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Outcome of Breast Cancer Management Comparative Cross Sectional Study in Sudan and Greece

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ABSTRACT

Introduction: Prognosis of breast cancer depends mainly on early detection of the disease it is also well known the stage at diagnosis is inversely associated with the five-year survival rate nodal involvement is main prognostic factor. Other factors are associated with the prognosis of breast cancer like the molecular subtype of the tumor, socioeconomic status of the patient, and the modalities of treatment received. The management of the patient is going to be planned according to stage at diagnosis, aggressiveness of the breast cancer disease; of course, the timing of investigation and treatment is influenced by the socioeconomic status of the patient. We have recorded invasive or non- invasive breast cancer at the time of diagnosis, site of the disease right, left or bilateral, type of surgery. Comparison of these factors in two countries both of them they have no national screening program for breast cancer like Sudan and Greece, but there is difference in population education. The breast cancer patients in Greece are treated at specialized breast units and in Sudan patients are treated in general hospitals by general surgeons.

General objectives: To evaluate different modalities of breast cancer treatment set up and outcomes of breast cancer in both countries Sudan and Greece.

Methods: The study is a comparative cross sectional case control study performed at Bashair Alneelain University Teaching & Elsharif Hospitals in Sudan, Hippokrateion General Hospital of the University of Athens and Alexandra General Hospital of the University of Athens in Greece.

Inclusion criteria: included female patients that were diagnosed with breast cancer underwent appropriate treatment and with five years survival rate. The study compared 100 breast cancer patients from Sudan and 94 breast cancer patients from Greece. Control 100 female patients from Sudan and 66 female patients from Greece diagnosed with a benign disease of the breast. Informed consent was obtained in all cases.

Results: The first result we found more invasive breast cancer in Sudan than in Greece (42.27%), and (9.28%) for noninvasive than Greece (29.8%), and (19.07%) respectively, the p-value of chi-square test (.001) more bilateral breast cancer in Greek patients. There is significant increase of mastectomy in Sudan than in Greece, more chemotherapy on the other hand more conservative breast surgery and hormonal therapy in Greece and recurrence occurs on the contralateral breast.

Conclusion: Breast cancer patients in Sudan presents at late stage, younger age group with negative estrogen receptors tumors and higher rate of local recurrence. Breast cancer cases in Greece are diagnosed at earlier stage and old age group than in Sudan, bilateral, estrogen receptors positive treated with hormonal therapy and conservative breast surgery.

Management of breast cancer at specialized breast clinics gives better outcome even in countries where there is no national screening program for early detection of breast cancer.

List of abbreviation:

ALN: Axillary lymph node; ER: Estrogen receptor; HER2: Human epidermal growth factor receptor 2; PR: Progesterone receptor; NOS: Non-otherwise specified; DIEP: Deep inferior epigastria perforator artery flap; MRM: Modified radical mastectomy; TRAM: Transverse abdominal muscle.

Introduction

Prognosis of breast cancer depends mainly on early detection of the disease, mainly the nodal state at diagnosis [1,2] it is also well known the stage at diagnosis is inversely associated with the five-year survival rate [3]. Other factors are associated with the prognosis of breast cancer like the socioeconomic status of the patient, the molecular subtype of the tumor and the modalities of treatment received. The management of the patient is going to be planned according to stage at the diagnosis, aggressiveness of the breast cancer disease, the biological type, the tumor receptors state it is well known triple negative breast cancer carry poor prognosis [4,5], in the old and new literature it has been mentioned the timing of investigation and treatment is influenced by the socioeconomic status of the patient [6-11]. Records has been taken reporting: invasive or non- invasive breast cancer at the time of diagnosis, site of the disease right, left or bilateral, type of surgery tumorectomy or mastectomy axillary clearance (MRM), reconstruction, neo-adjuvant or adjuvant or no chemotherapy, recurrence; time of recurrence after diagnosis, site of recurrence. Comparison of these factors in two countries both of them they have no national screening program for breast cancer applied, like Sudan and Greece [12], but there is difference in population education about breast cancer [13], another difference in Greece breast cancer patients are treated at specialized breast units and in Sudan patients are treated in general hospitals by general surgeons [14]. Breast cancer is the most encountered female cancer in Sudan [15] and Greece. As for Sudanese patients, there is lack of specialized multidisciplinary breast department and breast surgeons and lack of a national screening program has resulted in detecting breast cancer at advanced stage. Thus, treatment strategy seems more complicated and difficult and has greater impact on the social life of the patient. Moreover, the social stigma of the disease and the long-term treatment may influence patient's career and personal life. On the other hand, Greek patients are usually examined by specialized breast surgeons in multidisciplinary breast clinics accompanied by experienced radiologist on breast ultrasound and performing and reporting mammography, which results to an earlier detection and in most cases to less surgical and adjuvant interventions, less complications and lower rates of recurrence [16].

