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BREAST CARCINOMA IN WOMEN 40 YEARS OF AGE OR YOUNGER: EPIDEMIOLOGICAL PROFILE IN SERIES OF 135 CASES FROM EASTERN ALGERIA

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ABSTRACT

Background: Actually, breast cancer constitutes one of the most health problems in Algeria and the leading cause of death among Algerian women. Breast cancer in young women is a rare form, but it has an aggressive behavior associated with a poor prognosis. **Aims:** this study focuses to report breast cancer phenotype in Algerian young women. **Material and methods:** in order to better understand the determinants and tumor biology that may explain earlier onset and aggressive breast cancer characteristics in Algeria from December 2011 to July 2014, 135 patients aged 40 years and under diagnosed with breast cancer were included in the study. **Results:** Of the 135 patients recorded, 65.9% patients were aged between 36-40 years. The mean age was 36.29 years. A significantly higher proportion of women were overweight or obese (62.9%). 75.6% of patients had full-term pregnancy. 29.6% of breast cancers were diagnosed during pregnancy or after childbirth. Positive breast cancer family history was found in 34.1%. In 87.4% of cases the revealing sign was breast mass. Stage II and III associated with axillary lymph nodes involvement, higher pathological grade and hormone receptor positive were predominant. Neo-adjuvant was administered to 28.8%. 74.1% of patients underwent radical mastectomy using Patey technique with complete axillary dissection. Distant metastases at diagnosis were seen in 13.3%. The mean clinical tumor size was 4.80 cm. 71.1% of tumors were invasive ductal carcinoma. **Conclusion:**

early-onset Algerian breast cancer is more likely to present at an advanced stage with poor prognosis.

KEYWORDS: Algeria, breast cancer, young women, prognosis, advanced.

INTRODUCTION

The definition of breast cancer (BC) among young women varies, most studies referring to women under either age 35, 40 years or simply pre-menopausal as 'young'.[1] We have been focusing on women in their early 40s and younger. BC detected in young women is associated with an aggressive phenotype and poor prognosis than their older counterparts.[2,3,4,5,6] There are few studies examining BC in women 40 years of age and younger, particularly in Algerian population. This study aimed to assess epidemiological profile of BC in eastern Algeria.

BC is the most common female malignancy; accounting for about 23% of women malignant tumors, its incidence is particularly high in developed countries.[7] In young women, BC incidence is low (<17 cases/ 100,000 women or < 6% of breast cancer of all ages).[8,9] About 1% of patients with BC are below 30 years and 6.5% between 30 and 40 years. [1] BC is the leading cause of death among women in Europe.[10] It is also considered as the first female cancer in Morocco,[11] Algeria,[12] Tunisia,[13] and Jordan[14] particularly affecting young women. Age is considered to be the most worst prognostic factors.[6,15] Considering that BC occurs in younger women in our country, it is necessary to know their epidemiological features among women aged of 40 and under diagnosed with this tumor.

MATERIEL AND METHODS

This is a descriptive cross-sectional retrospective epidemiological approach focused on women diagnosed or treated with primitive BC at the age of forty years old and less from December 2011 to July 2014 in Medical Oncology unit of University Hospital Dr BENBADIS of Constantine, medical oncology of Anti cancer center of Batna and that of Setif, 135 patients from eastern Algeria were selected. Data collection including several determining factors of the disease such as age at diagnosis, puberty, parity, lactation. were performed during an interview for all patients in which they were interviewed on demographic, reproductive history and other known or suspected breast cancer risk factors using a validated questionnaire, participants provided many details. The patient's medical

records are used to collect the phenotypic characteristics of tumors and treatment protocols. The selected data were entered and analyzed using SPSS 20.0.

RESULTS

One hundred thirty five women were identified in the study period. The patients mean age was 36.29 years (23-40). 65.9% of patients aged between 36 and 40 years. Most patients were housewives (51.9%), married (74.8%), overweight (40%) or obese (22.9%), had full-term pregnancy (75.6%), used oral contraception (58.5%) for an average duration of 4.03 years, performed breastfeeding (65.9%), had a delay between the first signs of cancer and consultation varied from 1 to 6 months (51.7%), presented with tumors more often in the left breast (58.5%) and were located on the upper outer quadrant (38.5%), treated with mastectomy (74.1%). In our series, BC is less likely among white patients (41.5%). The menarche age was specified in 128 patients (94.8%), which varies between 10 and 18 years with an average age of 13.69 years. About 23% of cases had their first menarche at the age of 14th. Age of first pregnancy was between 17 and 38 years with a mean age of 25.72 years. The predominant breast cancer revealed sign was breast masse (87.4%). Inflammatory cancers represented 13.3%. BC was diagnosed during pregnancy in seventeen patients. From a total of 132 breast tumors (97.8%), 80 and 47 tumors were grade II and III tumors respectively. Young patients diseases were in most cases diagnosed in advanced stages (III A or III B). Histological examination of the surgical specimen found that invasive ductal carcinoma was the most common tumor (71.1%), followed by invasive lobular carcinoma (10.4%). 60%, 56.3% and 30.4% of tumors were oestrogen, progesterone and human epidermal growth factor receptor-2 positives, respectively. 25.2% of breast tumors are found to be triple-negative. Seventy-nine tumors were associated with lymph node involvement (N+) and it was accompanied with capsular rupture in 14.1% of cases. Vascular and lymph emboli were present in 25.9%, 17% respectively. Axillary lymphadenopathy were absent in 40% of cases. Neo-adjuvant chemotherapy was administered to 17.8% of patients. The majority of young patients received a protocol type FEC+TxT or AC- TxT, with treatment number varies from 3 to 16 and an average of 6. Nineteen patients underwent a second line chemotherapy. 60% of cases had no hormonal therapy and 20% of patients were treated with tamoxifen. Sixty-five patients received adjuvant radiotherapy. Over evolution plan; 61 events were finding: six as recurrence which five were local and one contralateral, fifty-five distant metastases were alive at mean follow-up of 5.04 months with predominantly bone secondary location (21.5%). A breast cancer family history in the 1st, 2nd or 3rd degree

