s, and 2% were in their 20s[13]. The National Breast Cancer Registry Program of Turkish Federation of Breast Diseases Societies documented 19,503 cases of breast cancer from 2005 to 2017, with 16.6% occurring in women under 40 years old[14]. Therefore, this study aims to compare immunohistochemical profiles, such as surrogate molecular classifications of breast carcinomas and histological findings, among women under and over 40 years of age.

METHODS

This was an observational, quantitative, and retrospective study based on data from the Instituto de Patologia de Araçatuba (IPAT), located in the countryside of the state of São Paulo, Brazil. Pathology reports from biopsy or surgical excision (149 biopsies and 222 excisions) recorded between January 1, 2017, and June 30, 2020 (42 months) were reviewed. Only data from malignant primary lesions of the female breast were included. In situ hybridization (FISH) was performed in all cases when necessary. Male specimens, metastases, benign lesions, carcinomas in situ, inconclusive molecular results for the Her-2 oncogene status, specimens for which FISH was not performed when indicated, and cases related to hereditary cancer syndrome and papillary carcinoma of the breast were excluded due to their high complexity. Only lobular and ductal carcinomas were histologically analyzed. Age, histological subtype, and immunohistochemical data of estrogen receptor, progesterone receptor, Her-2 and Ki-67 ($< 20\% \times \geq 20\%$) were analyzed according to international protocols. Paraffin samples underwent immunohistochemistry for ER (Clone: EP1; prediluted ready-to-use), PR (Clone: PgR636; prediluted ready-to-use), Her-2 (Clone: Polyclonal, dilution 1: 200), and Ki-67 (Clone: MIB-1; pre-diluted ready-to-use), according to the Dako® Immunhistochemistry Autostainer Plus manufacturer's protocols. Positive and negative internal and external controls were utilized. Sections were assessed by two pathologists, who determined the level of positivity of the markers. Specimens were categorized into two groups based on patient age at diagnosis ($\leq$ 40 years vs. > 40 years). Cases underwent approximate molecular classification according to the parameters of the WHO[3]. Both absolute and relative data (%) were considered. To assess potential statistical associations in the two groups, the p-value was calculated with a 95% confidence interval, and Fisher's exact test was employed to derive it.

The Research Ethics Committee of our institution approved the study under acceptance number CAAE: 36593120.0.0000.5379

RESULTS

We analyzed 329 samples from women aged over 40 years and 42 samples from women aged 40 years or below, totaling 371 samples. In the group aged ≤ 40 years, the estrogen receptor positivity was 74%, compared to 79% in the group aged >40 years. Both groups exhibited approximately 62% positivity for the progesterone receptor. Her-2 positivity was 76% in the ≤ 40 years group and 73% in the > 40 years group. There were no significant differences between the groups regarding hormone receptors, Her-2 status, or histological subtype (Table 1). The data on Ki-67 indicated that all tumors from women under 40 years of age exceeded the cutoff (p = 0.015). In the group aged 40 years and younger, over half of the cases were classified as Luminal B-like, Her-2 negative, and 19% were triple-negative. In the group of women over 40 years old, 57% of cases were classified as luminal B-like, Her-2 negative, 9% as luminal A-like, and only 13% as triple-negative. The mean age of the molecular subtypes ranged from 57 to 62 years, with a standard deviation (SD) varying from 13 to 16,3. No statistically significant difference (p = 0.197) was observed when considering both age groups and breast cancer molecular subtypes. All this data is presented in Table 2. Regarding Her-2 intensity, 38 cases exhibited a Her-2 score of 2+, seven of those in the ≤ 40 years group and 31 in the > 40 years group. In the group of younger women, only two samples showed amplification using FISH, whereas in the older age group, 19 samples exhibited amplification using this method.

Table 1 - Distribution of immunohistochemical markers by age with statistical analysis

Markers		Age		p-value
≤ 40 years		> 40 years		
Estrogen receptor	Positive	31 (73.8%)	261 (79.3%)	0.410
	Negative	11 (26.2%)	68 (20.7%)	
Progesterone receptor	Positive	26 (61.9%)	206 (62.6%)	0.929
	Negative	16 (38.1%)	123 (37.4%)	
Ki-67	≥ 20	42 (100%)	288 (87.5%)	0.015
	< 20	0 (0%)	41 (12.5%)	

Table 2 - Distribution of breast cancer molecular subtype by age

Molecular subtype		≤ 40 years	> 40 years	Mean	SD	p-value
Luminal A-Like	ER+, PR+, HER2- and KI-67 low	0	30 (9%)	61.8	13.01	0.197
Luminal B-like Her-2 negative	ER+, HER2- and KI-67 high and/or PR-	24 (57.2%)	185 (57%)	59.6	14.98	
Luminal B-like Her-2 positive	ER+, HER2+, KI-67 any and PR+/-	6 (14.3%)	46 (14%)	57.2	14.6	
Group Her-2	ER-, PR- and Her-2 +	4 (9.5%)	24 (7%)	58.7	16.37	
Triple-negative	ER-, PR- and Her-2 -	8 (19%)	44 (13%)	59.8	15.01	
Total		42	329			

DISCUSSION

In the population of the present study, the prevalence of breast cancer among women younger than 40 years of age was notable, despite this age group not being the target audience for screening programs worldwide[7,9-11].

