European Journal of Clinical and Experimental Medicine

ONLINE FIRST

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.

Authors: Yasmine El Kastit, Naoufel Ali Zeggwagh, Ahlam Aitouma, Hasna Ahyayauch

Article type: Original Article

Received: 16 July 2026

Accepted: 29 October 2026

Published online: 24 November 2026

eISSN: 2544-1361

Eur J Clin Exp Med

doi:10.15584/ejcem.2026.4.9

ONLINE FIRST Eur J Clin Exp Med

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our authors we are providing this early version of the manuscript. The manuscript will undergo copyediting and typesetting. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY 4.0) license.

Cancer-related fatigue and insomnia in Moroccan women with breast cancer – prevalence, co-occurrence, and associated factors

Yasmine El Kastit [1], Naoufel Ali Zeggwagh [1], Ahlam Aitouma [2], Hasna Ahyayauch [1]

[1] Higher Institute of Nursing Professions and Health Techniques (ISPITS), Rabat, Morocco

[2] Translational Oncology Research Team, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco

Corresponding author: Hasna Ahyayauch, e-mail: ahyayauch@hotmail.com

ORCID

YEK: https://orcid.org/0009-0006-3284-0970

NAZ: https://orcid.org/0009-0009-8607-4855

AA: https://orcid.org/0009-0003-3625-5355

HA: https://orcid.org/0000-0002-3324-2765

ONLINE FIRST Eur J Clin Exp Med

ABSTRACT

Introduction and aim. Cancer-related fatigue (CRF) and insomnia are highly prevalent, distressing symptoms in women with breast cancer, but their co-occurrence and associated factors remain understudied in Morocco. This study aimed to estimate the prevalence and severity of CRF and insomnia in Moroccan women with breast cancer, quantify the strength of their association, and identify the factors associated with each symptom.

Material and methods. A single-center, cross-sectional study was conducted at the National Institute of Oncology, Rabat, among 100 women with histologically confirmed breast cancer, assessed using the Arabic-validated Brief Fatigue Inventory (BFI) and Insomnia Severity Index (ISI). The fatigue–insomnia association was measured with Spearman's correlation and simple linear regression. Factors associated with each symptom were examined with multivariate linear regression.

Results. Severe fatigue (BFI ≥7) was reported by 78% of participants (mean 7.58±1.80), and clinically significant insomnia (ISI ≥15) by 75% (54% moderate, 21% severe). BFI and ISI scores were strongly correlated (ρ=0.78, $p<0.001$). In simple linear regression, approximately two-thirds of the variance in ISI scores was shared with BFI scores (R^2=0.67). In multivariate models, perceived stress was the factor most strongly associated with fatigue and insomnia.

Conclusion. Fatigue and insomnia were highly prevalent and strongly associated, and perceived stress was their strongest measured correlate. Because the study is cross-sectional and several potentially important

clinical and treatment-related confounders were not evaluated, these findings reflect associations and do not imply causation. They support the consideration of routine symptom assessment in Moroccan oncology settings.
Keywords. breast neoplasms, cancer-related fatigue, insomnia, Morocco, perceived stress, symptom burden

Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death among women worldwide, with an estimated 2.3 million new cases and 670,000 deaths in 2022[1]. In Morocco, breast cancer accounts for approximately one third of all female malignancies and increasingly affects women during their reproductive and economically productive years.[2,3] Earlier detection and improvements in systemic therapy have changed the clinical focus from survival alone to the long-term burden that erodes quality of life.[4,5]

Cancer-related fatigue (CRF) and insomnia are consistently rated by patients as among the most distressing symptoms, and by clinicians as among the most underrecognized and under-treated.[6-8] The National Comprehensive Cancer Network defines CRF as a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or its treatment, disproportionate to recent activity, and affecting usual functioning.[9] Insomnia is characterized by difficulty initiating or maintaining sleep, or by non-restorative sleep, accompanied by daytime impairment.[10] Reported prevalences in breast cancer cohorts range from 40–80% for CRF and 30–60% for insomnia,[11-13] and many patients continue to experience these symptoms long after active treatment has ended.[14,15] Assessing fatigue and insomnia together is clinically important because the two symptoms frequently co-occur in cancer patients,8,13 can share correlates, and call for different complementary management strategies.[17] Assessing only one of them may leave the other undetected, and neither is reliably identified without systematic screening.

Psycho-oncology research has proposed that fatigue, insomnia, and psychological distress can form a symptom cluster with shared biopsychosocial mechanisms, including hypothalamic-pituitary-adrenal (HPA) axis dysregulation, low-grade systemic inflammation, circadian disruption, and cognitive hyperarousal.[16-19] These symptoms are believed to reinforce one another-poor sleep may contribute to daytime fatigue, and fatigue and stress may promote nocturnal hyperarousal and rumination-forming a self-perpetuating loop that could compromise treatment adherence, immune function, and survival.[20,13] These mechanisms were not investigated in the present study.

Despite this global evidence, data from North Africa and the Middle East remain scarce. Moroccan studies have examined quality of life and anxiodepressive comorbidities in women with breast cancer,[21,22] but, to our knowledge, none has simultaneously assessed fatigue and insomnia or modeled their joint determinants in this population. Local cultural, socioeconomic, and health system characteristics, including limited health

ONLINE FIRST Eur J Clin Exp Med

literacy, low rates of formal psycho-oncology referral, and limited availability of non-pharmacological sleep interventions, make context-specific data essential for designing appropriate supportive care. The relationship between fatigue, insomnia, and psychological distress has been studied internationally; the contribution of the present study is regional rather than conceptual or methodological. Its main contribution is the simultaneous assessment of the severity of fatigue and insomnia, their association, and selected clinical and psychosocial correlates in a Moroccan population of breast cancer. By extending the existing literature to this setting, the study provides data to help identify unmet support care needs.