State of the problem

Early detection of breast cancer in a setting where is there is no national program for screening of breast cancer. In spite of the fact that breast cancer is the commonest female cancer in Sudan and Greece, and both countries have no national screening programs. There is reasonable outcome of breast cancer and acceptable survival rates ,the study is to discuss breast cancer treated patients the stage at presentation, management of breast cancer in a multidisciplinary setting unit in Greece or in a setting of general hospital in Sudan how does this affect the prognosis of breast cancer and the recurrence rate comparative study between African and European countries the study revised the records of the patients for type of the disease and the treatment modalities and the outcomes of the modalities of treatment the stage of the disease invasive or non-invasive tumor ,type of surgery , molecular type of the tumor, axillary dissection ,hormonal therapy and or chemotherapy and the recurrence rates and common sites of recurrence all these findings were compared to findings of a control group in the two countries.

General objectives

To evaluate different presentation of breast cancer, modalities of treatment and outcomes of breast cancer patients in Sudan and Greece.

Specific objectives

1- To compare the rate of early breast cancer detection and management in two countries where there is no applied national screening program for breast cancer detection like Sudan and Greece.

Compare invasive and non-invasive breast cancer in Greece and Sudan.

2- To discuss the facilities of management of breast cancer in Sudan and Greece.

Compare effect of specialized breast clinics on the prognosis of the breast cancer.

3- To detect the rate and site of recurrence of breast cancer and common sites of recurrence in Greece and Sudan.

Methodology

The study is a comparative cross sectional case control study performed at Bashair Teaching Hospital of Alneelain University & Elsharif Hospitals in Sudan, Hippokrateion General Hospital and Alexandra General Hospital of the University of Athens in Greece.

Inclusion criteria: included female patients that were diagnosed with breast cancer underwent appropriate treatment and with more than five years survival rate.

The first group included 100 breast cancer patients from Sudan and 94 breast cancer patients from Greece. These groups of patients were compared with a second control group that included 100 female patients from Sudan and 66 female patients from Greece diagnosed with a benign disease of the breast. Informed consent was obtained in all cases, either during their hospital follow-up visits or by telephone. The Ethical Committees of each Hospital had approved our study.

Data were retrieved from a questionnaire, transferred to an excel report and analyzed by a specialized Biostatistician with the use of SPSS and Fisher's exaction test. Fisher's test is a very significant statistical test used in the analysis of contingency tables and it is employed in small size sample, however it is valid for all size samples. It is named after its inventor, Ronald Fisher, and is one of a class of exact tests, so called because the significance of the deviation from a null hypothesis (e.g., P-value) can be calculated exactly, rather than relying on an approximation that becomes exact in the limit as the sample size grows to infinity, as with many statistical tests this test is known as ANOVA test as well.

Hospital setting in Greece

Patients in Greece were examined in specialized multidisciplinary breast clinics in two University Hospitals. Data were retrieved during their initial interview or by a telephone interview. Both breast clinics in Hippokrateion and Alexandra General Hospitals are Breast Accredited Units, utilizing all up to date means of mammography, sonography and biopsy.

Hospital setting in Sudan

On the other hand, patients in Sudan were examined in both Hospitals by only one specialized breast surgeon in collaboration with General Surgeons. Mammogram is available only in one public Hospital at the radiology department and in private Hospitals sonography and biopsy were available in both of the previously mentioned hospitals.

Results

The first result we found more invasive breast cancer in Sudan than in Greece. The frequency distribution the result of first biopsy showed significant increasing of invasive breast cancer in Sudan (82, 42.27%), and (18, 9.28%) for noninvasive than Greece (57, 29.8%), and (37, 19.07) respectively, the p-value of chi-square test (.001) (Figure 1).