was found in 46 cases (Study population characteristics of Algerian young patients are summarized in (Table 1).

Table. 1 Characteristics of the Study Population

Characteristics	Rate (%)
Epidemiologic characteristics	
Age at diagnosis (years) mean: 36.29 (23-40) 20-25 26-30 31-35 36-40	 01.5 11.1 21.5 65.9
Urban environment Rural environment	25.9 74.1
Profession Housewives Liberal profession Official State cadre	 51.9 25.2 14.8 08.1
Marital Status Married Single Divorced Widowed	 74.8 20.7 03.0 01.5
Patients Distribution according to BMI (kg/m^2) Underweight Normal weight Overweight Obesity	 03.0 34.1 40.0 22.9
Physical activity Any activity Aerobics Others	 89.6 04.4 06.0
Screening Yes No	 03.7 96.3
Alcohol	00.0
Smoking	00.0
Menarche age (years) ≤ 11 12-14 ≥ 15	 11.1 53.4 30.4
Age of first pregnancy (years) < 20 20-30 30-35 > 35	 09.7 45.8 15.4 04.4

Patients had full-term pregnancy	75.6
Nulliparity	24.4
Total cumulative duration of breastfeeding (months)	
24	15.6
Less than 24	46.7
More than 24	03.7
Breast cancer diagnosis period	
During pregnancy	12.6
During breastfeeding	17.0
Excluding these period	70.4
First consultation delay (months)	
< 3	15.5
3-6	36.2
6-12	39.9
> 12	17.7
Tumor characteristics	
Histology	
Invasive ductal carcinoma	71.1
Invasive Lobular carcinoma	10.4
Invasive ductal and lobular carcinoma	07.4
Invasive ductal carcinoma + ductal carcinoma in situ	03.7
Other	07.4
Stage	
0	01.5
I	05.9
II	27.5
III	43.7
IV	11.9
Unknown	09.6
Grade	
Grade I	0.70
Grade II	59.3
Grade III	34.8
Unknown	02.2
Laterality	
Right	40.7
Left	58.5
Bilateral	00.7
Tumor localization	
Upper outer quadrant	38.5
Upper inner quadrant	11.1
Entire breast	08.1
Retroareolar	06.7
Other	29.6
Human epidermal growth factor receptor-2	
Positive	30.4
Negative	69.6
Estrogen receptor status	

Positive Negative	60.0 40.0
Progesterone receptor status Positive Negative	 56.3 43.7
lymph node status N+ N- Unknown	 58.5 34.8 06.7
Axillary lymphadenopathy Unilateral Bilateral None fixed Mobile Unknown	 54.1 05.9 40.0 23.0 37.0 40.0
Treatment characteristics	
Surgery Mastectomy Lumpectomy Bilateral mastectomy Other	 74.1 09.6 00.7 15.6
Radiation Yes No	 48.1 51.9
Chemotherapy Neoadjuvant Adjuvant	 28.8 71.1
Hormonal therapy No TAM Nolvadex+Zoladex Zoladex	 60.0 20.0 16.3 02.2
Outcomes Distant metastases Bone secondary location Lung secondary location Recurrence Local Contralateral	 40.7 21.5 05.2 04.4 03.7 00.7

DISCUSSION

The increase breast cancer incidence in the last twenty years has been observed in world population.[16] In Lebanon and France, BC is the most common cancer with a high incidence among women.[17, 18, 19] Worldwide, BC estimation was more than 1.4 million new cases with 460,000 deaths in 2008.[20] In African countries, in general, BC is the second leading cause of death in women after cervical cancer.[21] In Algeria, in 2008, 7500 new BC cases diagnosed