The analysis of molecular subtypes revealed a higher frequency of triple-negativity in the group aged ≤ 40 years, as well as a more aggressive profile, lower levels of Luminal-A, and a more indolent subtype. Regardless of age, the most prevalent subtype was Luminal-B, Her-2 negative. These findings contrast with those of the WHO, which indicates that the Luminal-A subtype is the most prevalent. The Brazilian literature detailing the epidemiology of this tumor is limited, and the true prevalence and molecular subtypes of breast cancer among Brazilian women remain unknown[15,16].

There are numerous studies in the literature detailing the profile of breast carcinoma[17-21]. All surveys have shown

low percentages of breast cancer diagnoses among women under the age of 40[17-21]. Cortet et al. and Ushimado et al. reported high percentages of positivity for estrogen and progesterone receptors[17,21], as we did in the present study. Ductal carcinoma emerged as the predominant histological subtype in all populations[17-21]. Lobular carcinoma exhibited notably low rates across studies, with only one study reporting a percentage above 5%[19]. The studies presented discrepancies regarding molecular classification. Three studies indicated that the Luminal-A molecular subtype was most prevalent within the total sample[17,18,21], whereas two studies reported a prevalence of Luminal-B[19,20]. Only one study indicated Her-2 negative Luminal-B as the prevailing subtype[20], as we reported here. Only two studies assessed molecular classification among patients younger than 40 years[20,21]. In agreement with the present study, Ushimado et al. found that the Luminal-B Her-2 negative subtype was the most prevalent in this age group[21]. Jain et al. found that the two most prevalent subtypes in this age group mirrored those in our study; however, their results indicated triple-negative tumors as the most common, followed by Luminal-B Her-2 negative (24% and 20% respectively)[20].

There are limited studies that evaluate survival among women diagnosed with breast carcinoma under the age of 40[22-24]. Two studies demonstrated that women aged ≤ 40 years faced an increased risk of death from breast cancer of the Luminal A and Luminal B molecular subtypes[22,23]. One study indicated worse outcomes for triple-negative cancer, while outcomes were moderate for Luminal subtypes and not present for the Her-2 subtype[24]. Similarly, Partridge et al. found no worse outcomes in patients under 40 years of age with a Her-2 molecular diagnosis. Kim et al. identified poor prognostic factors in this age group, such as poor histological grade, negative ER expression, and higher PR levels compared to older patients[23]. Additionally, Partridge et al. demonstrated that the highest mortality rates in each molecular subtype occurred among women diagnosed at ≤ 40 years of age, with triple-negative breast cancer being the most lethal[22]. These findings suggest that public health programs should debate the poorer outcomes and the significant rates of breast cancer among women younger than 40 years.

Numerous studies discuss the risk factors for the development of breast carcinoma in young women[13,25-27]. Among non-modifiable factors, most studies suggest that a positive family history of breast cancer is a primary risk factor[13,25-27]. However, some studies indicate that women of African descent have higher incidence rates of breast cancer in youth than women of other ethnicities[26,28]. As for modifiable risk factors, all studies highlight a sedentary lifestyle, alcohol abuse, obesity, and nulliparity[13,25-27]. Lack of breastfeeding was also identified as a risk factor in some articles[25-27]. Long-term use of oral contraceptives remains a subject of debate[26]. While some studies suggest an increased incidence of breast cancer in young women using oral contraceptives, particularly over a prolonged duration[25,26,29,30], divergent results have been reported in other studies[26,31].

This study had certain limitations, as it was conducted solely within one institution and involved a limited number of samples. Nevertheless, our findings can contribute to consolidating national and international data concerning this age group, given the significant number of cases of breast carcinoma diagnosed in women under 40 years of age. Moreover, a proper understanding of the epidemiology of these tumors can influence public health policies to enhance screening methods and expedite earlier diagnosis, thereby improving outcomes.