Figure 1: Rate of Invasive and non-invasive breast cancer diagnosed among breast cancer patients in Greece & Sudan.

The frequency distribution of the side of the disease showed insignificant result, in Sudan (49, 25.26%) for the right side, and (49, 25.26%) for the left side, and (2, 1.03%) for Both sides, (57, 29.8%), and in Greece (37, 19.07), (40, 20.62%), (45, 23.20%), and (9, 4.64%) respectively the p-value of chi-square test (.069) (Figure 2), with increase of bilateral breast cancer in the Greek patients.



Figure 2: Bilateral breast cancer surgery performed among treated breast cancer patients in Greek and Sudanese breast cancer patients.

The frequency distribution of having surgery showed insignificant result, in Sudan (98, 51,042%%) for yes, and (1, .52%) for No, and (93, 48.44%) for yes in Greece the p-value of chi-square test (1.000).

The frequency distribution the type of surgery showed significant increasing of mastectomy in Sudan (59, 30.07%) than Greece (39, 20.21%), and the p-value of Fisher Exact test (.017) (Figure 3). This can be explained by late stage at diagnosis with larger tumor size.



Figure 3: Different type of breast Surgery performed among treated breast cancer patients in Sudan and Greece.

The frequency distribution of removing lymph-node showed significant increasing of yes removed in Sudan (58, 30.85%) than in Greece (55, 20.21%), and the p-value of Chi-square test (.006) (Figure 4).

The frequency distribution of removing ovaries showed

insignificant increasing of not removed in Sudan (95, 49.74%) than Greece (90, 47.12%), and the p-value of Chi-square test (.440).



Figure 4: Lymph node surgery performed among treated breast cancer patients in Sudan and Greece.

The frequency distribution of breast reconstruction showed significant increasing of not done in Sudan (90, 61.64%) than Greece (29, 19.86%), and the p-value of Chi-square test (.000) (Figure 5).



Figure 5: Breast reconstruction surgery performed among treated breast cancer patients in Sudan and Greece.

Using chemotherapy significantly increase in Sudan (83, 42.78%) than Greece (57, 29.38%), and the p-value of Chi-square test (.001) (Figure 6). Using hormonal therapy significantly increase in Greece (75, 43.60%) than Sudan (51, 29.65%), and the p-value of Chi-square test (.000) (Figure 7).

The early menopause was not noticed among patients from Greece in (68, 35.60%) in comparison with Sudanese (53, 27.75%), the frequency distribution was significant, the p-value of Chi-square test (.011) (Figure 8).



Figure 6: Rate of Chemotherapy administration among treated breast cancer patients in Sudan and Greece.







Figure 8: Incidence of early menopause among treated breast cancer patients in Sudan and Greece.

The recurrence of the tumor among Sudanese (19, 10.05%) patients was insignificantly more than among patients from Greece (12, 6.35%), the p-value of Chi-square test (.201).

The more common site of recurrence in Sudan was significantly the same breast (15, 83.3%) of total 19 cases with recurrence, and the more common site in Greece was the contralateral breast (6, 50%) of total 12 cases with recurrence, the p-value of Fisher Exact test (.000).

Discussion

It is known that breast cancer patients present at later stage at diagnosis when there is no proper national screening program this is the condition in Sudan, most of the patients are diagnosed at late stage with larger tumor size and involved axillary lymph nodes, this is not the condition in Greece in spite of the fact there is no national screening program for breast cancer in in Greece as well [13], we can attribute this to better socioeconomic status and literacy in Greece, furtherer more there are specialized certified breast clinics in Greece [13], while in Sudan the breast cancer patients are treated in the setting of general hospitals and there is scarcely specialized breast clinics or breast surgeons. This explains that there is more invasive cancer in Sudan figure [1].

Diagnosis of more bilateral breast cancer in Greece is explained by use of digital mammography in diagnosis of breast cancer, a paper from Sudan concluded to that (1.3%) of the breast cancer patients revealed bilateral cancer: (0.9%) synchronous and (0.4%) metachronous breast cancer [17]. Which is goes with the results of this study where bilateral breast cancer in Sudan is 1.03% where in Greek breast cancer patients represents of the cases (4.64%). Bilateral breast cancer is invariably advanced when diagnosed. Mammogram is a valuable tool in early detection. Whether synchronous or metachronous, both breasts often share the same histological type [18]. Most of the patients from Greece or Sudan underwent breast surgery, but most of the patients from Sudan underwent modified Radical Mastectomy (MRM) [19], while most the patients from Greece underwent tumorectomy or lumpectomy with or without axillary dissection.