each year with over 3500 deaths.[20] BC among women under 40th is the most frequently cancer; it represents 30 to 40% of female cancers.[6, 22, 23] In the United States the BC prevalence in women under 40th is less than 5%.[24] 10% of new BC cases in France are in women under 40 years.[25] BC in Algerian woman is a major public health problem that continues to increase largely. According to Pr. A. BENDIB, 12% of women with BC are under 35 and 20% are under 40 years.[26] BC is a rare disease in young women; however, it has attracted more interest because of its rapid evolution.[4] Breast tumors in younger women almost have a more aggressive biological behavior with poorer prognosis characteristics, higher risk of recurrence and mortality compared to older women.[27, 28, 29] BC prognosis has improved in these recent years, especially for the early stages. Young age is not just the only factor responsible for the poor prognosis.[6, 30, 31] BC in our study among patients aged of 40 years and below is characterized by: overweight and obesity among nearly two thirds of patients (63%). According to[17], 30.9% are overweight or obese. This high rate is influenced by many factors including the sedentary lifestyle, change of diet pattern (high in fat and low in fiber), westernized lifestyle of Algerian women. Studies among premenopausal women showed that BC increased risk associated with higher levels of endogenous estrogen[32], authors show clear associations between obesity, estrogen serum concentrations and increased risk of BC; the risk seems related to the exposure period.[33] 89.6% of patients do not practice any physical activity. 4.4% of cases practice aerobic exercise as regular activity. Several studies have evaluated the impact of physical activity and body size on breast cancer risk, these factors are among the few suspected factors who can change the risk.[34, 35] In young women, the current data suggest a greatly reduced breast cancer risk associated with physical activity.[36]

The mean age of patients was 36.29 years (23-40). It is less that than found in.[27, 37, 38] However, A. KWONG et al and JL. GNERLICH et al found a median age equal to 36 years, which in agreement with our result (ranges are respectively 24-39 and 11-39).[4, 39] This difference in the mean age noted between countries may be explained by the presence of genetic factors that may influence the age of early-onset breast cancer. Our data show that the dominant age group are those aged between 36-40 years which represent 65.9% of the total population. According to[8], less than 1% of BC patients were in the age group of 20-29, 6.5% were in the 30-39 age group and 15.2% were in 40-49 years age group. According to[29,40,41,42], age at diagnosis is an important prognosis factor particularly the young age is considered as poor prognosis indicator and a negative effect on survival and the relapse

occurrence. However, studies[43, 44, 45] reported no negative effect of young age on survival. Young women diagnosed with BC typically receive more aggressive treatment than their older counterparts which may explain their low survival rates. 41.5% of patients were blondes against 92.8% in series of.[8] According to[9,46], young black women under 40 had higher BC incidence rate. 51.9% of patients were housewives. In our study this layer is often characterized by poverty, a lack of health information and a high nervousness. 74.8% of patients were married, followed by 20.7% were single, this is consistent with results of [4]. The husband is an important pillar which plays a crucial role in the medico-psychological care of his wife. In 23% of subjects, the age at menarche was specified to 14 years (mean 13.69 years; range 10–18). Similar results were found in these studies.[47, 48] Early puberty (≤11 years) was founding in 11.1% of patients. According to[47], 19.01% of cases were identified with early menarche. Increased BC risk is strongly linked with early age at menarche.[33] 24.4% of patients were nulliparous, this is consistent with result of.[33] 75.6% of cases had full term pregnancies versus 80% in the series of[27] The long-term risk for women who have given birth to at least one child remains lower than that of nulliparous.[48] In our study, the average age at first pregnancy was 25.72 years (17-38 years), this result is similar to that found by[49] 25.9% of subjects had a late pregnancy. The average pregnancies number was 3.54 (1-11 pregnancies). 6.7% were primiparous, 48.9% were paucipares (2-4) and 19.2% were multiparous (5-8). Only one patient was grand multiparous (11 children). Early age at first full-term pregnancy and grand multiparity reduce BC risk.[46] It is constantly reported in the literature[50] that estrogen stimulation increases the BC risk and consequently increasing its frequency; this risk increases with early menarche, nulliparity and late pregnancy. Diagnosis with breast cancer two years after giving birth to a child is associated with a low survival rate, regardless disease stage. 58.5% of patients have been taking oral contraceptives for an average duration of 6.81 years (0.5-18). Age at the first time of using oral contraceptive was ranged from age 18 to 35 years (mean 25.95). Similar results were found in other studies.[17, 48] Taking oral contraceptives greatly increases the BC risk in young women.[46] The prevalence of breastfeeding practice among patients was 65.9% for an average period of 36.51 months (1-144). According to[47], 66.9% of cases were practiced breastfeeding. Breastfeeding reduces the risk of invasive BC, especially if they breastfeed for long period, even in BRCA1 carriers.[49] BC risk decreased by 7% for each new term pregnancy and 4.3% for each year of breastfeeding regardless of ethnic origin, age, menopausal status, number of children and age of women at first birth.[51] 74.1% of cases were from urban area. It is characterized by sedentary lifestyle. Over young patients

diagnosed with BC in our series, 23% had breast disease before the cancerous lesion confirmation, 8.9% of these cases had a fibroadenoma.

Only one patient has been using chewing tobacco for 15 years until cancerous conformation. Active smoking and alcoholism were not found in our study population which are considered taboo in Algerian society.

