Reproductive Risk Factors of Inflammatory Breast Cancer according to Luminal, HER2-Overexpressing, and Triple-Negative Subtypes: A Case Comparison Study

Nesrine Mejri^{a, b} Houda El Benna^{a, b} Haifa Rachdi^a Soumaya Labidi^{a, b}
Mahdi Benna^a Nouha Daoud^a Yosr Hamdi^b Sonia Abdelhak^b
Hamouda Boussen^{a, b}

^aMedical Oncology Department, Abderrahmen Mami Hospital, Faculty of Medicine Tunis, University of Tunis El Manar, Tunis, Tunisia; ^bLaboratory of Biomedical Genomics and Oncogenetics, LR16IPT05, Institut Pasteur de Tunis, University of Tunis El Manar, Tunis, Tunisia

Keywords

Inflammatory breast cancer · Risk factors · Breastfeeding

Abstract

Objective: We evaluated the risk factors of inflammatory breast cancer (IBC) compared to non-IBC and according to histological subtype. **Methods:** Cases of IBC ($n = 160$) and controls of non-IBC ($n = 580$) were collected from the cohort of breast cancer patients treated in two oncology centers matched based on age at cohort entry. Data about breast cancer risk factors were collected. We evaluated correlation and ORs using conditional logistic regression analysis for each case group versus the control group. We also evaluated those factors in three further subgroups: luminal (HR+, HER2–), HER2-overexpressing (HER2+, HR–), and triple-negative (TN) patients. **Results:** Long duration of breastfeeding of ≥ 12 months (OR = 4.64, 95% CI 2.97–7.26), body mass index ≤ 25 (OR = 2.48, 95% CI 1.71–3.58), and use of oral contraceptives (OR = 2.48, 95% CI 1.62–3.84) were the most significant risk factors in favor of IBC compared to non-IBC. There was no impact of contraceptives use in the luminal

subgroup and no impact of long duration of breastfeeding in the TN subgroup. The role of socioeconomic and educational levels was unclear. Age at menarche, age at first pregnancy, and age at menopause were nonsignificant risk factors of IBC. **Conclusion:** Reproductive risk factors were distinct in IBC patients reflecting the clinical entity of IBC.

© 2020 S. Karger AG, Basel

Introduction

A number of breast cancer risk factors have been well established for many years, especially those related to hormonal and genetic predisposition. Identification of genetic and environmental risk factors that contribute to the development of breast cancer will enhance prevention efforts. Recent reports showed that those risk factors can vary according to breast cancer subtypes [1]. Inflammatory breast cancer (IBC) is the most fatal form of breast cancer. It seems to occur at a younger age and to have poor nuclear grade, negative receptor status, and poor survival outcome. In 2008, the World IBC Consortium

Consensus Meeting defined it as the rapid onset of breast erythema (occupying at least one-third of the breast), edema and/or peau d'orange and/or warm breast, with or without an underlying palpable mass with duration of symptoms of no more than 6 months. Published literature about the risk factor of IBC is rare. The first study was published in 1998 and showed that IBC patients had a significantly higher body mass index (BMI) than both non-IBC patients and non-breast cancer patients [2]. The latest study including Tunisian patients showed similar results and found a significant role of longer cumulative duration of breastfeeding [3]. We conducted a case comparison study and aimed to evaluate the difference in terms of risk factors between IBC and non-IBC cases.

Methods

Cases and controls were collected from the cohort of breast cancer patients treated in two oncology centers – Taoufik Clinic and Abderrahmen Mami Hospital – between 2005 and 2016. IBC cases ($n = 160$) were confirmed according to the World IBC Consortium Consensus case definition or the American Joint Committee on Cancer criteria [4]. The inclusion criteria for the IBC group were histological confirmation of underlying carcinoma as well as clinical validation of the IBC by at least a surgeon and an oncologist. Controls ($n = 580$) were selected from the cohort of remaining non-IBC cases, matched based on age (± 2 years) at cohort entry. The inclusion criterion for the controls was histologically confirmed breast cancer not classified under the T4d criteria.

Several factors, such as medical and family history as well as reproductive and hormonal features, were collected at the time of cohort entry.

