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7 **Self-Reported Adherence to Oral Endocrine Therapy among Breast**  
8 **Cancer Patients in Jordan**

9 **\*Nour Faqeer,<sup>1</sup> Alia Al Gharabli,<sup>1</sup> Maha Dalbah,<sup>1</sup> Khawalah Ammar,<sup>2</sup>**  
10 **Randa Agha,<sup>1</sup> Hala Shannies,<sup>1</sup> Hala Sroji,<sup>1</sup> Rawaa Al Rabie<sup>1</sup>**

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12 <sup>1</sup>*Department of Pharmacy, King Hussein Cancer Center, Amman, Jordan;* <sup>2</sup>*Office of*  
13 *Scientific Affairs and Research, King Hussein Cancer Center, Amman, Jordan*

14 *\*Corresponding Author's e-mail: [nfaker@khcc.jo](mailto:nfaker@khcc.jo)*  
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16 Dear Editor,

17 Non-adherence to medications is a significant health issue, as it can reduce the efficacy of  
18 therapeutic management and increase the likelihood of relapse. <sup>1</sup> Ensuring that patients  
19 with breast cancer (BC) adhere to the prescribed duration of endocrine therapy (ET) is,  
20 however, difficult, because of the long duration of treatment. Several studies have  
21 evaluated adherence to ET. <sup>2-4</sup> To our knowledge, no studies have been conducted in the  
22 Middle East to evaluate adherence to ET. We conducted a study to evaluate the level of  
23 adherence to ET among patients with BC. The study also aimed to describe the patients'  
24 perceptions of ET and associations between adherence and patient-related factors.

25 This study was conducted between October 2017 and July 2018 at King Hussein Cancer  
26 Center. Ethics approval was granted by the institutional review board on the 5<sup>th</sup> October  
27 2017. The study involved administering a questionnaire to patients being treated for BC.  
28 Patients were recruited at the hospital's outpatient pharmacy and the chemotherapy  
29 infusion clinic. Those who had a refill for ET (tamoxifen, anastrozole, exemestane, or

30 letrozole) and had been on therapy for at least 1 month were included in the study. The  
31 questionnaire contained a statement in the first page which was considered as a consent  
32 form. Patients were consented as they agreed to participate in the study.

33 The questionnaire was developed by a survey specialist at our institution since, to our  
34 knowledge, there was no validated, well-established questionnaire in Arabic. The  
35 questionnaire contained items that were reported by Pourcelot et al.<sup>2</sup> The questionnaire  
36 included questions on adherence (the number of missed doses of ET during the previous  
37 month) and type and duration of ET, perception about ET. The survey specialist and the  
38 clinical investigators assessed the items in term for clarity and relevance for the patients  
39 to establish the face and content validity of the questionnaire. The questionnaire was pilot  
40 tested in a small group of patients for one week and modified based on the feedback  
41 received.

42 Continuous data were presented as means and SD, while categorical data were presented  
43 as numbers and percentages.  $P \leq 0.05$  was considered statistically significant. Anova test  
44 was used to determine any associations between adherence and continuous data while  
45 chi-square test was used for categorical data.

46 During the study period, 202 questionnaires were completed. The mean age of patients  
47 was 45.8 years  $\pm$  10.7(SD). Baseline demographics are summarized in Table 1. Among  
48 the enrolled patients, 113 (57.4%) were on tamoxifen, 34 (17.3%) on letrozole, 36  
49 (18.3%) on anastrozole, and 10 (5.1%) on exemastane. Four patients (2%) did not know  
50 the name of the ET they were taking, and five patients did not answer the question. ET  
51 had been taken for  $\leq$  6 months by 59 of the 202 patients (29.2%), for 6–12 months by 51  
52 patients (25.2%), for 1–3 years by 77 patients (38.1%), and for 3–5 years by 15 patients  
53 (7.4%).