Aim

This study aimed to: (i) describe the prevalence and severity of CRF and insomnia in women with breast cancer treated at the National Institute of Oncology (INO), Rabat; (ii) quantify the strength and direction of the fatigue–insomnia association; and (iii) identify the clinical, psychological and behavioural associated with each symptom. We hypothesized that fatigue and insomnia would be positively correlated and that psychological, clinical and behavioral factors, including perceived stress, would be associated with the severity of each symptom.

Material and methods

Study design and setting

We conducted a single-center, observational, cross-sectional study at the National Institute of Oncology (INO) in Rabat, the national reference center for cancer care in Morocco. Participants were recruited from the gyneco-mammary inpatient ward and the day hospital chemotherapy unit. Reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Participants

Eligible participants were women 18 years with a histologically confirmed diagnosis of breast cancer, currently receiving care at INO and able to understand and responding in Moroccan Arabic, French, or Modern Standard Arabic. Exclusion criteria were: a known severe cognitive or psychiatric disorder likely to compromise response reliability; a concurrent primary non-breast malignancy; or unavailability during the data collection window.

Sample size and sampling

Participants were recruited consecutively between August and October 2025. Eligibility, including the absence of exclusion criteria, was verified by reviewing the medical record prior to approach. No woman was excluded after being approached. The number of records screened prior to the approach was not recorded. All 100 eligible women were enrolled and none declined participation (response rate: 100%).

ONLINE FIRST Eur J Clin Exp Med

Because the sample size was determined by the number of eligible women available during the data collection window, we conducted a sensitivity power analysis instead of an a priori calculation. Using G*Power 3.1, (F tests: linear multiple regression, fixed model, increase in R2), a sample of n=100 provides 80% power at α=0.05 to detect an effect of f2 0.08 (between small and medium according to Cohen's conventions) for a single predictor (one predictor tested, 1 numerator degree of freedom) in a regression model with 9 predictors in total, as in the final models.

Data collection

Data were collected face-to-face by the principal investigator (YEK) in a private, confidential setting; mean administration time was 15–20 minutes. The questionnaire comprised a sociodemographic section, a clinical section, and two standardized symptom measures.

Sociodemographic and behavioral variables

Age (18–29, 30–44, 45–59, ≥ 60 years), marital status, parity, level of education, occupational status, perceived socioeconomic level, type of health insurance, residential area (urban/rural), tobacco and alcohol use, caffeine intake (cups per day), regular physical activity, and self-reported spirituality.

Clinical variables

Current oncological treatment, comorbidities, antidepressant use, appetite disturbance, intensity and perceived stress were recorded. The participant rated the intensity of pain and perceived stress on a 0–10 visual analog scale (VAS) 0-10, where 0=[no pain / no stress] and 10=[worst imaginable pain / maximum perceived stress]; higher scores indicate greater pain or stress. For description, pain was classified as none (0), mild (1–3), moderate (4–6), intense (7–9) or maximal (10), and perceived stress as low (0–3), moderate (4–6) or severe (7–10). In the regression models, pain intensity was entered as a continuous score and perceived stress as a categorical variable (reference: low stress).

Current oncological treatment was extracted from medical records and defined as the treatment received at the time of the interview. Participants were assigned to one of six mutually exclusive categories: no current treatment, hormonal therapy only, surgery alone, chemotherapy, radiotherapy or concurrent chemoradiotherapy (chemotherapy and radiation therapy administered during the same period).

Brief Fatigue Inventory (BFI)

Fatigue was assessed during the preceding 24 hours using the Arabic-validated BFI.[23,24] The BFI comprises nine items rated 0–10, yielding a total score of 0-10 with established cut-offs for mild (1–3), moderate (4–6), and severe (7) fatigue. The instrument has demonstrated strong internal consistency (Cronbach's α=0.96) and is widely used in cancer research.

ONLINE FIRST Eur J Clin Exp Med

Insomnia Severity Index (ISI)

Insomnia during the preceding two weeks was measured using the 7-item ISI,[25] scored 0 to 28 with conventional cutoffs of 0–7 (no clinically significant insomnia), 8 to 14 (subthreshold), 15–21 (moderate), and 22 to 28 (severe). ISI has good psychometric properties (Cronbach's α=0.87) and has been validated in Arabic.[26]

The BFI and ISI were administered in their validated Arabic versions, which are written in modern standard Arabic, and were read aloud by the investigator. Although eligible women could respond in Moroccan Arabic, French, or Modern Standard Arabic, all participants chose Moroccan Arabic. The items were explained orally in Moroccan Arabic when needed, without changing their content, and no formal translation or cross-cultural adaptation was undertaken in Moroccan Arabic. In our sample, Cronbach's α was 0.92 for the BFI and 0.80 for the ISI.

Completeness of the questionnaires was checked at the end of each interview. There were no missing values for any variable used in the analyzes (n = 100 for all analyzes).

Statistical analysis

Data were entered in Microsoft Excel and analyzed using IBM SPSS Statistics version 28 (IBM Corp., Armonk, NY). Continuous variables are expressed as mean±standard deviation (SD) and median (range); categorical variables as counts and percentages. Distributional normality was assessed using the Shapiro–Wilk test together with skewness statistics and visual diagnostics; Both scales showed marked negative skew, which justified nonparametric methods for the primary association analysis. The normality of the outcome scores is not required for linear regression; its assumptions concern the residuals of the model rather than the distribution of the outcome variables, and with n = 100 the inference on the coefficients is robust to moderate deviations from normality.

