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Research Article

HORMONAL PROFILE ABOUT 305 CASES OF BREAST CANCER AT THE MOHAMMED IV CENTER FOR THE TREATMENT OF CANCER OF CASABLANCA

***DRISSI Houda¹, IMAD Fatima Ezzahra¹, BENDAHHOU Karima², RADALLAH Driss¹ and BENIDER Abdelatif³**

¹Laboratory of Biology and Health, Research Unit Associated to CNRST, URAC-34, Faculty of Sciences Ben M'sik Hassan II University of Casablanca, Morocco

²Cancer Registry of the Greater Casablanca region, Morocco

³Mohammed VI Center for the Treatment of Cancers, Casablanca Morocco

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ABSTRACT

Breast cancer is the leading cancer for woman in terms of incidence and mortality in the world. The objective of our study is the determination of the risk factors, in particular the hormonal factors on the appearance of this pathology.

Our study included 305 newly diagnosed breast cancer patients at the Mohammed IV Center for the treatment of Casablanca. Data collection is done using a standardized survey, administered face-to-face and completed from patient records. The statistical analysis of the epidemiological data was done using the R software.

Our study population had a mean age of 50 years with a standard deviation of 11.35. More than half of the patients are married and most are housewives, living in urban areas. In our study population parity is on average of 3 and extremes ranging from 0 to 11 children. The average age at first pregnancy of our patients was 23.66 years and extremes ranging from 11 to 40 years. 96.41% of patients breastfed their children with an average cumulative duration of breastfeeding of 50.47 months. 56.1% of the patients were menopausal, the average age at menarche was 13.31 years and the average age of onset of menopause was 49.86 years.

The medical history of the study population shows that only 60% of patients used oral contraceptives with an average duration of 8.43 ± 6.54 years.

Invasive ductal carcinoma was the most common histologic type in our patients (77.7%) with SBR II grade in 68.3% of patients. Hormonal receptors are over expressed in 83.26% of cases, 29.9% of patients have HER2 positive and the triple negative represents only 13.22% of patients.

All of our results converge on the association of several factors with breast cancer risk, such as, the low level of education and the increased use of oral contraceptives. However, further studies are needed to conclude that there is a close association between hormonal factors in Moroccan women and the risk of breast cancer.

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INTRODUCTION

Breast cancer is the first cancer for women in the world. Its incidence is increasing steadily because of long life expectancy, increased urbanization and the adoption of Western lifestyles (WHO, 2003). In Morocco, it usually affects women over 45 years old. However, women of all ages can have breast cancer and in rare cases, breast cancer can also affect men. This pathology remains the main cause of female mortality in Morocco and in the world and remains a major

public health problem. (RCGC, 2016). There is sufficient evidence to affirm that exposure to hormonal and lifestyle factors play an important role in the etiology of this disease. Constant identification of risk factors, upon which action can be taken, should facilitate the implementation of effective prevention strategies (Nkondjock et Parviz, 2005)

The aim of this work is to describe the clinical, epidemiological characteristics and the exposure to hormonal factors in breast

*Corresponding author: **DRISSI Houda**

Laboratory of Biology and Health, Research Unit Associated to CNRST, URAC-34, Faculty of Sciences Ben M'sik Hassan II University of Casablanca, Morocco

cancer patients treated at the Mohammed VI center for the treatment of cancer.

PATIENTS AND METHODS

It is a cross-sectional epidemiological study of breast cancer cases newly diagnosed and collected at the Mohamed VI center of Casablanca for the treatment of cancers.

The inclusion of patients is done consecutively over a period of time between January 2015 and December 2016. Clinical information was recorded in a standardized survey administered face-to-face to patients and completed from medical records. Demographic information including age at diagnosis, marital status, delivery history, history of breastfeeding, menopausal status, work status, history of use of hormone therapy, anatomopathological features (histological type, histopronotic grade SBR, tumor stage), and results of immunohistochemical study regarding hormone receptor expression (estrogen, progesterone) and HER-2 status.

The statistical analysis of the results was carried out by software R. The values were expressed as percentage by population or as mean \pm standard deviation.

RESULTS

During the study period, 305 patients were treated in the Mohamed VI center for cancer treatments.

Sociodemographic data

The socio-demographic characteristics of these 305 patients are presented in Table I. These are data of age, marital status, educational level, occupation and place of residence.