BC was found in about 12.6% and 17% of pregnant and lactating women. Breast cancer is the most common type of cancer found during pregnancy. According to the literature, association between BC and pregnancy is a rare event which represents 0.2-3.8% of BCs.[25] A significant number of patients in our study have refused to end pregnancy. Diagnosed with BC during pregnancy significantly increase the risk of BC mortality.[52] Left breast tumors were present in 58.5% of patients, this rate is similar to those of.[4, 48] Most cancers were occurred in the upper outer quadrant, with more than 38.5%, the same result was found in these studies.[13, 48] Predominance of BC laterality can be explained by breastfeeding practices. Breast cancer bilateral form was found only in one patient in our series, this form is rare.

Breast self examination was the most revealer sign of cancer in our study, identical finding for.[13, 47, 48, 53] According to[54], breast self examination permits the detection of BC and reduce the cumulative BC mortality. The nipple retraction was found in 34.8% of cases. Axillary lymph nodes were present in 60% of cases, this rate is significantly higher than that found in.[27] 13.3% of patients were diagnosed three months after cancer symptom onset (mean: 8.27, 1-48 months). This result is in agreement with that of.[48] Lag time between onset of clinical symptoms and first diagnosis was more or less long and differs depending on the case, an extensive delay in consultation among BC patients in the present study was observed, it could be explained by the practice of traditional treatment before referral to the medical structure because a significant rate of women who believe that traditional medicine is more reliable on the one hand and on the other the fear of BC in this young age influencing its feminine prevents women to consult with a qualified physician since the onset of first sign. BC patients had relatively large tumor at diagnosis with an average size of 4.80 cm (1 to 18 cm). Younger women had tumors that were more likely to be higher.[4] According to[5], the tumor size plays a major role in predicting survival in BC patients. Given the lack of routine screening guidelines for women under 40th, it is not surprising that they are more likely to have tumors tend to be large. Rate of BC screening was very low among study subjects

(3.7%). Inflammatory BC was found in 13.3% of subjects, it is more likely to be diagnosed in women of African descent and young women[55], it is an especially aggressive type of BC frequently raised in developing countries (access to care). Stage Classification UICC was specified in 90.4% of patients, the common stages were IIIA, IIIB (16.3% and 17% respectively). According to studies[4, 39, 56, 57], young women are more likely to be diagnosed at an advanced stage. This diagnostic delay is explained by the late consultation among the majority of patients, but also by the lack of routine screening system especially in young women at higher BC risk and the backwardness of mammography appointments in hospitals which greatly influences the disease evolution. Given the BC advanced stage, 74.1% of patients underwent radical surgery with axillary dissection according to Patey technique and 9.6% had received conservative surgery, this is consistent with the results of.[17, 38, 48] According to[58], 59% of cases were treated with mastectomy. Young patients diagnosed with BC were more likely to be treated with mastectomy versus older women.[4, 6, 59] In developed countries, most patients with BC are treated by conservative treatment. The frequent use of Patey technique is explained primarily by the disease advanced stage and the lack of radiation therapy that is required in conservative surgery. Radical treatment reduces the risk of local recurrence. Histologically, the infiltrating ductal carcinoma represents 71.1% of cases in our series. This result is similar to those of.[27, 37, 38, 48, 56, 60] Carcinoma in situ was present in 1.4% of cases. Ductal invasive carcinoma associated with carcinoma in situ represent 03.7% of cases. Ductal carcinoma in situ rate is lower compared to that reported by the literature since it quickly can progress to become invasive cancer because of the diagnosis delay observed among patients in our study. 59.3% of tumors were grade II and 34.8% were grade III, this is consistent with results of.[11, 27] Some series had results which were different from ours.[5,27,37,38] Studies show that young women diagnosed with BC have high-grade tumors compared with their older counterparts.[4, 39, 59, 61] The lymph node invasion in our series was found in 58.5% of cases and in 68.6, 50, 52.5 and 67% according to.[5, 53, 58, 62] Young women are diagnosed with tumors that are more likely to have positive lymph nodes.[4, 59] Vascular emboli were found in 25.9% (35/78 cases) of cases in our series and in 25% and 30% of cases in series of.[48,53] Capsular rupture was found in 14.1% (19/107 cases) of patients and in 36.36% (8/22 cases) in the series of.[48] About 60% of tumors were estrogen receptor positive and 56.3% were progesterone receptor positive, this result is similar to that of.[38] The human epidermal growth factor receptor 2 was positive in 30.4% of cases. It varies from 30.2% according to[37] to 30.6% according to.[38] The majority of tumors among Chinese young women were estrogen receptor and progesterone receptor positive, but they had a higher