We also considered three different groups according to immunohistochemical expression of receptors: a group of luminal (ER+ and/or PR+) patients, a group with human epidermal growth factors receptors (HER2, ER–, and PR–) overexpression, and a group of triple-negative (TN) tumors (HR+ and HER2–). Positivity of HR was considered in case of $>10\%$ on immunohistochemistry and overexpression of HER2 was considered for score 3+ and positive (FISH/CISH) for 2+ score tumors.

Statistical Analysis

Unadjusted ORs and 95% CIs were calculated. Pearson χ^2 tests were used to test for distribution differences between risk factors for IBC cases and controls. Multinomial logistic regression was used to estimate ORs as a measure of the association between potential risk factors and tumor subtypes, with 95% CIs. Multivariate analysis was carried out using an unconditional logistic regression model expressed as an OR. To test the independence of the risk factors, the variables considered significant in the univariate analysis ($p < 0.15$) were entered into a multivariate logistic regression model with likelihood ratio forward selection and a significance criterion of $p < 0.05$. The factors included in the multivariate model were age at menarche, menopausal status, number of children, use of contraceptives, age at first pregnancy, breastfeeding duration, BMI, breast cancer family history, as well as socioeconomic and educational levels. We evaluated risk factors in the overall population and in three subgroups: we compared IBC to non-IBC risk factors in patients in the luminal (ER+ and/or PR+), HER2-overexpressing (with ER– and PR–), and TN subgroups.

Table 1. Tumor characteristics of the population

	IBC ($n = 160$)	Non-IBC ($n = 580$)	<i>p</i> value
Median age, years	48.5	49.0	–
Premenopausal, %	57.3	53.6	0.41
T stage, %			–
T1	–	16.4	
T2	–	52.5	
T3	–	9.1	
T4a–c	–	22.0	
T4d	100	–	
Stage N, %			
N0	8.3	61.3	0.004
N1	52.5	25.3	
N2	24.8	11.4	
N3	12.8	2.0	
De novo M1, %	16.3	16.0	0.4
SBR grade, %			0.002
I	2.6	10.6	
II	51.3	51.4	
III	46.2	36.1	
Hormonal receptors, %			<0.01
Positive	51.9	75.6	
Negative	48.1	24.4	
HER2 overexpression, %	31.8	20.6	<0.01
Triple-negative, %	23.1	14.5	<0.01
Ki-67, %			0.005
$<20\%$	27.2	43.6	
$\geq 20\%$	82.8	56.1	

IBC, inflammatory breast cancer; SBR, Scarff-Bloom-Richardson.

Results

Population

The median age was 48 years in IBC cases and 49 years in non-IBC cases. Around half of the patients were premenopausal (57.3% for IBC vs. 53.6% for non-IBC, $p = 0.31$). Non-IBC cases were T1 in 16.4%, T2 in 52.5%, T3 in 9.1%, and T4 in 22%. There was significantly higher clinical nodal involvement in IBC cases and also significantly more high-grade tumors (Scarff-Bloom-Richardson grade II–III). HER2 overexpression and TN tumors were more common in IBC (Table 1). Luminal breast cancer represented 64.4% of the population (51.9% IBC and 75.6% non-IBC), HER2 overexpression (ER– and/or PR–) was seen in 19.2% (31.8% IBC and 20.6% non-IBC), and TN represented 16.4% (23% IBC and 14.5% non-IBC).

Evaluation of risk factors showed that, when compared to non-IBC, there was no significant association between IBC and several reproductive factors such as early or late age at menarche, early or late age at first pregnancy, and breastfeeding. However, we observed that the use of contraceptives, breastfeeding ≥ 12 months, normal to low BMI, as well as low socioeconomic and education-