Table 1 General description of the population studied

Characteristics	Effective	Number of cases (%)	IC 95%
Average age (years)	305	50.15 \pm 11.35	
Age classes			
≤ 30	9	3	[0.61-4.00]
[30-34]	8	2.6	[2.14-6.95]
[35-39]	38	12.5	[9.07-16.82]
[40-44]	50	16.4	[12.52-21.14]
[45-49]	55	18	[13.98-22.91]
[50-54]	41	13.4	[9.92-17.91]
[55-59]	47	15.4	[11.65-20.07]
[60-64]	23	7.5	[4.94-11.25]
[65-69]	13	4.3	[2.39-7.36]
[70-74]	14	4.6	[2.63-7.76]
≥ 75	7	2.3	[1.01-4.88]
Marital status			
Single	52	17	[13.10-21.85]
Married	170	55.7	[49.96-61.31]
Divorced	44	14.4	[10.78-18.99]
Widow	39	12.8	[9.35-17.18]
Level of study			
Illiterate	146	47.9	[42.16-53.63]
Koranic school	21	6.9	[4.42-10.49]
Primary	71	23.3	[18.74-28.51]
Secondary	59	19.3	[15.16-24.32]
University	8	2.6	[1.22-5.30]
Profession			
Housewife	253	83	[78.15-86.90]
Worker	26	8.5	[5.75-12.39]
Official	19	6.2	[3.89-9.72]
High frame	2	0.7	[0.11-2.61]
Retirement	1	0.3	[0.02-2.10]
Other (student)	4	1.3	[0.42-3.55]
Middle of residence			

Urban	193	63.3	[57.57-68.65]
Suburban	26	8.5	[5.75-12.39]
Rural	86	28.2	[23.29-33.66]

The mean age of the patients was 50.15 with a standard deviation of 11.35 and extremes' ranging from 24 to 95 years and the median age was 49 years. More than half of our patients (55.7%) were married, 17% were single and 12.8% were widowed.

Regarding the level of study, our results showed that almost half of the population studied (47.9%) are illiterate, 23.3% have a primary level of education while only 19.3% have secondary level of education. The university level represents only 2.6% of the population. Of the women surveyed, 83% are housewives, over 8% are employed and only 0.7% of them are senior managers. 1.3% of them are female students. In the study population, 63.3% live in urban areas and 28.2% live in rural areas.

Gynecological Obstetric History

Data collected handle specifically on patients' gynecological and obstetrical history are shown in Table II.

Table 2 Obstetrical History of Patients

Characteristics	Effective	Mean \pm standard deviation	IC 95%
Average age at menarche (years)	305	13.31 \pm 1.69	
Average age of menopause (years)	171	49.86 \pm 5.11	
Average age of first pregnancy (years)	224	23.66 \pm 5.97	
Average number of pregnancy numbers	305	3.13 \pm 2.62	
Average duration of breastfeeding (months)	215	50.47 \pm 41.98	
Characteristics	Effective	Number of cases (%)	
Menopausal status			
Pre-menopausal	114	37.4	[31.98-43.10]
Perimenopausal	20	6.6	[4.15-10.10]
Postmenopausal	171	56.1	[50.29-61.69]
Distribution of the number of children			
0 Child	71	23.3	[18.74-28.51]
[1-2] Children	65	21.3	[16.94-26.42]
+ de 2 Children	169	55.4	[49.63-61.05]
Parity			
Yes (%)	223	73.1	[67.70-77.93]
No (%)	82	26.9	[22.07-32.30]
Breastfeeding (n=223)			
Yes (%)	215	96.41	[93.05-98.44]
No (%)	8	3.59	[1.56-6.95]

The age of menarche is on average 13.31 \pm 1.69 years, with extremes of 10 to 19 years. The average age of onset of menopause was 49.86 years with a standard deviation of 5.11 years and extremes ranging from 37 to 65 years. More than half of our patients are postmenopausal with a proportion of 56.1%, followed by patients with pre-menopausal status with a proportion of 37.4%. Finally, patients with peri-menopausal status are found with a proportion of 6.6%.

In our study population, the mean age of first pregnancy is 23.66 years with a standard deviation of 5.97 years and extremes ranging from 11 to 40 years. The parity is on average

3 children with a standard deviation of 2.62 and extremes ranging from 0 to 11 children. 73.1% of the women interviewed are multiparous while only 26.9% of the cases are nulliparous.

Of the 73.1% of multiparous women, 96.41% breastfed their children for an average cumulative breastfeeding duration of 50.47 months and extremes ranging from 1 to 196 months. Only 3.59% of patients did not breastfeed their children.