The association between BFI and ISI scores was examined using Spearman's rank correlation coefficient (ρ), with its 95% confidence interval (CI) and simple linear regression summarized by the coefficient of determination (R^2). The 95% CI for Spearman's ρ was calculated using Fisher's z transformation with the Bonett–Wright standard error, $SE = [(1 + \rho^2/2)/(n - 3)]$, and back-transformed to the correlation scale. The regression slope's 95% CI is based on the t distribution with $n - 2$ degrees of freedom [and was confirmed by BCa bootstrap with 2000 replicates].

Factors associated with each symptom were examined with multivariate linear regression and regression coefficients (B) are reported with 95% CI. Multivariate models included perceived stress, current oncological treatment, caffeine intake, pain intensity, and age, were selected a priori based on clinical relevance, and entered simultaneously. Perceived stress (reference: low stress) and current oncological treatment (reference: no current treatment) were entered as categorical variables with dummy coding;

ONLINE FIRST Eur J Clin Exp Med

caffeine intake, intensity of pain, and age were entered as continuous variables. Therefore, the model assumptions were evaluated in the residuals rather than in the outcome distributions: linearity and homoscedasticity were examined by plotting standardized residuals against predicted values, and normality of the residuals with histograms and normal probability plots; Multicollinearity was assessed with variance inflation factors (<3) and influential observations with Cook's distance (<1). Because the results were negatively skewed, bootstrap 95% CIs (bias-corrected and accelerated, 2,000 resamples) were computed as a sensitivity analysis to verify that the inference did not depend on normally distributed residuals. Statistical significance was established at $p<0.05$ (two-sided), with exact p values reported to three decimal places ($p<0.001$ when smaller).

Results

Characteristics of the participants

A total of 100 women with complete data on the BFI and ISI were included. The largest age group was 30 to 44 years (38%), followed by 45 to 59 years (33%); 23% were 60 years and 6% were 18–29 years old. Most were married (74%), had one or two children (60%), and lived in an urban area (72%). Education was generally low: 30% had no formal education, 31% had primary, 29% had secondary and 10% had higher education. Fifty-two percent were unemployed and 60% reported a low perceived socioeconomic level. Health insurance coverage included AMO Tadamoun (40%), CNSS (35%), FAR (10%), and CNOPS (4%); 11% had no coverage. Comorbidities were infrequent (78% reported none), the most common being hypertension (12%) and diabetes (10%). Regular physical activity was reported by 27%, 32% consumed two cups of caffeine per day, and only 1% was taking antidepressants. The complete characteristics are shown in Table 1.

Table 1. Sociodemographic, clinical, and behavioral characteristics of participants (n=100)*

Characteristic	Category	n (%)
Age (years)	18–29	6 (6)
	30–44	38 (38)
	45–59	33 (33)
	≥ 60	23 (23)
Marital status	Married	74 (74)
	Single	10 (10)
	Divorced	10 (10)
	Widowed	6 (6)
Children	None	12 (12)
	1–2	60 (60)

ONLINE FIRST Eur J Clin Exp Med

	3–4	24 (24)
	≥ 5	4 (4)
Education	None	30 (30)
	Primary	31 (31)
	Secondary	29 (29)
	Higher	10 (10)
Employment	Employed	34 (34)
	Unemployed	52 (52)
	Retired	14 (14)
Perceived SES	Low	60 (60)
	Medium	27 (27)
	High	13 (13)
Health insurance	AMO Tadamoun	40 (40)
	CNSS	35 (35)
	FAR	10 (10)
	CNOPS	4 (4)
	None	11 (11)
Residence	Urban	72 (72)
	Rural	28 (28)
Comorbidities	None	78 (78)
	Hypertension	12 (12)
	Diabetes	10 (10)
Current oncological treatment	Radiotherapy	33 (33)
	Chemotherapy	26 (26)
	None at present	25 (25)
	Hormonal therapy	8 (8)
	Surgery alone	5 (5)
	Chemo + radiotherapy	3 (3)
Physical activity	Yes	27 (27)
	No	73 (73)
Caffeine (cups/day)	0	24 (24)
	1	21 (21)
	2	32 (32)
	≥3	23 (23)

ONLINE FIRST Eur J Clin Exp Med

Antidepressant use	Yes	1 (1)
	No	99 (99)
Appetite disturbance	Yes	52 (52)
	No	48 (48)
VAS pain (0–10)	0 (none)	30 (30)
	1–3 (mild)	19 (19)
	4–6 (moderate)	13 (13)
	7–9 (intense)	29 (29)
	10 (maximal)	9 (9)
VAS stress (0–10)	Low	12 (12)
	Moderate	30 (30)
	Severe	58 (58)

* SES socioeconomic status, VAS – visual analog scale, AMO – Assurance Maladie Obligatoire, CNSS Caisse Nationale de Sécurité Sociale, FAR Forces Armées Royales, CNOPS – Caisse Nationale des Organismes de Prévoyance Sociale

Current oncological treatment: radiation therapy 33%, chemotherapy 26%, no current treatment 25%, hormonal therapy 8%, surgery alone 5%, and concurrent chemoradiotherapy 3%. 52% reported by 52%. On VAS stress, 58% reported severe stress, 30% moderate, and 12% low stress.