Table 2. Evaluation of risk factors in IBC and non-IBC patients

Variable	IBC (n = 160)	Non-IBC (n = 580)	p value	Case-only OR [95% CI]
Median age at menarche, years	13.0	13.0	0.9	–
Menarche ≥13 years, %	54.5	53.0	0.76	1.05 [0.72–1.54]
Menarche ≤10 years, %	3.1	8.1	0.054	0.4 [0.15–1.05]
Median age at first pregnancy, years	23.0	25.0	0.14	–
Age at first pregnancy ≤21 years, %	35.0	27.2	0.13	1.43 [0.88–2.32]
Age at first pregnancy ≥30 years, %	24.0	22.8	0.35	1.07 [0.63–1.82]
Median number of pregnancies	3.5	3.0	0.62	–
Nulliparity, %	11.7	13.5	0.59	0.86 [0.42–1.42]
Breastfeeding, %	62.0	65.3	0.57	–
Duration of breastfeeding ≥12 months, %	30.0	8.4	0.01	4.64 [2.97–7.26]
Use of oral contraceptives, %	30.8	52.7	<0.01	2.49 [1.62–3.84]
Body mass index >35, %	12.6	14.8	0.48	0.82 [0.49–1.39]
Body mass index ≤25, %	48.7	27.7	<0.01	2.48 [1.71–3.58]
Median body mass index	25.0	29.0	0.006	–
Family history of breast cancer, %	28.4	27.8	0.93	0.97 [0.57–1.67]
Age at menopause ≤45 years, %	15.4	31.5	0.089	0.39 [0.13–1.18]
Socioeconomic level, %			0.002	–
High	22.1	37.8		
Intermediate	45.4	47.2		
Low	32.5	15.0		
Educational level, %			0.018	–
Primary	30.0	15.8		
Secondary	26.6	37.4		
University	43.4	46.8		

IBC, inflammatory breast cancer.

al levels were significant risk factors of IBC compared to non-IBC. The duration of contraceptives use was reported in 63% of cases with a median of 3.4 years, without a significant difference between IBC and non-IBC (3.2 vs. 3.5 years, $p = 0.21$). Patients with a BMI ≤ 25 had a 2.48 times higher risk of developing IBC compared to non-IBC. Duration of breastfeeding was the most important risk factor; women who nursed ≥ 12 months had a 4.64 times higher risk of developing IBC compared to non-IBC (Table 2). The OR for use of oral contraceptives was 2.48 (95% CI 1.62–3.84) in favor of the non-IBC group.

When we consider only node-positive tumors, duration of breastfeeding ≥ 12 months remained a risk factor, with an OR of 4.1 (95% CI 2.6–6.3). Low BMI increased the risk of IBC by 2.3 (95% CI 1.3–3.32). Patients who used contraceptives had a 3.36 times higher risk of developing IBC compared with non-IBC (95% CI 1.95–4.7).

We evaluated those risk factors according to hormonal receptors and HER2 status, as shown in Tables 3–5. In luminal breast cancer, there was additionally an association between advanced age at first pregnancy (>30 years) and IBC compared to non-IBC (OR = 3.08, 95% CI 1.2–7.29).

When considering the TN subgroup, duration of breastfeeding ≥ 12 months was no longer a risk factor (Table 5).

Discussion

Our study found several differences in risk factors between IBC and non-IBC. Long breastfeeding duration ≥ 12 months, BMI ≤ 25 , and use of contraceptives were the most significant risk factors. In the TN subgroup there was no impact of long duration of breastfeeding.

The risk factors of breast cancer are nowadays well known, but it is not yet clear whether they are the same in IBC and whether they differ according to hormonal and HER2 receptors. It is commonly known that breastfeeding is a protective factor against the occurrence of breast cancer. Several mechanisms have been suggested to explain it, such as the differentiation of breast tissue and the reduction in the lifetime number of ovulatory cycles [5–7]. A review of the literature and meta-analysis published in 2017 showed that the relative risk was 0.72, 0.86, and 0.89 for women who breastfed their children exclusively, premenopausal women, and postmenopausal women, respectively [8].

Our results about breastfeeding and IBC subtype were contradictory with those reported by Atkinson et al. [9] and Lê et al. [3]. In the latter study, the authors found that long breastfeeding is a risk factor of IBC. It compared cases from North Africa and Europe with different breast-

Table 3. Evaluation of risk factors between IBC and non-IBC in luminal (ER+ and/or PR+) patients