proportion of cerbB2-positive tumors.[39] Young patients in our series had a positive rate of HR higher than expected, but similar to recent data reported in the literature. Neoadjuvant chemotherapy was administered to 28.9% and 71.1% of patients received adjuvant chemotherapy. 40% of cases were treated with hormonal therapy mainly type tamoxifen. It was administered in 20% of cases with positive hormone receptors, followed by 16.3% had received treatment consisting of TAM associated with zoladex. Actually, tamoxifen is the most important hormonal therapy administered to women with invasive breast carcinomas and hormone receptor-positive.[32] 27.4% of patients received targeted therapy with trastuzumab and only 48.1% of patients received radiotherapy. Postoperative radiotherapy and chemotherapy among young patients diagnosed with BC significantly reduce the rate of recurrence and mortality associated with this disease.[63, 64, 65] The largest shift observed in our series between the various therapeutic methods identified in BC patients and the treatment received could be explained by the lack of centers for radiation generating appointments far reaching more than 20 months after the end of chemotherapy. This treatment is very expensive in private institutions. In our series, the rate of local recurrence was 3.7%. The recurrence risk seems to be constant throughout life, so the young age at diagnosis is a cumulative risk of recurrence.[66] According to[57], among young women, the high triple-negative rate leads to a high risk of recurrence. We found that 40.7% of subjects had secondary localization. Patients were diagnosed with bone predominant metastatic disease (21.5%), followed by 5.2% of liver metastases. Metastases at diagnosis represent 13.3%. 9.6% of metastases were bony. BC is rapidly changing in a metastatic table. According to[13], 15.4% of tumors were metastatic at diagnosis, with 56% of bone metastases. 20.0% of patients received medical treatment before the diagnosis of cancerous lesions since their lesion considered as benign, while 16% was initially diagnosed with a benign disease in the series of.[27] Because mammography is not recommended or sensitive among young women due to the high density of breast tissue[67], we must identify relevant preventive approaches. The overall survival in this series was 20.33 months (2-48 months). It has been shown that the high tumor grade, lymph node status and the presence of distant metastases at diagnosis contribute to poor prognosis in women under 40 with BC.[3, 68, 69] The death rate from BC in our population during the study period was 3%. This finding is similar to that reported by.[47] Increase overall BC incidence rate among Algerian young women appears to be mainly the result of the increasing incidence of tumors expressing hormone receptor positive. We have observed that was an increased rate of tumors with hormone receptors positive among young women than previous years. Hormonal factors may explain the

explosion of BC that mostly affects young women. Studies suggest that nulliparity, early age at menarche, elevated BMI are associated with an increased risk of developing hormone-sensitive tumors. The lack of routine screening program for young women explains the tumor aggressive behavior in this age group.

A family history of BC in the 1st, 2nd or 3rd degree was found in 34.1% of patients. According to the literature[70], 20 to 30% of women diagnosed with BC have a family history, but only 5-10% of cancers have a genetic origin.[71]

CONCLUSION

The modern westernized lifestyle of Algerian young women influence significantly the increasing incidence of BC in Algeria (decline in age at marriage, late age at first pregnancy, overweight and obesity, decreased breastfeeding period, ...). Cancer in Algerian young women imperatively requires particular attention to the diagnostic, therapeutic and psychological plans to help these women overcome the heavy burden of this disease. Young women are particularly vulnerable to emotional distress and psychosocial issues and should receive appropriate help. Those at high risk of developing breast cancer should be followed carefully. Algerian women need an increased awareness for breast cancer.

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REFERENCES

1. M. ESPIE, PH. COTTU. Cancer du sein de la femme jeune: problèmes et questions. Path Biol, 2003; 51: 391-2.
2. D. COLAK, A. NOFAL, A. ALBAKHEET, M. NIRMAL, H. JEPREL, A. ELDALI, T. AL-TWEIGERI, A. TULBAH, D. AJARIM, OA. MALIK, MS. INAN, N. KAYA, BH. PARK, SM. BIN AMER. Department of Biostatistics, Epidemiology and Scientific Computing, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.
3. M. CHUNG, HR. CHANG, KI. BLAND, HJ. WANEBO: Younger women with breast carcinoma have a poorer prognosis than older women. Cancer, 1996; 77(1): 97-103.
4. JL. GNERLICH, AD. DESHPANDE, DB. JEFFE, A. SWEET, N. WHITE, JA. MARGENTHALER: Elevated Breast Cancer Mortality in Women Younger than Age 40 Years Compared with Older Women Is Attributed to Poorer Survival in Early-Stage Disease. Journal of the American College of Surgeons, 2009; 208(3): 341-347.