Prevalence and severity of fatigue and insomnia

Table 2. Descriptive statistics of total BFI and ISI scores (n=100)*

Statistic	**BFI total (0–10)**	**ISI total (0–28)**
n (valid/missing)	100/0	100/0
Mean	7.58	17.36
Median	8.00	18.00
Standard deviation	1.80	5.17
Variance	3.26	26.72
Skewness (SE)	–1.11 (0.24)	–0.59 (0.24)
Minimum	1	1
Maximum	10	28
Severity distribution	Mild 7%,	None 6%,
	Moderate 15%,	Subthreshold 19%,

ONLINE FIRST Eur J Clin Exp Med

	Severe 78%	Moderate 54%, Severe 21%

* Brief fatigue inventory, ISI – insomnia severity index, BFI severity: 1 to 3 mild, 4–6 moderate, ≥7 severe, ISI severity: 0 to 7 none, 8–14 subthreshold, 15 to 21 moderate, 22–28 severe

Severe fatigue (BFI ≥ 7) was reported by 78% of women; 15% had moderate and 7% mild fatigue. The mean total score was 7.58±1.80 (median 8; range 1–10; skewness 1.11), indicating clustering at the upper end of the scale (Table 2).

Insomnia was similarly prevalent. Using conventional ISI cutoffs, 75% had clinically significant insomnia at the moderate to severe level (ISI ≥ 15): 54% with moderate insomnia (ISI 15–21) and 21% with severe insomnia (ISI 22). A further 19% reported subthreshold insomnia (ISI 8–14) and only 6% had no clinically significant insomnia. The mean ISI total score was 17.36±5.17 (median 18; range 1–28; skewness <0.59).

Association between fatigue and insomnia

Fatigue and insomnia were strongly and positively associated. Spearman's rank correlation between BFI and ISI total scores was ρ=0.78 (95% CI 0.68 to 0.86; p<0.001; Table 3). In simple linear regression, ISI = 0.4 + 2.34 × BFI (slope 95% CI 2.01 to 2.67; R^2=0.67; Fig. 1): each 1 point higher BFI score was associated, on average, with a 2.34 point higher ISI score, and about two-thirds of the variance in ISI scores was shared with BFI scores in this sample. Given the cross-sectional design, these statistics describe an association only; they do not imply directionality, and R^2 should not be read as fatigue causing or explaining insomnia severity.and R^2 should not be read as fatigue causing or explaining insomnia severity.

Table 3. Spearman rank correlation between fatigue (BFI total) and insomnia (ISI total)

Variable pair	Spearman ρ	95% CI	2-sided p	n
BFI total×ISI total	0.784	0.68 to 0.86	<0.001	100

ONLINE FIRST Eur J Clin Exp Med

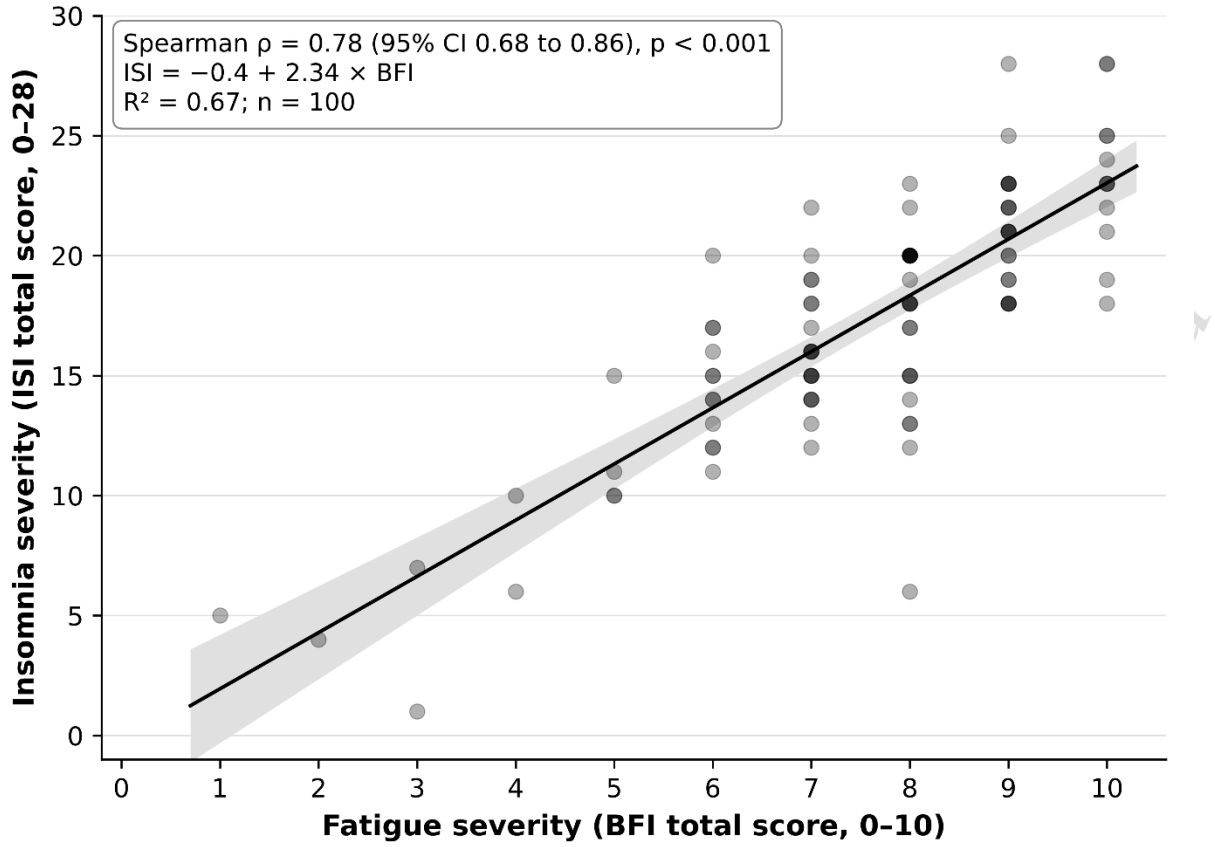


Fig. 1. Scatter plot of insomnia severity (ISI total) versus cancer-related fatigue (BFI total) in 100 Moroccan women with breast cancer, with linear regression line (ISI=–0.4+2.34×BFI; R^2=0.67; Spearman ρ=0.78, p<0.001)