Variable	IBC (n = 83)	Non-IBC (n = 438)	p value	Case-only OR [CI 95%]
Median age at menarche, years	13.0	13.0	0.9	–
Menarche ≥13 years, %	55.9	51.9	0.65	1.17 [0.58–2.37]
Menarche ≤10 years, %	5.9	6.7	0.86	0.87 [0.19–3.84]
Median age at first pregnancy, years	23.0	25.0	0.63	
Age at first pregnancy ≤21 years, %	16.7	21.2	0.26	0.53 [0.17–1.63]
Age at first pregnancy ≥30 years, %	45.8	21.6	0.008	3.08 [1.3–7.29]
Median number of pregnancies	3.0	3.0	0.9	
Nulliparity, %	23.3	14.5	0.19	1.79 [0.73–4.37]
Breastfeeding, %	73.8	64.7	0.24	2.18 [0.79–5.96]
Duration of breastfeeding ≥12 months, %	35.9	9.1	<0.001	5.57 [2.68–11.56]
Use of oral contraceptives, %	54.2	50.1	0.7	0.85 [0.37–1.95]
Body mass index >35, %	23.1	15.0	0.18	1.7 [0.77–3.76]
Body mass index ≤25, %	54.1	28.3	0.001	2.97 [1.5–5.87]
Body mass index	25.0	29.0	0.001	
Family history of breast cancer, %	23.3	27.7	0.59	1.26 [0.52–3.02]
Age at menopause ≤45 years, %	14.3	28.4	0.25	0.42 [0.09–1.95]
Socioeconomic level, %			0.25	–
High	25.7	34.0		
Intermediate	51.4	53.5		
Low	22.9	12.5		
Educational level, %			0.091	–
Primary	31.6	16.8		
Secondary	26.3	39.9		
University	42.1	43.4		

IBC, inflammatory breast cancer.

Table 4. Evaluation of risk factors between IBC and non-IBC in HER2-positive patients

Variable	IBC (n = 50)	Non-IBC (n = 120)	p value	Case-only OR [CI 95%]
Median age at menarche, years	13.0	13.0	0.29	–
Menarche ≥13 years, %	52.7	51.1	0.81	1.06 [0.61–1.83]
Menarche ≤10 years, %	5.4	10.1	0.28	0.5 [1.16–1.55]
Median age at first pregnancy, years	24.0	24.0	0.65	
Age at first pregnancy ≤21 years, %	31.2	31.2	0.99	1 [0.47–2.12]
Age at first pregnancy ≥30 years, %	27.1	21.5	0.45	1.35 [0.6–3]
Median number of pregnancies	3.0	3.0	0.49	
Nulliparity, %	11.9	19.6	0.16	0.55 [0.24–1.28]
Breastfeeding, %	60.0	60.6	0.945	0.97 [0.47–2]
Duration of breastfeeding ≥12 months, %	35.8	6.2	0.0001	8 [3.83–16.8]
Use of oral contraceptives, %	23.0	47.1	0.001	2.99 [1.51–5.92]
Body mass index >35, %	11.2	13.3	0.65	0.82 [0.36–1.87]
Body mass index ≤25, %	47.4	32.6	0.025	1.86 [1.07–3.22]
Body mass index	25.0	28.0	0.013	
Family history of breast cancer, %	36.7	30.6	0.5	0.76 [0.33–1.7]
Age at menopause ≤45 years, %	27.3	31.3	0.78	0.82 [0.2–3.35]
Socioeconomic level, %			0.036	
High	22.0	48.0		
Intermediate	48.7	34.0		
Low	29.3	18.0		
Educational level, %			0.046	
Primary	33.3	12.0		
Secondary	28.6	40.0		
University	28.1	48.0		

IBC, inflammatory breast cancer.

Table 5. Evaluation of risk factors between IBC and non-IBC in TN patients

Variable	IBC (n = 37)	Non-IBC (n = 84)	p value	Case-only OR [CI 95%]
Median age at menarche, years	13.0	13.0	0.31	–
Menarche ≥13 years, %	64.5	58.8	0.57	1.27 [0.54–3.01]
Menarche ≤10 years, %	0.0	11.2	0.051	1.12 [1.04–1.12]
Median age at first pregnancy, years	23.5	27.0	0.08	–
Age at first pregnancy ≤21 years, %	35.6	27.7	0.46	1.45 [0.53–1.96]
Age at first pregnancy ≥30 years, %	14.2	25.5	0.25	0.48 [0.14–1.68]
Median number of pregnancies	3.5	3.0	0.61	–
Nulliparity, %	6.7	5.6	0.84	1.19 [0.2–6.9]
Breastfeeding, %	45.0	61.4	0.2	0.51 [0.18–1.44]
Duration of breastfeeding ≥12 months, %	24.3	10.7	0.053	2.67 [0.96–7.43]
Use of contraceptives, %	42.2	67.2	0.02	2.78 [1.16–6.66]
Body mass index >35, %	13.5	19.3	0.44	0.65 [0.22–1.94]
Body mass index ≤25, %	48.6	23.1	0.007	3.14 [1.35–7.34]
Body mass index	25.0	28.0	0.01	–
Family history of breast cancer, %	26.3	33.8	0.53	1.42 [0.46–4.37]
Age at menopause ≤45 years, %	16.4	42.1	0.23	0.27 [0.02–2.58]
Socioeconomic level, %			0.032	–
High	28.6	60.6		
Intermediate	33.3	27.3		
Low	38.1	12.1		
Educational level, %			0.075	–
Primary	30.0	6.5		
Secondary	20.0	22.6		
University	50.0	71.1		