History of hormonal treatments use in patients

Data of the use of hormonal treatments for the patients are shown in Table III.

Table 3 History of Hormonal Therapy use in Patients

Characteristics	Effective	Number of cases (%)	IC 95%
Hormone substitutif therapy			
Yes	10	3.3	[1.69-6.14]
No	295	96.7	[93.86-98.33]
Ovulation inducers			
Yes	33	10.82	[7.67-14.99]
No	272	89.18	[85.01-92.33]
Treatment of the irregularity of the cycle			
Yes	26	8.52	[5.75-12.39]
No	279	91.48	[93.45-98.09]
Treatment of breast mastosis			
Yes	11	3.61	[1.91-6.55]
No	294	96.39	[93.45-98.09]
Oral contraception (OC)			
Yes	183	60	[53.25-64.55]
No	122	40	[35.45-46.75]
Average duration of use of OC (years)	183	8.43±6.54	
Distribution of the duration of OC			
≤ 5years	69	37.70	[30.66-45.15]
≥ 5years	114	62.30	[54.85-69.34]

The medical history of the study population shows that few patients had undergone hormone replacement therapy or treatment for breast mastosis with a small percentage estimated respectively at 3.3% and 3.61%. Similarly, 10.82% of patients were treated with ovulation inducers and 8.52% were followed for treatment of irregular cycle.

In addition, the use of oral contraceptives has been found in 60% of cases. The average duration of oral contraceptive use is 8.43 years with a standard deviation of 6.54 and extremes ranging from 1 month to 27 years.

The histopathological features of the patients

Table IV reports the distribution of patients according to histopathological features. Invasive ductal carcinoma was the dominant histological type (n = 237, 77.7%). Other histological types were invasive mammary carcinoma (13.7%), invasive lobular carcinoma (3.6%), ductal carcinoma in situ (1.3%), and other histological types (medullary carcinoma; Lobular carcinoma in situ, neuroendocrine carcinoma, sarcoma and phyllode tumor) with a proportion of 2.2%. The histopronostic grade SBR II is the most frequent grade with a proportion of 68.3%.

Almost three-quarters of patients (70.8%) were diagnosed at an early stage and only 29.2% were seen at an advanced stage.

The immunohistochemical profile study identified 83.26% of hormone receptor-positive cancers, 29.9% of HER2-positive

patients and 13.22% of patients were triple negative, neither hormone-receptor nor on coprotein-expressing HER2.

Table 4 Histopathological Characteristics of patients with breast cancer

Characteristics	Effective	Number of cases (%)	IC 95%
Histological type			
Invasive ductal carcinoma	237	77.7	[72.53-82.17]
Invasive breast carcinoma	42	13.7	[10.21-18.27]
Invasive lobular carcinoma	11	3.6	[1.91-6.55]
In situ ductal carcinoma	4	1.3	[0.42-3.55]
Other types	11	3.6	[1.91-6.55]
SBR grade			
Grade 1	19	7.1	[4.32-10.85]
Grade 2	183	68.3	[62.35-73.81]
Grade 3	66	24.6	[19.59-30.24]
Stade			
Stade 1 and stade 2	126	70.8	[63.52-77.35]
Stade 3 and stade 4	52	29.2	[22.65-36.48]
Estrogen receptor			
Positive	186	81.9	[76.31-86.72]
Negative	41	18.1	[13.28-23.69]
Progesterone receptor			
Positive	163	72.1	[65.79-77.87]
Negative	63	27.9	[22.13-34.21]
HER2			
Positive	60	29.9	[23.62-36.69]
Negative	141	70.1	[63.31-76.38]
Ki67			
Low (≤ 14%)	119	85.4	[77.34-89.96]
High (≥ 14%)	22	14.6	[10.04-22.66]
Molecular classification			
Luminal A (ER+ et /ou PR + HER - ki67 ≤ 14%)	119	52.42	[45.71-59.07]
Luminal B (ER+ et /ou PR + HER +/- ki67 ≥ 14%)	16	7.05	[4.08-11.19]
HER-2 or No luminal (ER- et PR- HER + ki67 ≥ 14%)	8	3.52	[1.53-6.83]
Basal or Triple negative (ER- et PR- HER -)	30	13.22	[9.10-18.33]
Unclassified	54	23.79	[18.40-29.87]

DISCUSSION

Breast cancer is a major public health problem. Its incidence varies across regions and the environment, which necessitates the local study of risk factor profiles.