Factors associated with fatigue and insomnia

Factors associated with fatigue and insomnia were examined using multivariate linear regression, with BFI total score and the total ISI score as separate outcomes. Perceived stress, current oncological treatment, caffeine intake, pain intensity, and age were entered simultaneously (n=100; 9 estimated coefficients; residual df=90). Perceived stress was, by a clear margin, the strongest measured correlate of fatigue: compared to low stress, BFI total scores were on average 1.71 points higher with moderate stress (95% CI 0.67 to 2.74, p=0.001) and 3.19 points higher with severe stress (95% CI 2.20 to 4.19, p<0.001). None of the treatment categories, caffeine intake, pain intensity or age reached statistical significance for fatigue once stress and the other covariates were accounted for. The model explained a modest proportion of the variance in fatigue scores (R^2=0.40, adjusted R^2=0.34).

The pattern was similar for insomnia. Moderate stress was associated with a 3.46-point increase in the ISI total score (95% CI 0.44 to 6.48, p=0.025) and severe stress with a 7.79-point increase (95% CI 4.89 to 10.70, p<0.001), relative to low stress. Among treatment categories, only combined chemotherapy plus

ONLINE FIRST Ed

radiation therapy differed from current treatment (including hormonal therapy only) (B= –5.32, 95% CI -10.53 to –0.11, p=0.046); as only three women received this combination, this estimate is imprecise and should be interpreted with caution. Caffeine intake, pain intensity, and age were not significantly associated with insomnia. The model accounted for a similar proportion of variance (R^2=0.37, adjusted R^2=0.31). Collinearity diagnostics were reassuring for both models (all variance inflation factors<3), and no observation exerted an undue influence (Cook's distance<1 for all cases). Bootstrap resampling (bias-corrected and accelerated, 2000 replications) produced confidence intervals closely matching the parametric estimates above.

Table 4. Multivariate linear regression of factors associated with fatigue (BFI total) and insomnia (ISI total) (n=100)

Predictor	**BFI: B (95% CI)**	**BFI: p**	**ISI: B (95% CI)**	**ISI: p**
Perceived stress: moderate vs low	1.71 (0.67 to 2.74)	0.001	3.46 (0.44 to 6.48)	0.025
Perceived stress: severe vs low	3.19 (2.20 to 4.19)	<0.001	7.79 (4.89 to 10.70)	<0.001
Treatment: surgery alone vs no current treatment*	–0.04 (–0.84 to 0.75)	0.915	0.12 (–2.19 to 2.44)	0.915
Treatment: chemotherapy vs no current treatment*	0.54 (–0.20 to 1.29)	0.151	1.05 (–1.13 to 3.22)	0.341
Treatment: radiotherapy vs no current treatment*	0.61 (–0.60 to 1.82)	0.320	2.81 (–0.72 to 6.34)	0.117
Treatment: concurrent chemoradiotherapy vs no current treatment*	–0.96 (–2.74 to 0.83)	0.289	–5.32 (–10.53 to –0.11)	0.046
Caffeine intake, per 1 cup/day	0.24 (–0.05 to 0.52)	0.102	0.13 (–0.69 to 0.96)	0.750
Pain intensity, per 1 point increase (0-–10)	0.01 (–0.22 to 0.24)	0.958	0.09 (–0.57 to 0.76)	0.780

ONLINE FIRST Eur J Clin Exp Med

Age, per 1 year	0.005 (–0.02 to 0.03)	0.676	0.02 (–0.05 to 0.09)	0.561
Model fit	R^2=0.4, adj. R^2=0.34, F(9,90)=6.60, p<0.001		R^2=0.37, adj. R^2=0.31, F(9,90)=5.94, p<0.001	

*no current treatment (including hormonal therapy only)

Discussion

In this cross-sectional study of 100 Moroccan women with breast cancer, severe fatigue (78%) and clinically significant insomnia (75%) were highly prevalent and strongly associated with perceived stress.

Symptom burden in international context

The prevalence of fatigue and insomnia was at the upper end of published ranges,[11-13,27] plausibly reflecting active chemotherapy / radiation therapy in most participants,[14,28] marked sociodemographic vulnerability (60% low socioeconomic status, 30% without formal education, 11% uninsured),[22,29] physical activity (27%, despite its evidence base for CRF),[30,31] and under-recognized psychological distress 58% reported high stress, but only one patient received antidepressant therapy. The prevalence of severe fatigue (78%) and clinically significant insomnia (75%) in our cohort is at the upper end of the international range and exceeds it in several published series. Several context-specific factors may be relevant. First, most of the participants were recruited during active chemotherapy or radiation therapy, modalities previously associated with worsening in other cohorts, although in our adjusted multivariate model current oncological treatment was not independently associated with either symptom once stress was considered.

Co-occurrence of fatigue, insomnia, and stress

The fatigue–insomnia correlation in our sample (ρ=0.78, 95% CI 0.87-8.86) is at the upper end of published values. In the Arabic BFI validation study among Jordanian cancer patients, the correlation between BFI and ISI scores was 0.70.[24] The correlation between BFI and ISI scores (ρ=0.78) is markedly higher than typical values reported in the literature on breast cancer symptoms cluster, which generally range from 0.40 to 0.65.[16,32,33] Part of this difference may reflect our sample, which was predominantly under active treatment, and the use of self-report scales for both symptoms at the same interview, which can inflate associations through variance from shared method. A strong association between two symptoms is not sufficient to establish a formally defined symptom cluster, which requires dedicated methods, such as cluster or factor analysis in a broader set of symptoms, ideally with longitudinal data. Therefore, our findings should be read as an association between two symptoms only.

