

# The Impact Of The Economic Crisis And Covid-19 Pandemic On The Characteristics Of Breast Cancer In Lebanon

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## Abstract

Pregnancy interruption policies are distinguished by orienting opinions, decisions and behaviors towards the individual request for abortion, even when the literature indicates that the choice of partner is defined by the group closest to the person, government strategies seem Focus on the personal reasons of the person requesting the service. The objective of this work was to establish the sociopolitical and sociocognitive dimensions of abortion. A documentary, exploratory and psychometric work was carried out with a sample of 100 students from a public university selected for their internships and professional service in public health institutions. The results show a reduction to three factors of the six reported in the literature. The reduction to three factors and eleven indicators is recommended in order to adjust the instrument to the sample and its scenario of expectations of termination of pregnancy.

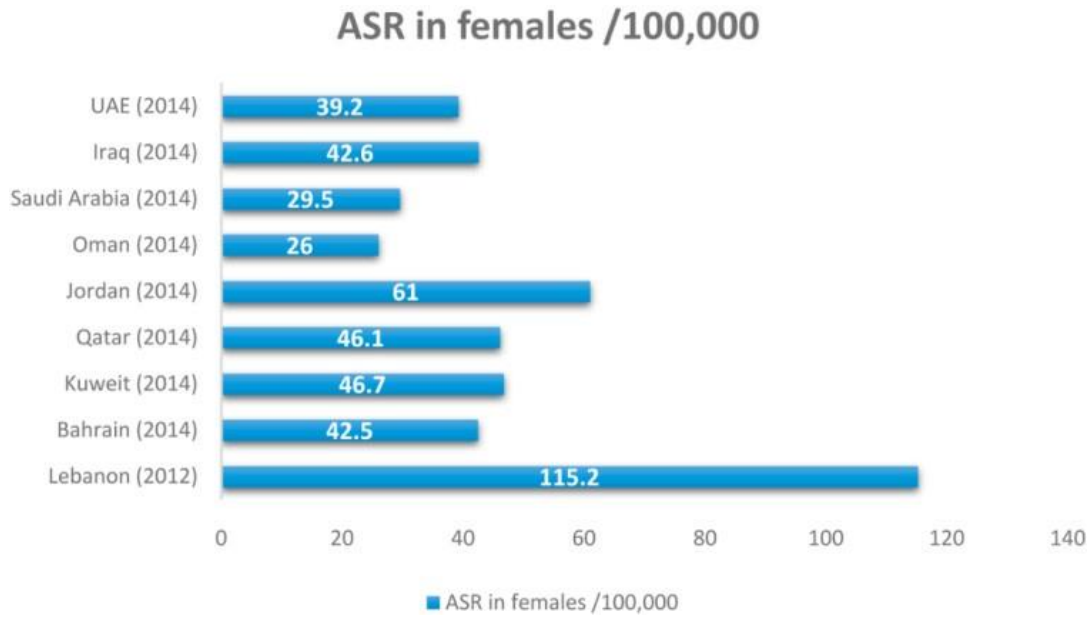
**Key words:** attitudes; abortion; knowledge; beliefs; factor model

## Introduction

Breast cancer is the most common cancer worldwide, with 2.3 million cases per year. It constitutes the second cause of cancer-due-mortality after lung cancer with 684996 cases in 2020 (1).

Particularly in Lebanon, breast cancer constitutes 38.2% of all cancer cases according to the national register between the years of 2004 and 2018 (2) (3). The average incidence of breast cancer between the years 2008 and 2015 rose to 44.84 cases per 100000; and is considered among the highest worldwide (3), with a mortality rate of 10.2% (4). These incidences are higher when compared to those found in other Arab countries [figure 1] partly due to the implementation of screening programs nationally, following the example of developed countries. Indeed, since 2002, the Ministry of

Public Health in Lebanon has organized awareness campaigns for breast cancer screening, which aims to encourage women over the age of 40 to have their annual mammogram at reduced costs (4) (5). Between the years 2003 and 2012, there was a reduction of 1.9% per year in the mortality rate due to breast cancer (6). Several studies conducted at Hôtel Dieu de France and AUBMC (two university hospitals located in Beirut, which constitute the two most important centers in Lebanon) highlighted - before 2015 - the prevalence of early stages (I and II) of breast cancer compared to advanced stages (III and IV) (8) (9) (10). These satisfactory results were most likely the outcome of the great progress in the field of systematic breast cancer screening and awareness campaigns.



**Figure 1:** incidence of breast cancer in Lebanon compared to neighboring countries (7)

However, with the arrival of the COVID-19 pandemic towards the end of 2019, repercussions were detected at the international level in various ranges, especially in the health field. Health establishments lost, especially during the peak of the pandemic in 2020, their capacity to offer preventive medicine services. In the United States, for example, the cancer screening rate has seen a major decrease, reaching 94% (11); the same in Brazil with an 84% drop in the number of consultations, as well as a reduction in paraclinical examinations, especially mammograms and ultrasounds by 95% (12).