CONCLUSION

While not targeted by national or international screening programs, the incidence of breast carcinomas in women under forty years of age is significant. In terms of the molecular profile, these cancers differ from those found in older women, exhibiting a higher index of cell proliferation with a predominance of Luminal-B Her-2 negative and triple-negative subtypes.

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REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin [Internet]. 2021;71(3):209–49. Doi: http://dx.doi.org/10.3322/caac.21660

2. Instituto Nacional do Câncer (Brasil). Estimativa 2020: Incidência de Câncer no Brasil. Rio de Janeiro: Instituto Nacional do Câncer, 2020. https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/

document//estimativa-2020-incidencia-de-cancer-no-brasil.pdf.

3. WHO Classification of Tumours Editorial Board. Breast tumours. Lyon (France): International Agency for Research on Cancer; 2019. (WHO classification of tumours series, 5th ed.; vol. 2).

4. Eroles P, Bosch A, Pérez-Fidalgo JA, Lluch A. Molecular biology in breast cancer: intrinsic subtypes and signaling pathways. Cancer Treat Rev [Internet]. 2012;38(6):698-707. Doi: http://dx.doi.org/10.1016/j.ctrv.2011.11.005

5. Vasconcelos I, Hussainzada A, Berger S, Fietze E, Linke J, Siedentopf F, et al. The St. Gallen surrogate classification for breast cancer subtypes successfully predicts tumor presenting features, nodal involvement, recurrence patterns and disease free survival. Breast [Internet]. 2016;29:181-5. Doi: http://dx.doi.org/10.1016/j.breast.2016.07.016

6. Deus Moura R, Carvalho FM, Bacchi CE. Breast cancer in very young women: Clinicopathological study of 149 patients ≤25 years old. Breast [Internet]. 2015;24(4):461-7. Doi: http://dx.doi.org/10.1016/j.breast.2015.04.002

7. Ministério da Saúde. Diretrizes para a Detecção Precoce do Câncer de Mama no Brasil. Rio de Janeiro. Instituto Nacional do Câncer. https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//diretrizes_deteccao_precoce_cancer_mama_brasil.pdf.

8. Urban LABD, Chala LF, Bauab S di P, Schaefer MB, Dos Santos RP, Maranhão NM de A, et al. Breast cancer screening: updated recommendations of the Brazilian College of Radiology and Diagnostic Imaging, Brazilian Breast Disease Society, and Brazilian Federation of Gynecological and Obstetrical Associations. Radiol Bras [Internet]. 2017;50(4):244-9. Doi: http://dx.doi.org/10.1590/0100-3984.2017-0069

9. Oeffinger KC, Fontham ETH, Etzioni R, Herzig A, Michaelson JS, Shih Y-CT, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society: 2015 Guideline update from the American cancer society. JAMA [Internet]. 2015;314(15):1599-614. Doi: http://dx.doi.org/10.1001/jama.2015.12783

10. Perry N, Broeders M, de Wolf C, Törnberg S, Holland R, von Karsa L. European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition--summary document. Ann Oncol [Internet]. 2008;19(4):614-22. Doi: http://dx.doi.org/10.1093/annonc/mdm481

11. Lee EH, Park B, Kim N-S, Seo H-J, Ko KL, Min JW, et al. The Korean guideline for breast cancer screening. J Korean Med Assoc [Internet]. 2015;58(5):408. Doi: http://dx.doi.org/10.5124/jkma.2015.58.5.408

12. Hamashima C, Japanese Research Group for the Development of Breast Cancer Screening Guidelines, Hamashima C C, Hattori M, Honjo S, Kasahara Y, et al. The Japanese guidelines for breast cancer screening. Jpn J Clin Oncol [Internet]. 2016;46(5):482-92. Doi: http://dx.doi.org/10.1093/jjco/hyw008

13. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast cancer before age 40 years. Semin Oncol [Internet]. 2009;36(3):237-49. Doi: http://dx.doi.org/10.1053/j.seminoncol.2009.03.001

14. Özmen V, Özmen T, Doğru V. Breast cancer in Turkey; An analysis of 20.000 patients with breast cancer. Eur J Breast Health [Internet]. 2019;15(3):141-6. Doi: http://dx.doi.org/10.5152/ejbh.2019.4890

15. Moraes AB de, Zanini RR, Turchiello MS, Riboldi J, Medeiros LR de. Estudo da sobrevida de pacientes com câncer de mama atendidas no hospital da Universidade Federal de Santa Maria, Rio Grande do Sul, Brasil. Cad Saude Publica [Internet]. 2006;22(10):2219-28. Doi: http://dx.doi.org/10.1590/s0102-311x2006001000028