ONLINE FIRST Eur J Clin Exp Med

Perceived stress showed by far the strongest association with both symptoms, which is consistent with biopsychosocial frameworks:[16-18,34], possibly through biological pathways linking stress to fatigue and sleep disturbance, though these were not measured and this remains a hypothesis. One possible explanation is that stress-related hyperarousal disturbs sleep, which in turn increases daytime fatigue. We did not measure cortisol, inflammatory markers, or objective sleep, so this remains a hypothesis that must be tested in longitudinal studies. In the multivariate model, perceived stress was the strongest measured correlate of both symptoms: relative to low stress, severe stress was associated with a 3.19-point increase in fatigue and a 7.79-point increase in the severity of insomnia (both $p<0.001$). One possible explanation is that stress engages biological pathways linked to both fatigue and sleep disturbance; because these pathways were not measured in this study. In addition, anxiety and depression were not assessed; because they overlap with perceived stress and are closely related to both fatigue and insomnia, part of the association attributed to perceived stress may reflect broader psychological distress.

Current oncological treatment

In the present study, only concurrent chemoradiotherapy was associated with insomnia scores, but in the opposite direction. Women who received this combination had lower ISI scores than the reference group ($B = 5.32$, $p = 0.046$), without any difference in fatigue. Chemotherapy and radiation therapy have been reported to alter circadian rhythms, cortisol secretion, and inflammation.3537 However, this finding should be interpreted with caution, as only three patients were included in this treatment category. This small sample size limits the reliability of the estimate; therefore, no definitive conclusion can be drawn regarding the association between combined chemotherapy and radiotherapy and insomnia.

As treatment duration and cumulative exposure were not recorded, lower scores in untreated women cannot be attributed to treatment itself; a preexisting symptom profile or disease differences may also contribute.[38] Because treatment duration and cumulative exposure were not measured and the design is cross-sectional, no causal interpretation is possible.

Variables not associated with fatigue or insomnia

Age, pain, and caffeine intake did not show a significant association with fatigue and insomnia. The absence of age effect is consistent with CRF relating more to biological/psychological factors than age,39, and with the effect potentially absorbed by stress and treatment.[40,41] Whether behavioral factors such as caffeine intake matter primarily under high psychological load is a question for targeted testing.[42]

Clinical and nursing implications

These findings suggest that routine screening for fatigue, insomnia, and perceived stress with BFI and ISI could help identify women with a high burden of symptoms. Stress reduction and sleep interventions

ONLINE FIRST Eur J Clin Exp Med

delivered by advanced practice nurses are a promising option, but their effect on fatigue and insomnia in this population has not been tested and should be evaluated in intervention studies.

These findings support the systematic screening of fatigue and insomnia in Moroccan oncology practice using the BFI and ISI, both of which are brief, validated, and well tolerated. Because perceived stress was the strongest measured correlate of both symptoms stress-reduction interventions are a promising target for the future evaluation, including cognitive-behavioral.

This study adds context-specific data from a Moroccan breast cancer population, in which, to our knowledge, fatigue and insomnia have rarely been assessed together. Its contribution is descriptive and regional, rather than conceptual: it documents a high burden of both symptoms, quantifies their association, and identifies perceived stress as the factor most strongly associated with them in this setting. These data can help to identify supportive-care needs in Moroccan oncology care, but, given the single-centre, cross-sectional design, they do not establish causal effects or the effectiveness of any intervention and require confirmation in larger, multicenter longitudinal studies.

Study limitations and strengths

Strengths of this study include the use of internationally validated Arabic-translated scales (BFI, ISI), recruitment in a national reference center, simultaneous measurement of fatigue, insomnia, stress, and pain, and a combined analytical strategy integrating correlation, linear regression, and multivariate regression modelling with bootstrap sensitivity analysis. To our knowledge, this is one of the first studies to explicitly quantify the association and the factors associated with it in a Moroccan population of breast cancer.

These cross-sectional associations are limited by unmeasured clinical confounders (cancer stage, metastatic status, hemoglobin level, anxiety and depression, duration of treatment, cumulative exposure to chemotherapy, and radiotherapy dose); the association of stress with the severity therefore cannot be considered independent of these factors.

Limitations include: single-center design and consecutive sampling limiting external generalizability; the number of women screened through medical records was not documented, so selection processes cannot be fully assessed; cross-sectional design precluding causal inference; reliance on self-reported outcomes introducing potential shared-method variance; absence of dedicated instruments for anxiety, depression, and social support; the assessment of perceived stress using a single item visual analogue scale rather than validated multidimensional psychological distress instruments; lack of a cancer-free comparison group, unmeasured clinical confounders (cancer stage, metastatic status, hemoglobin level, treatment duration, cumulative chemotherapy exposure, and radiotherapy dose); the association of stress with symptom severity cannot be considered independent of these factors. Larger, multicentre studies incorporating biomarkers of inflammation and HPA function, together with longitudinal and interventional designs, are needed.

ONLINE FIRST Eur J Clin Exp Med

Conclusion

In this single-centre, cross-sectional study of Moroccan women with breast cancer, severe fatigue and clinically significant insomnia were highly prevalent (78% and 75%) and strongly associated, and perceived stress showed the strongest association with both symptoms. Because several potentially important clinical and treatment-related factors were not assessed, these findings reflect only associations and should be interpreted cautiously; they do not establish causation. They support the consideration of routine symptom assessment and further evaluation of supportive care strategies, whose effectiveness was not investigated in this study.