Together with the COVID-19 pandemic, and starting October 2019, the country began to suffer from one of the most serious economic crises ever recorded. It has further worsened the state of health in the country by closing several medical imaging centers, prompting insurance companies to stop covering many exams, pushing hundreds of doctors to leave the country (and therefore leaving thousands of patients without alternatives) (13), and making it more challenging for patients to obtain medications whether because of the cost or their unavailability (14). Certain immunotherapies and targeted therapies, which constitute incredible progress in the treatment of several types of cancer, unfortunately became unavailable in Lebanon (15).

**Objective and methodology of the study**

The impact of the COVID-19 pandemic on breast cancer screening has been proven in several countries as well as that of the Lebanese financial crisis on the general and especially economic situation of the people.

Indeed, since the start of these events, which both began towards the end of 2019, awareness campaigns have decreased at the national level, as well as the number of screening mammograms. This would have a potential effect on the discovery of breast cancer at a later stage with subsequent harmful consequences since early detection is fundamental for rapid and correct treatment.

And given that this concept has not yet been studied in our country, we carried out a study whose objective would be to compare the characteristics of breast cancer between two groups of

Lebanese women using information collected from the pathology laboratories in "Hôtel Dieu de France" consisting of pieces of mastectomies from 747 female patients between 2015 and 2023:

-Group 1: patients diagnosed before the crisis/pandemic (between 2015 and October 2019)

-Group 2: patients diagnosed after the crisis/pandemic (between October 2019 and August 2023).

The collected data included:

- Age of the patients
- Size of the tumor (T)
- The lymph nodes (N)
- The molecular and histological types
- The grade of the tumor
- The index of proliferation (Ki67)
- The administration or not of neoadjuvant chemotherapy

**Statistical analysis**

All the data analyses were performed using R 4.3.1 (The R Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel. Continuous and categorical data were summarized by a variable's mean and standard deviation or proportions, respectively. For continuous data, Jarque- Bera test was used to assess population normality and Fisher's F-test for equality of variances. If the preceding tests were insignificant, Student's T-test was performed to compare population

means; otherwise, Mann-Whitney non-parametric test was used. For categorical data, the Z-test was used to compare the groups' binomial proportions; if the test's assumptions were not met,

Fisher's exact test was carried out. Additionally, Pearson's Chi-squared test or Fisher's exact test were used if a variable had more than 2 proportions.

**Results**

Variable	Pre crisis/pandemic (n = 486)	Post crisis/pandemic (n = 261)	P-value
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<b>Age</b>	57.09 ± 12.2	56.73 ± 12.26	0.7
<b>Ki67</b>	18.93 ± 16.96	18.55 ± 18.52	0.45
<b>T</b>			< 0.001***
T1	247 (50.82%)	97 (37.16%)	< 0.001***
T2	185 (38.06%)	101 (38.69%)	0.710
T3-T4	48 (9.87%)	61 (23.37%)	< 0.001***
Tx	6 (1.23%)	2 (0.76%)	0.720
<b>N</b>			
N0	214 (44.03%)	86 (32.95%)	< 0.001***
N1	148 (30.45%)	76 (29.12%)	0.785
N2	62 (12.75%)	47 (18%)	0.036*
N3	46 (9.46%)	44 (16.86%)	0.003**
Nx	16 (3.29%)	8 (3.06%)	0.930
<b>ER</b>			0.135
Negative	73 (15.02%)	51 (19.54%)	
Positive	399 (82.09%)	204 (78.16%)	
<b>PR</b>			0.192
Negative	156 (32.09%)	98 (37.54%)	
Positive	316 (65.02%)	157 (60.15%)	
<b>Her2</b>			0.75
0	288 (60.13%)	164 (63.57%)	0.360
+1	79 (16.49%)	42 (16.28%)	0.940
+2	70 (14.61%)	31 (12.02%)	0.330
+3	42 (8.77%)	21 (8.14%)	0.770
<b>Her2</b>	36 (7.41%)	20 (7.66%)	0.910
<b>TN</b>	34 (6.95%)	28 (10.72%)	0.125
<b>Histological type+ grade</b>			< 0.001***
DUC grade 1	49 (10.27%)	9 (3.5%)	< 0.001***
DUC grade 2	176 (36.90%)	85 (33.73%)	0.307
DUC grade 3	155 (32.49%)	91 (36.11%)	0.371
DUC x	21 (4.4%)	30 (11.9%)	< 0.001***
MED grade 3	1 (0.21%)	2 (0.79%)	0.250
MUC grade 2 et 3	1 (0.21%)	5 (1.97%)	0.010**
LOB grade 2	63 (13.21%)	24 (9.52%)	0.120
LOB grade 3	6 (1.26%)	6 (2.38%)	0.400
<b>Neoadjuvant chemotherapy</b>			< 0.001***
Yes	56 (11.52%)	70 (26.32%)	
No	430 (87.58%)	191 (73.18%)	

ER: estrogen receptors, PR: progesterone receptors, TN: triple negative, DUC: ductal, MED: medullar, MUC: mucinous, LOB: lobular  
Concerning the age of the patients, the proliferation index Ki67 and the molecular type: There was no significant difference between the 2 groups. Nonetheless, we must emphasize this increase in the percentage of the “triple negative” category (from 6.95% to 10.72%).