Regarding modalities of breast surgery while in Greece the discussion with the patient is about conservative breast surgery and most of the patients diagnosed with ductal carcinoma in situ [20], in Sudan the discussion is about surgery after neo-adjuvant chemotherapy in patients diagnosed with locally advanced breast cancer.

Axillary lymph node dissection is still the goal standard of surgical management in patients diagnosed with breast cancer in Sudan [21], in general axillary lymph node dissection is indicated in women who had breast tumors larger than 5 cm in diameter, women with three or more positive sentinel lymph nodes, women who received chemotherapy or hormone therapy before surgery, and women who underwent mastectomy instead of breast-conserving surgery with radiation, still there is a lot to learn about the need for ALND in

other treatment settings [21] on the other hand women with stage I or II breast cancer may benefit of senile lymph node dissection. A sentinel lymph node biopsy is a procedure to examine the lymph node closest to the tumor because this is where the cancer cells have most likely spread. First, the surgeon will want to identify the "sentinel lymph node," the lymph node (or nodes) closest to the tumor, to be able to identify the sentinel lymph node, the surgeon will inject dye or radioactive substances into the tissue near the tumor. The lymph nodes that are the most susceptible to the cancer's spread will be marked by the dye or radioactive substance. During surgery, the nearest lymph nodes will be removed and checked for the presence of cancer cells. For patients who are having a lumpectomy and the sentinel node is positive for cancer completion surgery towards axillary dissection or clearance should be performed. This applies to postmenopausal patients who are over age 70 and whose cancer is estrogen receptor-positive. Radiation to the underarm area and upper chest wall may be part of the treatment.

Breast cancer is the most common malignant tumor in women, once the treatments have been completed, patients can proceed to the recovery of the breast, and Patients' desire for breast reconstruction after surgery has increased. In addition to conventional methods with local flaps or implants, new prospects were provided by autologous tissue repair (Falous or free flap). In Greece all rehabilitation with implants or autologous tissue (predominantly TRAM or free Diep flap) are available both in private or general hospital. Microsurgical abdominal tissue transplantation (Diep or TRAM) offers the patient more natural form and long-lasting results. On the other hand, in Sudan breast cancer surgery is mostly mastectomy or modified radical mastectomy with no construction, in a paper from Sudan it is mentioned that breast cancer management should be tailored to the needs of the patient, stage of the disease. There is no agreement on the approach to breast cancer patients so as to standardize the management. There is no consensus on which type of surgery to be done by what type and level of surgeons. This has implications on the management of the patients [20].

Most of the patients from Sudan used to receive chemotherapy because of the negative estrogen receptors, larger tumor size at presentation and involvement of axillary lymph nodes [21], the patients from Greece used to receive hormonal therapy (due to positive estrogen receptors) with or without radiation therapy figure 7. The early menopause is not noticed among patients from Greece in comparison with the Sudanese patients (Figure 8). We can explain early menopause among breast cancer survivors in Sudan by the effect of chemotherapy.

The recurrence of the tumor among Sudanese patients was significantly more than among patients from Greece, in a study done at Gezira university the recurrence rate is found to be 31.1% and the major risk factor is young age group, size of the tumor and number of lymph nodes involved [22].

The more common sight of recurrence in Sudan was significantly the same breast, and the more common one in Greece was Contralateral breast, the use of radiotherapy, targeted chemotherapy therapy and Zoledronic acid reduces the recurrence rate in locally advanced disease, on the contralateral breast or distant metastasis [23].

Conclusion

- Breast cancer patients in Sudan presents at late stage, with negative estrogen receptors tumors and higher recurrence rate.
- Breast cancer cases in Greece are diagnosed at earlier stage and old age group than in Sudan with better modalities of treatment.
- Bilateral breast cancer is more common in Greece than in Sudan.
- Contralateral heterogeneous breast cancer is common in Greek breast cancer patients.
- Local recurrence on the same breast is common in Sudanese breast cancer patients.
- Management of breast cancer at specialized breast clinics gives better out comes even in countries where there is no national screening program for early detection of breast cancer.