In our series, the mean age and the median age of the population are 50.15 years and 49 years, respectively. This average age is comparable to that (50 years) found in a Tunisian series (Ben Ahmed *et al*, 2002). In contrast, breast cancer in the West occurs at a later age (median age 55) and only 3% of patients are under 35 years of age (Blamey *et al*, 2010).

A prospective study conducted in Iceland between 1982 and 2004 on a population aged 20-64 found a positive association between breast cancer risk and the level of education (Vidarsdottir *et al*, 2008). For our patients, 47.9% are illiterate. These results are comparable to those reported in the literature (Cleggand *et al*, 2009) and highlight the difficulties of access to information for our patients and their lack of knowledge of the risk factors and symptoms related to breast cancer.

Numerous studies have shown that the onset of mumps before the age of 12 and/or menopause after age 50 increases the risk of breast cancer (Nkondjock *et al.*, 2005). This association corresponds to the early and prolonged exposure to hormonal impregnation (estrogen and progesterone) that exists during the period of ovarian activity (Nkondjock *et al.*, 2005). However, this association is not found by our patients, since this period of hormonal exposure is relatively small; the age of menarche averages 13.31 years and menopause occurs at an early age of 49 years.

In addition, the use of oral contraception is strongly implicated in the occurrence of breast cancer in our study population. In fact, 60% of women routinely took oral contraceptives. This is also the case for a meta-analysis of case-control studies, which suggests that the use of oral contraception, especially at a young age (before the first pregnancy), is linked to an increased risk of breast cancer (Oukili, 2006). The same finding was reported by the study of Barouagui *et al.*, (2012) on a population of western Algeria, showing that 64.15% of patients with breast cancer take oral contraceptives.

Regarding hormone replacement therapy, a 2002 American Women's Health Initiative (WHI) confirmed a slight increase in breast cancer among women treated. Indeed, the promoting effect of sex steroids could go through an increase in insulin resistance induced by artificial progestins. This link cannot be established in our population, since only 3% of patients had taken hormone replacement therapy (Lyytinen and *et al.*, 2009). The same is true for ovulation-inducing treatments. Our results, with only 10.82% of patients treated, did not show a significant association between exposure to ovulation inducer treatments and risk of breast cancer. This data is consistent with a meta-analysis of 20 selected studies (Gabriele *et al.*, 2017).

Multiparity does not appear to be a protective factor for breast cancer in our study population. Indeed, 73.1% of our patients are multiparous and the parity is on average 3 children. These data go against many epidemiological studies that have shown the long-term protective effect of the number of pregnancies. Thus, it has been shown that this protective effect increases with the number of children; each birth reduces the relative risk of breast cancer by an average of 7 to 9% (Espie *et al.*, 2001; Collaborative Group, 2002). Different pathophysiological mechanisms are involved in reducing breast cancer risk induced by pregnancy, such as cell differentiation of the mammary epithelium (Brettes *et al.*, 2007).

The age of the first pregnancy seems to be also a fundamental parameter in many works. The risk of developing breast cancer is increased 4 to 5 times in women whose first pregnancy occurs after age 35 (Anderson *et al.*, 2009). In our series, the proportion of women with their first child after the age of 35 represents only 5.57%.

On the other hand, there is much evidence for the protective role of breast cancer breastfeeding. This reduction in the risk of breast cancer is all the greater as the cumulative duration of breastfeeding is long (Russo *et al.*, 2005). This protective effect of breastfeeding is thought to be due to an elevation of prolactin and a decrease in estrogen production, which reduces the duration of estrogen exposure overall and thus their promoter effect *via* cell signaling pathways breast

carcinogenesis. For Russo, the mammary gland reaches its maximum development and differentiation during pregnancy and lactation, which makes it less sensitive to the action of carcinogens (Russo *et al.*, 2005). These protective effects attributed to breastfeeding do not seem to be acting in our cohort, since the majority of our breast cancer patients (96.41%) breastfed their children with an average breastfeeding duration of 50.47 ± 41.98 months.