IBC, inflammatory breast cancer; TN, triple-negative.

feeding habits, which may represent a pitfall of the study. However, in our study all patients were Tunisian and had more or less the same breastfeeding traditions. In the study by Atkinson et al. [9], women with a history of breastfeeding had a lower risk of TN (OR = 0.30, 95% CI 0.15–0.62) and luminal IBC (OR = 0.35, 95% CI 0.18–0.68). In that study the control group were cancer-free women, in our study the control group were non-IBC patients, and there was no role of long duration of breastfeeding in the TN group.

Previous studies have found that TN breast cancer and TN IBC are associated with lower frequency and duration of breastfeeding compared to non-TN breast cancer and non-TN IBC, respectively [10]. Reproductive risk factors and TN breast cancer have also been observed in other studies [11, 12]. The review by Anderson et al. [11] reported that the single protective factor most consistently associated with TN breast cancer was longer duration of breastfeeding. Increased parity, younger age at first birth, older age at menarche, and oral contraceptive use were less consistently shown to be associated with TN breast cancer. Conversely, a case-control study by Woodward [13] looking at potential correlations between breastfeeding and the risk of IBC-specific subtypes reported that breastfeeding was not a risk factor for either TN or ER+ IBC.

In contrast with our results, previous studies have shown that high BMI was associated with an increase in the risk of IBC. As reported by Schairer et al. [14], high BMI was associated with a substantially increased risk of ER-positive and ER-negative IBC in both pre- and peri-/postmenopausal women. It seems that there is a relationship between inflammatory cytokines caused by overweight and angiogenesis in IBC [15]. Those observations do not necessarily mean that normal or low weight is not associated with IBC. In some studies, low BMI was a risk factor of locoregional recurrence after constructive therapy of breast cancer, which may be explained by to a potential role of low BMI and skin involvement in breast cancer [16, 17]. Such observations need to be validated by other studies.

Studies of breast cancer risk among women who receive hormonal contraceptives show inconsistent findings from no elevation in risk to a 20–30% increase in risk. Most studies have assessed women according to whether they were current, recent, or past users of oral contraceptives or whether they had ever used oral contraceptives [18]. The authors also concluded that the risk of increasing breast cancer is correlated with the estrogen level in the pill and with family history of breast cancer.

A recent Chinese study by Zhang et al. [19] examined the relationship between hormonal contraception and IBC. Fouad et al. [20] found that the use of birth control and hormone replacement therapy did not increase the risk of IBC ($p = 0.29$, HR = 1.419, 95% CI 1.4–0.7). Furthermore, Manai et al. [21] in their recent study about 210 Tunisian IBC cases revealed that contraception was not associated with an increase in the risk of IBC, regardless of molecular subtypes. In our study, we found a consistent relationship between the use of oral contraceptives use and the risk of having IBC, especially for the HER subtype (OR = 2.99, 95% CI 1.51–5.92), but we could not evaluate the role of duration of oral contraceptives. In Tunisia, high-dose estrogen-based contraceptives were used in the first decades of birth control programs starting from 1960. This contraception protocol might have led to subsequent higher risk of breast cancer and IBC.

In our study the choice of non-IBC patients, including very-low-risk patients, leads to the question whether the noted differences are really locally advanced versus node-negative, especially given the substantial difference in nodal stage in our population. However, the results in node-positive patients show that those risk factors remain stable even in node-positive non-IBC patients.