Acknowledgments

The authors thank the patients at INO Rabat for their participation, and the nursing and medical teams of the gyneco-mammary inpatient ward and the day hospital unit of chemotherapy for their support during data collection.

Declarations

Funding

No specific funding was received for this work.

Author contributions

Conceptualization, Y.E.K. and N.A.Z.; Methodology, Y.E.K.; Software, not applicable; Validation, N.A.Z.; Formal Analysis, Y.E.K.; Investigation, Y.E.K., H.A. and A.A.; Resources, not applicable; Data Curation, Y.E.K.; Writing – Original Draft Preparation, Y.E.K.; Writing – Review & Editing, H.A., A.A. and N.A.Z.; Visualization, not applicable; Supervision, N.A.Z.

Conflicts of interest

The author(s) declare no competing interests.

Data availability

De-identified data are available from the corresponding author on reasonable request.

Ethics approval

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee for Biomedical Research, Faculty of Medicine and Pharmacy of Rabat, Mohammed V

ONLINE FIRST Eur J Clin Exp Med

University (Project identification code: CERB 80/23). Institutional authorisation was obtained from the Direction of INO Rabat prior to data collection. No personally identifying information was collected.

References

1. Kim J, Harper A, McCormack V, et al. Global patterns and trends in breast cancer incidence and mortality across 185 countries. *Nat Med*. 2025;31(4):1154-1162. doi:10.1038/s41591-025-03502-3
2. Khalis M, El Rhazi K, Charaka H, et al. Female breast cancer incidence and mortality in Morocco: comparison with other countries. *Asian Pac J Cancer Prev*. 2016;17(12):5211-5216. doi:10.22034/APJCP.2016.17.12.5211
3. Hashim MJ, Al-Shamsi FA, Al-Marzooqi NA, Al-Qasemi SS, Mokdad AH, Khan G. Burden of breast cancer in the Arab world: findings from Global Burden of Disease, 2016. *J Epidemiol Glob Health*. 2018;8(1-2):54-58. doi:10.2991/j.jegh.2018.09.003
4. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. *Br J Radiol*. 2022;95(1130):20211033. doi:10.1259/bjr.20211033
5. Devi S. Projected global rise in breast cancer incidence and mortality by 2050. *Lancet Oncol*. 2025;6:S1470-2045. doi:10.1016/S1470-2045(25)00136-6.
6. Curt GA, Breitbart W, Cella D, et al. Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. *Oncologist*. 2000;5(5):353-360. doi:10.1634/theoncologist.5-5-353
7. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-related fatigue: the scale of the problem. *Oncologist*. 2007;12(suppl 1):4-10. doi:10.1634/theoncologist.12-S1-4
8. Palesh OG, Roscoe JA, Mustian KM, et al. Prevalence, demographics, and psychological correlates of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. *J Clin Oncol*. 2010;28(2):292-298. doi:10.1200/JCO.2009.22.5011
9. Berger AM, Abernethy AP, Atkinson A, NCCN clinical practice guidelines in oncology: cancer-related fatigue. *J Natl Compr Canc Netw*. 2010;8(8):904-931. doi:10.6004/jnccn.2010.0067
10. American Academy of Sleep Medicine. International Classification of Sleep Disorders. 3rd ed. American Academy of Sleep Medicine; 2014.
11. Abrahams HJG, Gielissen MFM, Schmits IC, Verhagen CAHHVM, Rovers MM, Knoop H. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12,327 breast cancer survivors. *Ann Oncol*. 2016;27(6):965-974. doi:10.1093/annonc/mdw099

ONLINE FIRST Eur J Clin Exp Med

12. Al Maqbali M, Al Sinani M, Al Naamani Z, Al Moundhri M, Mansour L. Prevalence of fatigue in patients with cancer: a systematic review and meta-analysis. *J Pain Symptom Manage*. 2021;61(1):167-189. doi:10.1016/j.jpainsymman.2020.07.037
13. Roscoe JA, Kaufman ME, Matteson-Rusby SE, et al. Cancer-related fatigue and sleep disorders. *Oncologist.* 2007;12(suppl 1):35-42. doi:10.1634/theoncologist.12-S1-35
14. Bower JE, Ganz PA, Desmond KA, Rowland JH, Meyerowitz BE, Belcin RB. Fatigue in breast cancer survivors: occurrence, correlats, and impact on quality of life. *J Clin Oncol*. 2000;18(4):743. doi:10.1200/JCO.2000.18.4.743
15. Bower JE, Lamkin DM. Inflammation and cancer-related fatigue: mechanisms, contributing factors, and treatment implications. *Brain Behav Immun.* 2013;30(suppl):S48-S57. doi:10.1016/j.bbi.2012.06.011
16. Bower JE. Cancer-related fatigue: mechanisms, risk factors, and treatments. *Nat Rev Clin Oncol.* 2014;11(10):597-609. doi:10.1038/nrclinonc.2014.127
17. Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. *J Clin Oncol.* 2001;19(3):895-908. doi:10.1200/JCO.2001.19.3.895
18. Miaskowski C, Barsevick A, Berger A, et al. Advancing symptom science through symptom cluster research: expert panel proceedings and recommendations. *J Natl Cancer Inst*. 2017;109(4):djw253. doi:10.1093/jnci/djw253
19. Saligan LN, Olson K, Filler K, et al. The biology of cancer-related fatigue: a review of the literature. *Support Care Cancer*. 2015;23(8):2461-2478. doi:10.1007/s00520-015-2763-0
20. Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. *Brain Behav Immun.* 2007;21(8):1038-1049. doi:10.1016/j.bbi.2007.04.002
21. El Kherchi O, Aquil A, Elkhoudri N, et al. Relationship between sleep quality and anxiety-depressive disorders in Moroccan women with breast cancer: a cross-sectional study. *Iran J Public Health.* 2023;52(7). doi:10.18502/ijph.v52i7.13247
22. El Kherchi O, Aquil A, Elkhoudri N, et al. Anxiety and depression comorbidities in Moroccan patients with breast cancer. *Front Psychiatry.* 2021;11:584907. doi:10.3389/fpsyt.2020.584907
23. Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer*. 1999;85(5):1186-1196. doi:10.1002/(sici)1097-0142(19990301)85:5<1186::aid-cncr24>3.0.co;2-n
24. Suleiman K, Al Kalaldeh M, AbuSharour L, et al. Validation study of the Arabic version of the Brief Fatigue Inventory (BFI-A). *East Mediterr Health J.* 2019;25(11):784-790. doi:10.26719/emhj.19.032