From a histological point of view, invasive ductal carcinoma was the dominant histological type ($n = 237$, 77.7%). Other histological types were invasive mammary carcinoma (13.7%), invasive lobular carcinoma (3.6%), ductal carcinoma in situ (1.3%), and other histological types (medullary carcinoma; Lobular carcinoma in situ, neuroendocrine carcinoma, sarcoma and phyllode tumor) with a proportion of 2.2%. These data are in agreement with those of the literature. In Fès-Boulemane, a retrospective study of 265 patients from the north-eastern region of Morocco, aged between 18 and 80 years old and collected at the CHU between January 2007 and September 2009, reported that the predominant histological type of tumors was infiltrating ductal carcinoma (CCI) in 87.8% of cases, followed by infiltrating lobular carcinoma with a rate of 4.7% (Abbass *et al.*, 2011). In Casablanca, between 2005 and 2007, the most common histological type was infiltrative ductal carcinoma with 75.2% of cases, and 7% of cases corresponded to invasive lobular carcinoma (RCRC, 2012). Comparable rates of infiltrating ductal carcinoma were found in Tunisia with 90% of cases (Ben Ahmed *et al.*, 2002).

In addition, the percentage of grade I tumors diagnosed is very low (7.1% instead of 30% in Europe), while grades III are almost of the same order of magnitude (24.6% versus 30%). Grade II tumors are the most common, but more markedly in Morocco (68.3%) than in Europe (42%) (Blamey *et al.*, 2010). Almost three-quarters of patients (70.8%) were diagnosed at an early stage and only 29.2% were seen at an advanced stage. This encouraging result is the result of the establishment in recent years of a national screening strategy in the greater Casablanca region where the study center is located.

According to Carey *et al.*, the percentages of basal and luminal A subtypes were 27% and 47%, respectively, versus 13.22% and 52.42% in our study. We note that the prevalence of basal subtype was 2 times lower than in the literature and the HER2 + / ER- status was 3.52% in our patients versus 9% represented by Carey *et al.*, 2006.

Our study shows that luminal subtype B is the least common molecular subtype, accounting for 7.05% of cases. These results are comparable to many data reported in the literature (Goran *et al.*, 2010; Munirah *et al.*, 2011).

CONCLUSION

Our study of the epidemio-hormonal profile of breast cancer in a population of Moroccan women allowed the identification of patients at risk. In our study, the overriding factor associated with breast cancer risk is the frequent use of oral contraceptives. The frequency of the multiparity rate and the average long duration of breastfeeding do not appear to be protective factors.

This description of the risk factors already mentioned in the literature may raise causal hypotheses in these patients. However, an analytical case-control study to study this association is desirable to quantify the significance of the link that may exist between each of the risk factors and the occurrence of breast cancer.