16. Schneider IJC, d'Orsi E. Sobrevida em cinco anos e fatores prognósticos em mulheres com câncer de mama em Santa Catarina, Brasil. Cad Saude Publica [Internet]. 2009;25(6):1285-96. Doi: http://dx.doi.org/10.1590/s0102-311x2009000600011

17. Cortet M, Bertaut A, Molinié F, Bara S, Beltjens F, Coutant C, et al. Trends in molecular subtypes of breast cancer: description of incidence rates between 2007 and 2012 from three French registries. BMC Cancer [Internet]. 2018;18(1). Doi: http://dx.doi.org/10.1186/s12885-018-4080-8

18. Pandit P, Patil R, Palwe V, Gandhe S, Patil R, Nagarkar R. Prevalence of molecular subtypes of breast cancer: A single institutional experience of 2062 patients. Eur J Breast Health [Internet]. 2020;16(1):39-43. Doi: http://dx.doi.org/10.5152/ejbh.2019.4997

19. Sharma JD, Khanna S, Ramchandani S, Kakoti LM, Baruah A, Mamidala V. Prevalence of molecular subtypes of breast carcinoma and its comparison between two different age groups: A retrospective study from a tertiary care center of northeast India. South Asian J Cancer [Internet]. 2021;10(4):220-4. Doi: http://dx.doi.org/10.1055/s-0041-1731905

20. Jain S, Narang V, Jain K, Paul D, Singh J, Sohi AS, et al. Prevalence of molecular subtypes in operated cases of breast cancer and its clinicopathological correlation: A single institute study from a tertiary cancer centre in north India. Indian J Surg Oncol [Internet]. 2021;12(3):538-44. Doi: http://dx.doi.org/10.1007/s13193-021-01374-w

21. Ushimado K, Kobayashi N, Hikichi M, Tsukamoto T, Kuroda M, Utsumi T. Differences in clinicopathologic features and subtype distribution of invasive breast cancer between women older and younger than 40 years. Fujita Med J [Internet]. 2019;5(4):92-7. Doi: http://dx.doi.org/10.20407/fmj.2019-001

22. Partridge AH, Hughes ME, Warner ET, Ottesen RA, Wong Y-N, Edge SB, et al. Subtype-dependent relationship between young age at diagnosis and breast cancer survival. J Clin Oncol [Internet]. 2016;34(27):3308-14. Doi: http://dx.doi.org/10.1200/jco.2015.65.8013

23. Kim NH, Bang HW, Eom YH, Choi SH. The different prognostic impact of age according to individual molecular subtypes in breast cancer. Ann Surg Treat Res [Internet]. 2022;103(3):129-44. Doi: http://dx.doi.org/10.4174/astr.2022.103.3.129

24. Liedtke C, Rody A, Gluz O, Baumann K, Beyer D, Kohls E-B, et al. The prognostic impact of age in different molecular subtypes of breast cancer. Breast Cancer Res Treat [Internet]. 2015;152(3):667-73. Doi: http://dx.doi.org/10.1007/s10549-015-3491-3

25. Velentgas P, Daling JR. Risk factors for breast câncer in younger women. J Natl Cancer Inst Monogr [Internet]. 1994;(16):15-24.

26. Daly AA, Rolph R, Cutress RI, Copson ER. A review of modifiable risk factors in young women for the prevention of breast cancer. Breast Cancer (Dove Med Press) [Internet]. 2021;13:241-57. Doi: http://dx.doi.org/10.2147/BCTT.S268401

27. Yeo W, Lee H-M, Chan A, Chan EY, Chan MC, Chan K-W, et al. Risk factors and natural history of breast cancer in younger Chinese women. World J Clin Oncol [Internet]. 2014;5(5):1097-106. Doi: http://dx.doi.org/10.5306/wjco.v5.i5.1097

28. Joslyn SA, Foote ML, Nasseri K, Coughlin SS, Howe HL. Racial

and ethnic disparities in breast cancer rates by age: NAACCR Breast Cancer Project. Breast Cancer Res Treat [Internet]. 2005;92(2):97-105. Doi: http://dx.doi.org/10.1007/s10549-005-2112-y

29. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Lancet [Internet]. 1996;347(9017):1713-27. Doi: http://dx.doi.org/10.1016/s0140-6736(96)90806-5

30. Mørch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard Ø. Contemporary hormonal contraception and the risk of breast cancer. N Engl J Med [Internet]. 2017;377(23):2228-39. Doi: http://dx.doi.org/10.1056/NEJMoa1700732

31. Westhoff CL, Pike MC. Hormonal contraception and breast cancer. Am J Obstet Gynecol [Internet]. 2018;219(2):169.e1-169.e4. Doi: http://dx.doi.org/10.1016/j.ajog.2018.03.032

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