#### Concerning the size of the tumor (T):

A significant difference was noted with a decrease in T1 tumors (50.82% to 37.16%) and an increase in T3-T4 tumors (9.87% to 23.37%).

#### Concerning the lymph nodes number (N):

A significant difference was noted with a decrease in N0 tumors (44.03% to 32.95%) and an increase in N2 (12.75% to 18%) and N3 (9.46% to 16.86%) tumors.

#### Concerning the histological type of the cancer:

A significant difference was noted in the ductal subtype with a decrease in grade 1 (10.27% to 3.5%), and the mucinous subtype with the increase in grade 2 and 3 (0.21% to 1.97%).

#### Concerning the use of neoadjuvant chemotherapy:

We have noticed a significant increase in the use of neoadjuvant chemotherapy (11.52% to 26.32%).

#### Discussion

Before discussing the main objective of our study, it will be necessary to dwell on an important notion emerging from these data: indeed, there is evidence of a remarkable increase in the use of neoadjuvant chemotherapy in Lebanon in accordance with international recommendations, where neoadjuvant chemotherapy has become the first-line treatment with the aim of reducing the extent of mastectomy and performing conservative surgeries (16).

The parameters of breast cancer underwent notable changes according to data collected from Hôtel Dieu de France. Thus, we found ourselves facing more aggressive stages of cancer with an increase in the rate of large tumors

(increase in T3-T4), tumors with positive nodes (increase in N2 and N3) and a reduction in tumors (increase in particularly of the ductal type) grade 1.

This impressive new character of aggressiveness in Lebanon follows the same model of that of breast tumors in various regions of the world:

-Indeed, according to a study carried out in Brazil in October 2021, it was found that patients who presented to the clinic for the first time during the pandemic (between September 2020 and January 2021) had a more aggressive tumor than those who presented before the pandemic (between September 2019 and January 2020): 37.3% of cases were stage III in the first group while 23.2% of these cases were in the second group (17).

-Likewise, we wanted to estimate the impact of diagnostic delay due to the COVID-19 pandemic in Japan. It was then demonstrated that the percentage of patients with a stage greater than or equal to IIB was superior in the pandemic group (between April 2020 and October 2022) compared to the non-pandemic group (between April 2019 and October 2019). Additionally, the percentage of cases with a Ki-67 proliferation index greater than 20% was higher in the pandemic group compared to the non-pandemic group (18).

-In France, the stages of breast cancer were compared between the years 2019 and 2020, and we found an increase in the size and in the rate of invasive cancers in 2020 (19).

-Another study in Turkey (20) carried out in 2021 compared the characteristics of breast cancer in the group treated between 2020 and 2021 (study group) with that treated between 2019 and 2020 (control group) in İstanbul Florence Nightingale Hospital. Several significant results were collected, including: an increase in the number of pre-

menopausal women in the study group (57.7% vs 45%); an increase in stage IV cancer in the study group (10.8% vs 4%); an increase in PRDT (patient-related delay time) in the study group ([2.58±2.1) months vs [1.82±1.4) months).

-In Portugal (21), we noticed an increase in the proportion of patients diagnosed with a grade 3 tumor, as well as those already having locally advanced or even metastatic cancer at presentation.

Therefore, it is crucial to restore screening programs in order to detect these tumors in their early stages to improve patient survival.