ONLINE FIRST Eur J Clin Exp Med

25. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med.* 2001;2(4):297-307. doi:10.1016/S1389-9457(00)00065-4
26. Suleiman KH, Yates BC. Translating the Insomnia Severity Index into Arabic. *J Nurs Scholarsh.* 2011;43(1):49-53. doi:10.1111/j.1547-5069.2010.01374.x
27. Hendy A, Abd Elaziz N, Hussein A. Sleep disturbance, cancer-related fatigue and depression as determinants of quality of life among breast cancer patients undergoing chemotherapy: a cross-sectional study. *BMC Cancer*. 2025;25(1):1122. doi:10.1186/s12885-025-14538-6
28. Pirl WF, Greer JA, Traeger L, et al. Depression and survival in metastatic non-small-cell lung cancer: effects of early palliative care. *J Clin Oncol.* 2012;30(12):1310-1315. doi:10.1200/JCO.2011.38.3166
29. Traoré BM, El Fakir S, Charaka H, et al. Evolution of quality of life of breast cancer patients during the first year of follow-up in Morocco. *BMC Cancer*. 2018;18(1):109. doi:10.1186/s12885-018-4008-3
30. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev*. 2012;(11):CD006145. doi:10.1002/14651858.CD006145.pub3
31. Mustian KM, Alfano CM, Heckler C, et al. Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: a meta-analysis. *JAMA Oncol.* 2017;3(7):961-968. doi:10.1001/jamaoncol.2016.6914
32. Fiorentino L, Rissling M, Liu L, Ancoli-Israel S. The symptom cluster of sleep, fatigue and depressive symptoms in breast cancer patients: severity of the problem and treatment options. *Drug Discov Today Dis Models.* 2011;8(4):167-173. doi:10.1016/j.ddmod.2011.05.001
33. Berger AM, Wielgus K, Hertzog M, Fischer P, Farr L. Patterns of circadian activity rhythms and their relationships with fatigue and anxiety/depression in women treated with breast cancer adjuvant chemotherapy. *Support Care Cancer*. 2010;18(1):105-114. doi:10.1007/s00520-009-0636-0
34. Harvey AG. A cognitive model of insomnia. *Behav Res Ther.* 2002;40(8):869-893. doi:10.1016/s0005-7967(01)00061-4
35. Wang XS, Woodruff JF. Cancer-related and treatment-related fatigue. *Gynecol Oncol.* 2015;136(3):446-452. doi:10.1016/j.ygyno.2014.10.013
36. Dhruva A, Aouizerat BE, Cooper B, Kober K, Leutwyler H, Miaskowski C. Differences in morning and evening fatigue in oncology patients and their family caregivers. *Eur J Oncol Nurs.* 2013;17(6):841-848. doi:10.1016/j.ejon.2013.06.002

ONLINE FIRST Eur J Clin Exp Med

37. Abercrombie HC, Giese-Davis J, Sephton S, Epel ES, Turner-Cobb JM, Spiegel D. Flattened cortisol rhythms in metastatic breast cancer patients. *Psychoneuroendocrinology*. 2004;29(8):1082-1092. doi:10.1016/j.psyneuen.2003.11.003
38. Goedendorp MM, Gielissen MFM, Verhagen CAHHVM, Bleijenberg G. Development of fatigue in cancer survivors: a prospective follow-up study from diagnosis into the year after treatment. *J Pain Symptom Manage.* 2013;45(2):213-222. doi:10.1016/j.jpainsymman.2012.02.009
39. Schmidt ME, Blickle P, Steindorf K. Cancer-related fatigue: benefits of information booklets to improve patients' literacy and ability to cope with challenges. *Support Care Cancer*. 2022;30(6):4813-4821. doi:10.1007/s00520-022-06833-w
40. Theobald DE. Cancer pain, fatigue, distress, and insomnia in cancer patients. *Clin Cornerstone*. 2004;6(suppl 1D):S15-S21. doi:10.1016/s1098-3597(05)80003-1
41. Davidson JR, MacLean AW, Brundage MD, Schulze K. Sleep disturbance in cancer patients. *Soc Sci Med.* 2002;54(9):1309-1321. doi: 10.1016/s0277-9536(01)00043-0
42. Rehman A, Drake CL, Shiramizu V, Fleming L. Sleep reactivity predicts insomnia in patients diagnosed with breast cancer. *J Clin Sleep Med.* 2022;18(11):2597-2604. doi:10.5664/jcsm.10170

ONLINE FIRST Eur J Clin Exp Med