It is important to highlight that our study was conducted in breast cancer patients; there was not healthy control group. The evaluated risk factors should not be considered as true demographic risk factors applicable to the general population. The major limitation in our study concerns the absence of a healthy control group. Thus, we do not know whether our results apply to the general population. The sample size of the HER2 and TN subgroups was also small due to the rarity of those two subtypes. It is possible that the absence of associations between some risk factors and IBC subtypes was due to the limited power of the study. In our study those biomarkers were available for most patients. However, we could not further classify luminal tumors into luminal A and luminal B due to lack of more biomarkers [22].

Our results were contradictory with many published data. The Tunisian population is young, with early age at IBC onset. Breastfeeding is very common and long breastfeeding is widely encouraged in the North African cultural context [23, 24]. IBC is more common in the North African population [25]. The risk factors observed in our study could be specific to our region; to our knowledge, they are reported for the first time. Research on breastfeeding mechanisms should be implemented more in order to understand the relationship between breastfeeding and IBC. Underlying normal breast tissues may play a role in enhancing features of IBC. Puberty, pregnancy, breastfeeding, and menopause are major milestones in breast tissue evolution. Early onset of those events may alter normal breast tissue.

Mammary gland involution after the pregnancy-lactation cycle increases the duration of the breast remodeling period, with an increase in mammary progenitor cells and anti-inflammatory mediators [26]. High blood flow to the mammary gland for a long period of time between pregnancy and weaning may be favorable for a vascular tropism of cell proliferation and clonal expansion and after years may lead to breast cancer with vascular emboli and inflammatory aspect [27].

Statement of Ethics

None of the authors has any conflict of interest to declare. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No ethics committee approval is needed for retrospective studies in our national ethical guidelines. There was no use of identifying information for this retrospective study, and no informed consent was needed.

Disclosure Statement

None of the authors has any disclosures to make.

Funding Sources

This study did not receive any grant.

Author Contributions

N. Mejri: idea, data collection, statistical analysis, writing, revision. H. El Benna: data collection, writing. H. Rachdi: writing, statistical analysis. S. Labidi: idea, revision, statistical analysis. M. Benna: idea, statistical analysis revision. N. Daoud: data collection, revision. Y. Hamdi: idea, revision, evaluation of tables. S. Abdelhak: revision. H. Boussen: data collection and revision.

References

- 1 Colditz GA, Rosner BA, Chen WY, Holmes MD, Hankinson SE. Risk factors for breast cancer according to estrogen and progesterone receptor status. *J Natl Cancer Inst.* 2004 Feb;96(3):218–28.
- 2 Chang S, Buzdar AU, Hursting SD. Inflammatory breast cancer and body mass index. *J Clin Oncol.* 1998 Dec;16(12):3731–5.
- 3 Lê MG, Arriagada R, Bahi J, Pfeiffer F, Cammoun M, Tabbane F, et al. Are risk factors for breast cancer similar in women with inflammatory breast cancer and in those with non-inflammatory breast cancer? *Breast.* 2006 Jun; 15(3):355–62.
- 4 Dawood S, Merajver SD, Viens P, Vermeulen PB, Swain SM, Buchholz TA, et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. *Ann Oncol.* 2011 Mar;22(3):515–23.