5. NS. EL SAGHIR, M. SEOUD, MK. KHALIL, M. CHARAFEDDINE, ZK. SALEM, FB. GEARA, et al. Effects of young age at presentation on survival in breast cancer, BMC Cancer., 2006; 6: 194, doi: 10.1186/1471-2407-6-194.
6. H. FREDHOLM, S. EAKER, J. FRISELL, L. HOLMBERG, I. FREDRIKSSON, H. LINDMAN. Breast cancer in young women: poor survival despite intensive treatment, PLoS ONE., 2009; 4: e7695, doi: 10.1371/journal.pone.0007695.
7. DM. PARKIN, F. BRAY, J. FERLAY, P. PISANI: Global cancer statistics, 2002. Ca-a Cancer Journal for Clinicians, 2005; 55(2): 74-108.
8. GM. SWANSON, CS. LIN: Survival patterns among younger women with breast cancer: the effects of age, race, stage, and treatment. J Natl Cancer Inst Monogr, 1994; 16: 69-77.
9. LA. BRINTON, ME. SHERMAN, JD. CARREON, WF. ANDERSON: Recent Trends in Breast Cancer Among Younger Women in the United States. Journal of the National Cancer Institute, 2008; 100(22): 1643-1648.
10. F. MOLINIE et al. Incidence et pronostiques des cancers du sien découverts au cours et en dehors du programme de dépistage organize en loire –Atlantique (1991-2002). Revue d'epidémiologie et de santé publique., 2008; 56: 41-49.
11. F. ABBASS, S. BENNIS, K. ZNATI, Y. AKASBI, J.K AMRANI, O. EL MESBAHI et A. AMARTI. Le profil épidémiologique et bilogique du cancer du sein à Fès-Boulemane (maroc) EMHJ., 2011; 17(12).
12. Y. BELKACEM, H. BOUSSEN, M. HAMDI CERIF, A. BENIDER, H. ERRIHANI, H. MRABTI, K. BOUZID, A. BENSALEM, S. FETTOUKI, M. BEN ABDALAH, L. ABID, J. GLIGOROV. Epidémiologie des cancers du sein de la femme jeune en Afrique du nord, 32es J de la SFSPM, Strasbourg, nov 2010.
13. S. BEN AHMED, S. ALOULOU, M. BIBI, A. LANDOLSI, M. NOUIRA, L. BEN FATMA, L. KALLEL, O. GHARBI, S. KORBI, H. KHAIRI, C. KRAIEM. Pronostic du cancer du sein chez les femmes tunisiennes: analyse d'une série hospiyalière de 729 patientes. Santé publique, 2002; 14(13): 231-241.
14. AA. Abalkhail, HM ZAHAWI. NM ALMASRI. O K HAMEED. The role of young population structure in determining age distribution of breast cancer in Jordan. Journal of the Bahrain Medical Society; Majallat Jam'īyat al-Atibbā'al-Bahraynīyah 01/20 03; 15(1): 28-33.
15. E. Yildirim, Dalgic T, Berberoglu U: Prognostic significance of young age in breast cancer. Journal of Surgical Oncology, 2000; 74(4): 267-272.

16. L. BOULANGER, D. VINATIER. Epidémiologie du Cancer du sein. CHRU de Lille., 2012.
17. H. GUENDOUZ, W. CHETIBI, A. ABDELOUAHAB, A. BENDIB. Cancer du sein de la femme de moins de 35 ans: étude rétrospective à propos de 612 cas. 32es journées de la SFSPM à Strasbourg nov. 2010.
18. American Cancer Society: Cancer Facts and Figures, 2004; 3(10).
19. SM. ADIB, AA. MUFARRIJ, AI. SHAMSEDDINE, SG. KAHWAJI, P. ISSA, NS. EL-SAGHIR: Cancer in Lebanon: An Epidemiological Review of the American University of Beirut Medical Center Tumor Registry (1983-1994). Annals of Epidemiology, 1998; 8: 46-51.
20. A. MAHNANE, M. HAMDI CHERIF, Epidémiologie du cancer du sein en Algérie. Actualités dans la prise en charge multidisciplinaires des cancers du sein en 2012.SAOM.2012.
21. GAETAN Mac GROGAN: Les néoplasies mammaires non invasives et invasives (le rôle du pathologiste). VII journée franco-africaines de pathologie. Niamey 11 au 13 février 2003.
22. BOTTOM, O'LEARY, SHEAFFER, PHILLIPS, SHU et al. Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975–2000. National Cancer Institute, NIH Pub. No. 06–5767. Bethesda, MD 2006.
23. LD. MARRETT, J. FROOD, D. NISHRI, AM. UGNAT. Cancer incidence in young adults in Canada: preliminary results of a cancer surveillance project. Chronic Dis Can, 2002; 23: 58–64.
24. K. ZABICKI, J. COLBERT et al. Breast cancer diagnosis in women lower 40 versus 50 to 60 years: increasing size and stage disparity compared with older women over time. Annals of surgical oncology, 2006; 13: 1072-1077.
25. E. MATHIEU, P. MERVIEL, E. BARRANGER, J.M ANTOINE, S. UZAN. Journal de gynéco-obstétrique et de biologie de la reproduction. Paris.
26. A. BENDIB. Algérie: 12% des femmes atteintes du cancer du sein ont moins de 35 ans. http://www.algerie-focus.com/blog/2013/10/algerie-12-des-femmes-atteintes-du-cancer-du-sein-ont-moins-de-35-ans/ Par Djamila Ould Khettab| octobre 2013; 5.
27. JR. CUAN MARTINEZ, FE. MAINERO RATCHELOUS, IU. AGUILAR GALLEGOS, AB. MIRANDA, MA. BUENROSTRO PINEDA, IB. PORTILLO, A. EDELMIRA, A. CORTES HERRERA, JJ. BURGUETE VERA. Comparacion de las caracteristicas de

pacientes de 40 o menos y 70 anos o mas de edad con carcinoma mamario. Ginecol Obstet Mex, 2008; 76(6): 299-306.