54 We assessed the patients' perceptions about ET. About two-third of the patients (63%)  
55 reported that they didn't know to what extent they needed ET and about half of the  
56 patients (47%) didn't know whether ET could help in reducing recurrence of  
57 BC. However, the majority of the patients were aware of their treatment plan (90%) and  
58 reported understanding of their disease (91%). Most of the patients (86%) reported that

59 they had received information on the importance of ET from their physicians but only  
60 half of the patients (52 %) reported having received medication counseling from a  
61 pharmacist.

62 The only factor that was significantly associated with adherence was the duration of  
63 treatment ( $P = 0.048$ ); the shorter the duration of ET, the fewer reported missed doses.

64 We found a relatively high rate of adherence to ET. Patients were considered adherent if  
65 they took at least 80% of their prescribed medication over a certain period.<sup>5</sup> In our study,  
66 the majority of patients (99.5%) reported adherence rates of 80% or more over 1 month.  
67 Studies have reported high as well as low rates of adherence.<sup>2,3,5</sup>

68 In our study, most participants reported that they had received information on the  
69 importance of ET, but interestingly, this information was mostly from their physicians  
70 rather than pharmacists. We found no association between the high adherence and the  
71 information provided by physicians which might be due to the nature of the study as there  
72 was no objective measure of the physician's role in patient's counseling. The only factor  
73 associated with adherence was the duration of treatment. A similar association was  
74 reported by Robinson et al. who found that the rate of adherence decreased from year 1 of  
75 treatment throughout year 5 by 50%.<sup>4</sup> We were unable to draw any conclusion about  
76 adherence over the course of ET because of the short duration of follow-up in this study.

77 Several studies have evaluated the association between adherence and patient-related  
78 factors.<sup>2,5</sup> In cross-sectional survey, the risk factors associated with non-adherence were  
79 comorbid conditions, poly-pharmacy, younger age.<sup>2</sup> In our study, age and whether the  
80 patient was taking other medications were not significantly associated with adherence.  
81 The present study has limitations. First is the use of a self-administered questionnaire as  
82 there was no objective measure of adherence for more accurate assessment, which might  
83 have resulted in overestimation of adherence. In addition, the small number of patients  
84 that have taken the ET for more than 3 years, response rate which defined as the  
85 percentage of patients who answered the questionnaire from the total number of patients  
86 was not calculated, and the included patients were on ET for more than one month which

87 might affect the adherence as the behaviors of patients would change over the period of  
88 treatment.

89 We found a relatively high level of adherence to ET among patients with BC. However,  
90 there was a gap in the counseling provided by pharmacists. Further studies should be  
91 conducted to assess adherence of longer duration and to further investigate the factors  
92 that may be associated with non-adherence, such as socioeconomic status.

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#### 94 **Authors' Contribution**

95 NF and KA Conceptualized and designed the manuscript. AG, MD, RA, HS, HS and RR  
96 Collected and assembled the data. KA analyzed the data. NF, AG and KA wrote the  
97 manuscript. All authors approved the final version of the manuscript.

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Accepted Article

119 **Table 1:** Baseline demographics of 202 patients with breast cancer.

Demographic	Item	Number of patients (%) who answered the question
Marital status	Married	163/200 (81.5%)
	Single	19/200 (9.5%)
	Widowed	13/200 (6.5%)
	Divorced	5/200 (2.5%)
Educational level	Bachelor's degree	59/199 (29.6%)
	High school	58/199 (29.1%)
	Diploma	51/199 (25.6%)
	Master's or doctoral degree	13/199 (6.5%)
	Others	18/199 (9%)
Area of residence	Amman	127/190 (66.8%)
	Outside Amman	55/190 (28.9%)
	Outside Jordan	8/190 (4.2%)
Family income per month (JD <sup>*</sup> )	< 500	98/190 (51.6%)
	500–1000	72/190 (37.9%)
	1000–2000	16/190 (8.4%)
	> 2000	4/190 (2.1%)
Nationality	Jordanian	179/199 (89.9%)
	Others	20/199 (10.1%)
Family history of breast cancer	Yes	55/199 (27.6%)
On other medications	Yes	55/187 (29 %)

120 <sup>\*</sup>**JD:** Jordanian dinar, the currency of Jordan.

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