Recommendations

- Establishment of specialized breast clinics in Sudan for better management out comes of breast cancer patients.
- National and international efforts are needed to improve management and quality of life for breast cancer patients' especially in Sudan and to some extent in Greece.
- More studies are needed to pick the differences on the pathology of breast cancer in Sudan and Greece.

RESEARCH QUESTIONNAIRE

For 'Impact of Breast Cancer on Marital Status" Please only complete this questionnaire if you HAVE had a breast biopsy. NAME:

DATE:

DATE OF BIRTH:

SECTION I – BREAST CANCER DIAGNOSIS, TREATMENT AND DETECTION

Please answer the following questions based on the timing of your first breast biopsy.

RESULTS

1. How many breast biopsies have you had? _____ Please answer the following in regards to your first breast biopsy:

2. When was your first breast biopsy? _____(MM/YYYY)

- a. Name of hospital:
- b. Name of doctor:

3. Which breasts were biopsied?

••Left ••Right ••Both

4. What was the result of your first biopsy? (Check all that apply)An invasive cancer

- A non-invasive cancer (early stage breast cancer)
- I. Was it Ductal Carcinoma In-situ (DCIS)? ••Yes ••No
- II. Was it Lobular Carinoma In-situ (LCIS)? ••Yes ••No
- Both an invasive and non-invasive cancer
- Benign breast disease
- Normal
- Other:

If you have had a diagnosis of breast cancer, please complete the following section on breast cancer treatment. If you have not had a history of breast cancer, please continue to section II.

TREATMENT

- 5. Did you have surgery for the first breast cancer?
- No
- Yes Year of surgery: _____

If yes, what type of surgery did you have? (Check one)

- □ Lumpectomy (tumour removed, breast remains)
- □ Mastectomy (one breast removed)
- □ Bilateral mastectomy (both breasts removed)
- 6. If you had a mastectomy; did you undergo breast reconstruction
- (i.e., plastic surgery with surgical implants)?
- No
- Yes
- 7. Was there lymph node involvement?
- No
- Yes List number of involved lymph nodes: ______
- 8. Did you receive chemotherapy for the first breast cancer?
- No
- Yes

9. Did you experience early menopause as a result of your breast cancer and its treatment?

- No
- Yes

10. Did you have your ovaries surgically removed as a result of your breast cancer?

- No
- Yes

11. Did you receive chemotherapy for the first breast cancer?

• No

• Yes

12. Have you had a recurrence of your first breast cancer?No

• Yes - Date: ____ / ___ / ___ (mm / dd / yyyy)

If yes, where did this cancer recur? (Check all that apply)

- Breast
- Lung

• Brain • Liver		
• Bone		
• Other:		
	City Province/State Postal Code	
SECTION II –MARITAL RELATIONSHIP AT THE TIME		
OF YOUR FIRST BREAST BIOPSY	23. What type of community do you live in? (Mark all that apply)	
	• Rural	
13. Were you married at the time of your first breast biopsy?	• Urban	
• No - Please go to Section III	• Suburban	
• Yes	• Farming	
	• Other:	
14. When were you married? : (MM/YYYY), to:	24. What is your major ancestry?	
(MM/YYYY)	a. Ethnic Background:	
15. Your age when married: (years), Partner's age	b. Country of Origin:	
when married:(years)		
	25. What was your work status at the time of your first breast	
16. What is your current relationship with this spouse?	biopsy: (Mark all that apply)	
Still married	• Retired	
• Widowed	• Homemaker	
• Separated, Date of separation: (MM/YYYY)	• Work Full-time, Occupation:	
• Divorced, Date of divorce: (MM/YYYY)	Work Part-time, Occupation:	
o If separated first, date of separation: (MM/YYYY)	• Unemployed or laid off, Duration of unemployment:	
	(vears, months)	
17. Did you have any children with this spouse?	□ Previous occupation:	
• No	• Other (please specify):	
• Yes - Number of children: List the years of birth of your		
children:	26. What is your current work status? (Mark all that apply)	
	• Retired	
18. In the first year following your first breast biopsy, how	• Homemaker	
did your relationship with your partner change [compared to	• Work Full-time. Occupation:	
your relationship before your breast biopsyl? (Check the most	• Work Part-time. Occupation:	
appropriate box)	• Unemployed or laid off. Duration of unemployment:	
• It staved the same	(vears, months)	
• It got better	— Previous occupation:	
• It got slightly worse	• Other (please specify):	
• It deteriorated		
	27 What is the highest level of education that you have achieved?	
19 Overall what was the impact of your first breast biopsy on this	(Check the most appropriate box)	
relationship?	Elementary School	
Positive	• High School	
Negative	• College (diploma)	
• No Impact	• University (degree)	
Tto Impuor	Postgraduate Program (Please check: Masters PhD)	
SECTION III - PERSONAL INFORMATION	Postgraduate Professional School Program (e.g. Medical school	
SECTION III - I ERSONAL INFORMATION	dental school)	
20. Date of Birth: (MM/DD/YYYY)	dental sensor)	
	28. What is your current relationship status? (Check the most	
21 Place of birth	appropriate box)	
	□ Married	
	Engaged/Long Term Relationship	
	Common-law	
City Province/State	\Box Divorced not remarried	
	\Box Divorced remarried \Box Widowed not remarried	
22. Current Residence:	□ Widowed, remarried	