28. HO ADAMI, B. MALKER, L. HOLMBERG, et al. The relation between survival and age at diagnosis and breast cancer.NEngl J Med., 1986; 315: 559–563.
29. A. DE LA ROCHEFORDIERE, F. CAMPANA, J. FENTON, et al. Age as a prognostic factor in premenopausal breast cancer. Lancet., 1993; 341: 1039–1043.
30. P. TAI, G. CSERNI, J. VAN DE STEENE, G. VLASTOS, M. VOORDECKERS, et al. Modeling the effect of age in T1-2 breast cancer using the SEER database. BMC Cancer, 2005; 5: 130.
31. M. SANT, R. CAPOCACCIA, A. VERDECCHIA, J. ESTEVE, G. GATTA, et al. Survival of women with breast cancer in Europe: variation with age, year of diagnosis and country. The EUROCARE Working Group., Int J Cancer, 1998; 77: 679–683.
32. HV. THOMAS, GK. REEVES, TJ. KEY. Endogenous estrogen and postmenopausal breast cancer: a quantitative review. Cancer Causes Control, 1997; 8*:* 922-928.
33. R. CLARKE, M. C LIU, K. B BOUKER, Z. GU, R. Y LEE, Y. ZHU, T. C SKAAR, GOMEZ. B, O'BRIEN. K, WANG. Y, A HILAKIVI-CLARKE. L. Antiestrogen resistance in breast cancer and the role of estrogen receptor signaling. Oncogene, 2003; 22: 7316-7339.
34. RG. ZIEGLER. Anthropometry and breast cancer. J. Nutr, 1997; 127: 924S-928S.
35. A. MCTIERNAN, C. ULRICH, S. SLATE, J. POTTER. Physical activity and cancer etiology: associations and mechanisms. Cancer Causes Control, 1998; 9: 487-509.
36. CM. FRIEDENREICH, I. THUNE, LA. BRINTON, D. ALBANES. Epidemiologic issues related to the association between physical activity and breast cancer. Cancer (Phila.), 1998; 83(Suppl)*:* 600-610.
37. B. MCAREE, ME. O'DONNELL, A. SPENCE, LIOE, TF. MCMANUS DT, RA. SPENCE. Breast cancer in women under 40 years of age: a series of 57 cases from Northern Ireland. Breast., Apr 2010; 19(2): 97-104. doi: 10.1016/j.breast.2009.12.002. Epub 2010. Jan.
38. Elrasheid AH KHEIRELSEID, Jennifer ME BOGGS, Catherine CURRAN1, Ronan W GLYNN, Cara DOOLEY, Karl J SWEENEY and Michael J KERIN. Younger age as a prognostic indicator in breast cancer: A cohort study. BMC Cancer, 2011; 11: 383 doi: 10.1186/1471-2407-11-383.

39. Ava KWONG, Polly CHEUNG, Stephanie CHAN, Silvia LAU. Breast Cancer in Chinese Women Younger than Age 40: Are They Different from Their Older Counterparts? World Journal of Surgery., December 2008; 32(12): 2554-2561.
40. Jp. BOURGEOIS. Traitement du cancer du sein. Rev. Prat., 1990; 10: 914-916.
41. L. PIANA, F. BONNIER. Tumeur du sein: Epidémiologie, dépistage, diagnostic, évolution, pronostic, principe du traitement. Rev. Prat. Paris; 1992; 4211.
42. J. ROUESSE et al. Facteurs épidémiologique et pronostiques des cancers du sein. Rev. Prat. Paris, 1990; 40: 909-913.
43. HY. AL-IDRISSI, EM. IBRAHIM, NY. KURASHI, SA. SOWAYAN: Breast Cancer in a Low Risk Population. The Influence of Age and Menstrual Status on Disease Pattern and Survival in Saudi Arabia. Int J Cancer, 1992; 52: 48-51.
44. KS. CHIA, WB. DU, R. SANKILA, H. WANG, J. LEE, A. SEOW, HP. LEE: Do younger female breast cancer patients have a poorer prognosis? Results from a population-based survival analysis. Int J Cancer, 2004; 108: 761-765.
45. E. RAPITI, G. FIORETTA, HM. VERKOOIJEN, G. VLASTOS, P. SCHAFER, AP. SAPPINO, J. KURTZ, I. NEYROUD-CASPAR, C. BOUCHARDY: Survival of young and older breast cancer patients in Geneva from 1990 to 2001. Eur J Cancer, 2005; 41: 1446-1452.
46. DR. Pathak, JR. Osuch, He J. Breast carcinoma etiology: current knowledge and new insights into the effects of reproductive and hormonal risk factors in black and white populations. Cancer., Mar 2000; 88(5 Suppl): 1230-8.
47. J. ROBLES-CASTILLO, E. RUVALCABA-LIMON, A. MAFFUZ, S. RODRIGUE Z-CUEVAS. Cancer de mama en mujeres mexicanas menores de 40 anos. Ginecol Obstet Mex, 2011; 79(8): 482-488.
48. A. AYYAD et al. Cancer du sein chez la femme jeune de moins de 35 ans (a propos de 48 cas). Université Sidi Mohammed BEN ABDELLAH.FES.MAROC. 2010.
49. C. FREUNDA, L. MIRABELA, K. ANNANE, C. MATHELIN. Allaitement maternel et cancer du sein. Gynécologie Obstétrique & Fertilité., Oct 2005; 33(10): 739–744.
50. N. Kroman, J. Wohlfahrt, KW. Andersen, et al. Time since childbirth and prognosis in primary breast cancer: population based study. BMJ, 1997; 315: 851-855.
51. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 woment with breast cancer and 96973 women without the disease. Collaborative Group on Hormonal Factors in Breast Cancer. Lancet, 2002; 360: 187-95.