References

- Abbass F., Bennis S., Znati K., Akasbi Y., Amrani K.J., El Mesbahi O., and Amarti A. 2011. Epidemiological and biologic profile of breast cancer in Fez-Boulemane, Morocco. *Easten Mediterranean Health Journal*, 17, 12.
- Andersson T.M., Johansson A.I., Hsieh C.C., Cnattingius S., and Lambe M. 2009. Increasing incidence of pregnancy-associated breast cancer in Sweden. *Obstetrics and gynecology*, 114, 568-72.
- Barouagui S., Zaoui C., Senhadji R., and El Kébir F.Z. 2012. Age, Endogenous and Exogenous Hormonal Factors and Risk of Breast Cancer in Western Algeria. 34th Days of the French Society of Senology and Mammary Pathology, Acquisitions and limits in Senology, p.422.
- Ben Ahmed S., Aloulou S., Bibi M., Landolsi A., Nouira M., Ben Fatma L., Kallel L., Gharbi O., Korbi S., Khaïri H., and Kraïem C. 2002. Breast cancer prognosis in Tunisian women: an analysis of a hospital trial involving 729 patients. *Santé Publique*, 14(3), 231-241.
- Blamey R.W., Hornmark S.B., Ball G., Blichert T.M., Cataliotti L., Fourquet A., Gee J., Holli K., Jakesz R., Kerin M., Mansel R., Nicholson R., Pienkowski T., Pinder S., Sundquist M., van de Vijver M., Ellis I. 2010. Oncopool – A European Database For 16,944 Cases Of Breast Cancer. *European Journal of Cancer*, 46:56–71.
- Brettes J.P., Mathelin C., Gairard B., and Bellocq J.P. 2007. Rôle des hormones stéroïdes dans la cellule normale et dans la carcinogenèse mammaire: les mécanismes intracrines intramammaires. *on: Cancer du sein*. Editions Masson, 358: 77-91.
- Carey L.A., Perou C.M., Livasy C.A., Dressler L.G., Cowan D., Conway K., Karaca G., Troester M.A., Tse C.K., Edmiston S., Deming S.L., Geradts J., Cheang M.C., Nielsen T.O., Moorman P.G., Earp H.S., and Millikan R.C. 2006. Race, Breast Cancer Subtypes, And Survival In The Carolina Breast Cancer Study. *Journal American medical association, Jama*, 295, 2492-2502.
- Clegg L.X., Reichman M.E., Miller B.A., Hankey B.F., Singh G.K., Lin Y.D., Goodman M.T., Lynch C.F., Schwartz S.M., Chen V.W., Bernstein L., Gomez S.L., Graff J.J., Lin C.C., Johnson N.J., Edwards B.K. 2009. Impact Of Socioeconomic Status On Cancer Incidence And Stage At Diagnosis: Selected Findings From The Surveillance, Epidemiology, And End Results: National Longitudinal Mortality Study. *Cancer Causes And Control*, 20(4), 417-435. Doi:10.1007/S10552008-9256-0.
- Collaborative Group on Hormonal Factors In Breast Cancer. 2002. Breast Cancer and Breastfeeding: Collaborative Reanalysis of Individual Data From 47 Epidemiological Studies In 30 Countries, Including 50302 Women With Breast Cancer And 96973 Women Without The Disease. *Lancette*, 360, 187-95.
- Espie M., Tournant B., Cuvier C., and Cottu P.H. 2001. *Epidémiologie Des Lésions Malignes Du Sein*. Encycl Med Chir, Gynécologie, 840,A, 15, 10 P.
- Gabriele V., Benabu J.C., Ohl J., Youssef C.A., and Mathelin C. 2017. Does fertility treatment increase the risk of breast cancer? current knowledge and meta-analysis. *Gynécologie Obstétrique Fertilité & Sénologie*, 45 (5), 299-308.
- Göran J., Johan S., Johan V.C., Markus R., Karolina H., Cecilia H., Haukur G., Rainer F., Carina S., Bjarni A.A., Outi K., Lena L., Päivi H., Kristiina A., Carl B., Niklas L., Per M., Håkan O., Oskar T.J., Adalgeir A., Heli N., Rosa B.B., and Åke B. 2010. Genomic Subtypes Of Breast Cancer Identified By Array-Comparative Genomic Hybridization Display Distinct Molecular And Clinical Characteristics. *Breast Cancer Research* 12, R42.
- Lyytinen H., Pukkala E., and Ylikorkala O. 2009. Breast Cancer Risk In Postmenopausal Women Using Estradiol-Progestogen Therapy. *Obstetrics and gynecology*, 113, 65-73
- Munirah M.A., Siti-Aishah M.A., Reena M.Z., Sharifah N.A., Rohaizak M., Norlia A., Rafie M.K., Asmiati A., Hisham A., Fouad I., Shahrin N.S., Das S. 2011. Identification Of Different Subtypes Of Breast Cancer Using Tissue Microarray. *Romanian Journal Morphology and embryology*, 52(2), 669-677
- Nkondjock A., Parviz G., 2005. Facteurs De Risque Du Cancer Du Sein. *Médecine and sciences*, 21, 175-180.
- Oukili M.A., 2006.- *Epidémiologie Et Facteurs De Risqué Du Cancer Du Sein A Propos De 816 Cas*. Thèse Université Mohammed V faculté médecine et pharmacie. Rabat, 115p.
- RCGC, 2012. *Registre Des Cancers de La Région du Grand Casablanca, fait Au CHU Ibn Rochd pour les années 2005, 2006, 2007* (Edition 2012).
- RCGC, 2016. *Registre Des Cancers de La Région du Grand Casablanca, fait Au CHU Ibn Rochd pour les années 2008, 2009, 2010, 2011, 2012* (Edition 2016).
- Russo J., Moral R., Balogh G.A., Mailo D., Russo H.I. 2005. The Protective Role of Pregnancy In Breast Cancer. *Breast Cancer Research*, 7, 131-42.
- Vidarsdottir H., Gunnarsdottir H.K., Olafsdottir E.J., Olafsdottir G.H., Pukkala E., and Tryggvadottir L. 2008. Cancer Risk By Education In Iceland; A Census-Based Cohort Study. *Acta oncologica*, 47(3), 385-390. Doi:10.1080/02841860801888773
- World Health Organization Classification Of Tumours. Tavassoli F.A., and Devilee P. 2003. *Pathology And Genetics Of Tumors Of The Breast And Female Genital Organs*. Lyon, France, IARC Press 2003.
- Writing Group for the Women's Health Initiative. 2002. Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women. Principal results from the Women's Health Initiative Randomized Controlled Trial. *Journal American medical association, JAMA*, 288, 321-333.