□ Single

Other (please specify): ______

29. How many people were living in your household, including yourself, at the time of your first breast biopsy? _____ (Number of people)

30. Who did you live with at the time of your first breast biopsy? (Check all that apply)

□ My own children, number

□ My relatives' children, number

 \square My husband

□ My In-laws

 \Box My mother \Box My father

 \Box My sister(s)

 \Box My brother(s)

□ Relatives of my spouse

Other:

31. How many people are currently living in your household, including yourself?

_____ (Number of people)

32. Who do you currently live with? (Check all that apply)

□ My own children, number ____

□ My relatives' children, number _____

 $\ \square \ My \ husband$

 $\ \square \ My \ In-laws$

 \square My mother \square My father

 \Box My sister(s)

 \Box My brother(s)

 \square Relatives of my spouse

□ Other: _____

SECTION IV – PARTNER INFORMATION

Please complete the following questions in regards to the partner you were married to at the time of your first breast biopsy. If you were not married at the time of your first breast cancer diagnosis, please go to CONTACT INFORMATION).

33. Birth date of partner: ____/ ____ (month-day-year)

34. What is this partner's major ancestry?

a. Ethnic Background:

b. Country of Origin: _____

35. What was your spouse's occupational status at the time of your first breast biopsy: (Mark all that apply)

Retired

• Homemaker

Work Full-time, Occupation:

Work Part-time, Occupation:

• Unemployed or laid off, Duration of unemployment: (years, months)

Previous occupation: ______

Other (please specify):

36. What is your partner's current work status? (Mark all that apply)

• Retired

- Homemaker
- Work Full-time, Occupation:
- Work Part-time, Occupation:
- Unemployed or laid off, Duration of unemployment: ______(years, months)

□ Previous occupation:

• Other (please specify):

37. What is the highest level of education that this partner has achieved?

• Elementary School

- High School
- College (diploma)
- University (degree)
- Postgraduate Program (Please check: _____Masters _____PhD)

• Postgraduate Professional School Program (e.g. Medical school, dental school)

CONTACT INFORMATION

Thank you for taking the time to complete this questionnaire. Should the need arise, may we call you again?

- No
- Yes Telephone number: ______ Email : _____

In the case that we are unable to reach you at this number, please provide a telephone number of a relative that we can call to obtain your new contact information:

Name: _____ Relationship:

Telephone number: _____ Email: _____

If you are changing you contact information, please call us at:+249115848962.

FOR OFFICE USE (to be completed by Study Personnel):

	Participating centre:,	Contact
	person:	
	Interviewer (if by phone):	
ſ	Individual Identification No:	
	Date questionnaire sent: Month – Day – Year	
:	Date questionnaire received: Month – Day – Year	

Information received by: mail _____ telephone _____ email in clinic ____

PATIENT CONSENT:

I.....

Agree to be considered a volunteer and to provide information and investigations about my condition to participate in the study research done by Mrs. Ayda Hussein Omer Mustafa, about breast cancer and its effects on marital status.

I have been fully informed beforehand.

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