52. VF. Guinée, H. Olsson, T. Moller, et al. Effect of pregnancy on prognosis for young women with breast cancer. Lancet, 1994; 343: 1587-1589.
53. I. Bouamama, Z. Bourhaleb, M. Moukhlissi, N. Benchakroun, H. Jouhadi, N. Tawfiq, S. Sahraoui, A. Benide. Le cancer du sein chez la femme jeune: particularités épidémiologiques, génétiques, pathologiques, biologiques et thérapeutiques. Doi:10.1016/j.canrad.2 009. 08.124.
54. VF. Semiglazov, VN. Sagaidak, VM. Moiseyenko, EA. Mikhailov. Study of the role of breast self-examination in the reduction of mortality from breast cancer. The Russian Federation/ World Health Organization Study. Eur J Cancer., 1993; 29A (14): 2039-46.
55. http://www.cancer.ca/fr-ca/cancer-information/cancertype/breast/pathology-and-staging/malignant-tumours/inflammatory-breast-cancer/?Region=bc#ixzz 3EVSpUkhP.
56. S. Thangjam, RS. Laishram, K. Debnath. Breast carcinoma in young females below the age of 40 years: A histopathological perspective. South Asian J Cancer, 2014; 3: 97-100.
57. EA. Rakha, Reis-Filho JS, Ellis IO. Basal-like breast cancer: A critical review. J Clin Oncol, 2008; 26: 2568-81.
58. Csaba Gajdos .Paul I Tartter, Ira J Bleiweiss. Carol Bodian. Steven T Brower. Stage 0 to stage III breast cancer in young women. Journal of the American College of Surgeons., May 2000; 190(5): 523–529.
59. A. Bharat, Aft, R. L., Gao, F. and Margenthaler, J. A. Patient and tumor characteristics associated with increased mortality in young women (≤40 years) with breast cancer. J. Surg. Oncol, 2009; 100: 248–251.doi: 10.1002/jso.21268.
60. Filomena M. Carvalho, Livia M. Bacchi, Priscila P. C. Santos, Carlos E. Bacchi. Triple-negative breast carcinomas are a heterogeneous entity that differs between young and old patients. Clinics, 2010; 65(10): São Paulo.
61. Melinda A MAGGARD, Jessica B O'Connell, Karen E Lane, Jerome H Liu, David A
62. Etzioni, Clifford Y Ko. Do young breast cancer patients have worse outcomes? Journal of Surgical Research., July 2003; 113(1): 109–113.
63. Foo, C. S., Su, D., Chong, C. K., Chng, H. C., Tay, K. H., Low, S. C. and Tan, S. M. Breast cancer in young Asian women: Study on survival. ANZ Journal of Surgery, 2005; 75: 566–572. doi: 10.1111/j.1445-2197.2005.03431.x.
64. EBCTCG: Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials. Lancet, 2000; 355(9217): 1757-1770.

65. IH. Kunkler, Williams LJ, King CC, Jack W: Breast radiotherapy: considerations in older patients. Clinical Oncology, 2009; 21(2): 111-117.
66. O. Abe, Abe R, Enomoto K, Kikuchi K, Koyama H, Nomura Y, Sakai K, Sugimachi K,
67. Tominaga T, Uchino J, et al. Polychemotherapy for early breast cancer: an overview of the randomised trials. Lancet, 1998; 352(9132): 930-942.
68. M. Kimura, Yanagita Y, Fujisawa T, Koida T: Study of time-course changes in annual recurrence rates for breast cancer: Data analysis of 2,209 patients for 10 years post-surgery. Breast Cancer Research and Treatment, 2007; 106(3): 407-411.
69. N. Houssami, Irwig L, Simpson JM, McKessar M, Blome S, Noakes J. Sydney Breast Imaging Accuracy Study: Comparative sensitivity and specificity of mammography and sonography in young women with symptoms. AJR Am J Roentgenol., 2003; 180(4): 935–940.
70. A. Sidoni, A. Cavaliere, G. Bellezza, M. Scheibel, E. Bucciarelli: Breast cancer in young women: clinicopathological features and biological specificity. Breast, 2003; 12(4): 247-250.
71. L. Livi, I. Meattini I, C. Saieva, S. Borghesi, V. Scotti, A. Petrucci, A. Rampini, L. Marrazzo, V. Di Cataldo, S. Bianchi, et al. The impact of young age on breast cancer outcome. Eur J Surg Oncol, 2010.
72. C. GOHFIB et al, Familial breast cancer: collaborative reanalysis of individual data from 52 espidemiological studies including 58209 woman with breast cancer and 101986 women without the disease. Lancet., 2001; 358: 1389-99.
73. J. GEST et al. Cancer du sein étiologie et histoire naturelle. EMC paris Gynéco, 1975; 4: 865.