- 5 Yang L, Jacobsen KH. A systematic review of the association between breastfeeding and breast cancer. *J Womens Health (Larchmt)*. 2008 Dec;17(10):1635–45.
- 6 do Carmo França-Botelho A, Ferreira MC, França JL, França EL, Honório-França AC. Breastfeeding and its relationship with reduction of breast cancer: a review. *Asian Pac J Cancer Prev*. 2012;13(11):5327–32.
- 7 Palmer JR, Boggs DA, Wise LA, Ambrosone CB, Adams-Campbell LL, Rosenberg L. Parity and lactation in relation to estrogen receptor negative breast cancer in African American women. *Cancer Epidemiol Biomarkers Prev*. 2011 Sep;20(9):1883–91.
- 8 Unar-Munguía M, Torres-Mejía G, Colchero MA, González de Cosío T. Breastfeeding Mode and Risk of Breast Cancer: A Dose-Response Meta-Analysis. *J Hum Lact*. 2017 May; 33(2):422–34.
- 9 Atkinson RL, El-Zein R, Valero V, Lucci A, Bevers TB, Fouad T, et al. Epidemiological risk factors associated with inflammatory breast cancer subtypes. *Cancer Causes Control*. 2016 Mar;27(3):359–66.
- 10 Bambhroliya A, Van Wyhe RD, Kumar S, Debeb BG, Reddy JP, Van Laere S, et al. Gene set analysis of post-lactational mammary gland involution gene signatures in inflammatory and triple-negative breast cancer. *PLoS One*. 2018 Apr;13(4):e0192689.
- 11 Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. *Breast Cancer Res Treat*. 2014 Feb;144(1):1–10.
- 12 Stecklein SR, Reddy JP, Wolfe AR, Lopez MS, Fouad TM, Debeb BG, et al. Lack of Breastfeeding History in Parous Women with Inflammatory Breast Cancer Predicts Poor Disease-Free Survival. *J Cancer*. 2017 Jul;8(10): 1726–32.
- 13 Woodward WA. Inflammatory breast cancer: unique biological and therapeutic considerations. *Lancet Oncol*. 2015 Nov;16(15):e568–76.
- 14 Schairer C, Li Y, Frawley P, Graubard BI, Wellman RD, Buist DS, et al. Risk factors for inflammatory breast cancer and other invasive breast cancers. *J Natl Cancer Inst*. 2013 Sep;105(18):1373–84.
- 15 Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr*. 2004 Sep;92(3):347–55.
- 16 Chen CH, Lo YF, Tsai HP, Shen SC, Chao TC, Chen MF, et al. Low body mass index is an independent risk factor of locoregional recurrence in women with breast cancer undergoing breast conserving therapy. *Chang Gung Med J*. 2009 Sep–Oct;32(5):553–62.
- 17 Marret H, Perrotin F, Bougnoux P, Descamps P, Hubert B, Lefranc T, et al. Low body mass index is an independent predictive factor of local recurrence after conservative treatment for breast cancer. *Breast Cancer Res Treat*. 2001 Mar;66(1):17–23.
- 18 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*. 2017 Dec; 377(23):2228–39.
- 19 Zhang L, Huang Y, Feng Z, Wang X, Li H, Song F, et al. Comparison of breast cancer risk factors among molecular subtypes: a case-only study. *Cancer Med*. 2019 Apr;8(4):1882–92.
- 20 Fouad TM, Ueno NT, Yu RK, Ensor JE, Alvarez RH, Krishnamurthy S, et al. Distinct epidemiological profiles associated with inflammatory breast cancer (IBC): a comprehensive analysis of the IBC registry at The University of Texas MD Anderson Cancer Center. *PLoS One*. 2018 Sep;13(9):e0204372.
- 21 Manai M, Finetti P, Mejri N, Athimni S, Birnbaum D, Bertucci F, et al. Inflammatory breast cancer in 210 patients: A retrospective study on epidemiological, anatomo-clinical features and therapeutic results. *Mol Clin Oncol*. 2019 Feb;10(2):223–30.
- 22 Ades F, Zardavas D, Bozovic-Spasojevic I, Pugliano L, Fumagalli D, de Azambuja E, et al. Luminal B breast cancer: molecular characterization, clinical management, and future perspectives. *J Clin Oncol*. 2014 Sep;32(25): 2794–803.
- 23 Bouanene I, ElMhamdi S, Sriha A, Bouslah A, Soltani M. Knowledge and practices of women in Monastir, Tunisia regarding breastfeeding. *East Mediterr Health J*. 2010 Aug;16(8): 879–85. French.
- 24 Laamiri F, Barich F, Bennis A, Bouslah A, Soltani M. Connaissances et pratiques des mères en matière d'allaitement maternel. *J Pédiatr Pueric*. 2019;32(3):128–39.
- 25 Duke TJ, Jahed NC, Veneroso CC, Da Roza R, Johnson O, Hoffman D, et al. A cluster of inflammatory breast cancer (IBC) in an office setting: additional evidence of the importance of environmental factors in IBC etiology. *Oncol Rep*. 2010 Nov;24(5):1277–84.
- 26 Betts C, Pennock N, Goddard E, Guo Q, Jindal S, Borges V, et al. Postpartum tissue remodeling drives breast cancer metastasis. *Cancer Res*. 2018;78(13 suppl):SY38-02.
- 27 Zaragoza R, García-Trevijano ER, Lluch A, Ribas G, Viña JR. Involvement of Different networks in mammary gland involution after the pregnancy/lactation cycle: implications in breast cancer. *IUBMB Life*. 2015 Apr;67(4): 227–38.