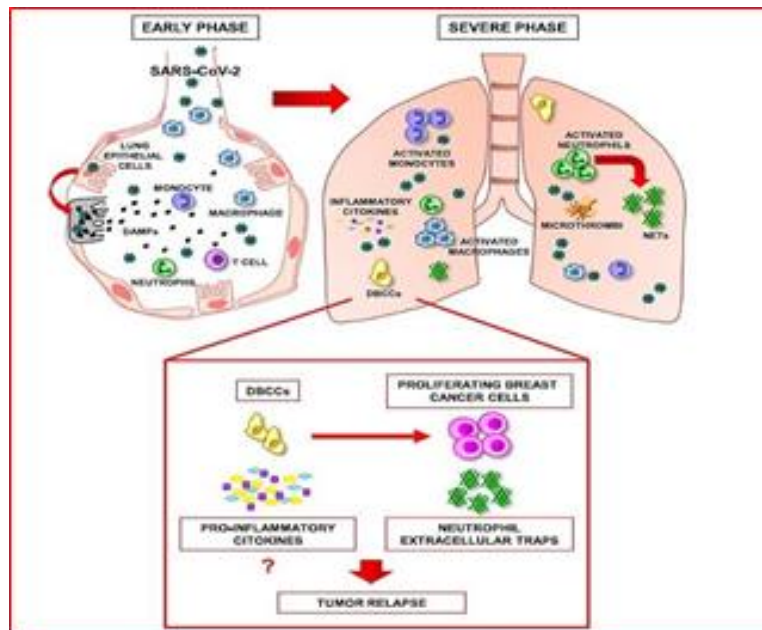
### The relation between COVID-19 infection and cancer:

The problem of breast cancer aggressiveness found these recent years may not be exclusively due to a lack/delay in screening. Some studies raise the possibility of a pathogenicity link between breast cancer and COVID-19 infection. This theory is summarized as the following:

SARS-CoV-2 infection activates proteins that play a role in cell replication, DNA damage and epigenetic regulation, and therefore in cancer pathophysiology (22). Indeed, it has been

demonstrated that SARS-CoV-2 is involved in a stage of the tumor cycle linked to dormant cancer cells (DCC). These DCCs are resistant to cancer treatment and survive asymptotically in regions prone to metastasis (23). And these can reactivate in response to inflammation.

Particularly, SARS-CoV-2 is responsible for the genesis of an inflammatory cycle with the recruitment of various inflammatory cells, leading to the formation of NETs (neutrophil extracellular traps) [figure 2]. The latter are the most involved in the awakening of CCDs, thus producing reactivation and pulmonary metastasis (24).



the inflammatory cycle caused by SARS-CoV-2 infection

Another hypothesis has been put forward by attributing the awakening of CCDs to hypoxia which can be caused by SARS-CoV-2 (25). Hypoxia also constitutes an environment favorable to the risk of metastasis because of the neovascularization that it causes, thus facilitating the dissemination of tumor cells (26).

Thus, the SARS-CoV-2 infection can aggravate the cancer progression, with the genesis of metastasis and increase of the mortality rate (27) (28).

### The relation between COVID-19 infection and breast cancer:

An American study published in 2022 (29) highlighted the relationship with breast cancer in particular by demonstrating several effects:

-The M protein of SARS-CoV-2 stimulates migration, invasion, and expression of genes responsible for EMT (epithelial to mesenchymal transition) in both types of breast cancer (triple negative and hormone-dependent),

-The triple negative type most expresses the ACE2 receptor (which is a receptor for SARS-CoV-2), which could mean that infection can worsen the progression of this particular type of cancer. Indeed, the binding of SARS-



CoV-2 with ACE2 will reduce the functional number of the latter. And it is known that ACE2 has anti-tumor effects such as suppressing angiogenesis and metastases (30).

-The M protein activates NFkB responsible for the regulation of EMT genes and tumor progression, as well as angiogenesis.

-Triple negative tumor cells can induce a more aggressive transformation of initially less aggressive tumor cells due to cytokine shock.

Other studies focused on the role of pro-inflammatory cytokines in tumor genesis like the TGF-  $\beta$ 1 that promotes metastases, VEGF (elevated during SARS-CoV-2 infection) that is a stimulator of angiogenesis (31), IL-6, crucial in cytokine shock, that has a direct effect on the stimulation of tumor cells, as well as on angiogenesis and inhibition of apoptosis (32) ...

## Limitations

It is true that our study concerns a significantly high number of individuals, but our data were drawn only from a single institution which is effectively an oncological reference center.

Collecting these same data from various regions of the country, where resources are more limited, would allow us to determine in a more realistic and general way the impact of the pandemic and the economic crisis on the characteristics of cancer in Lebanon. Also, it could have been interesting to know if these patients were subject to the SARS-CoV-2 infection and/or vaccination to study whether the latter practically influences the aggressiveness of the tumor.

## Conclusion

Breast cancer is the most common type of neoplasia worldwide. Systematic screening is an extremely important tool for detecting cancer at a relatively early stage and establishing more effective therapy. However, this entity was marginalized with the occurrence of the COVID-19 pandemic, which was combined with the Lebanese economic crisis. This has negatively impacted the characteristics of breast cancer in Lebanon, with the appearance of more aggressive tumors. Hence, it is crucial to restore the previous screening programs. In addition, several resources have studied a pathogenicity relationship between the SARS-CoV-2 virus and cancers in general, constituting an additional argument to explain the recently encountered aggressiveness of breast cancer. However, the latter only constitutes a theory that other studies should focus on confirming or disproving in order to evaluate the severity of this still ongoing virus on cancers in general.

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