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Adherence and Beliefs to Adjuvant Hormonal Therapy in Patients with Breast Cancer: A Cross-Sectional Study (Conference Paper)[#]

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Abstract

Breast cancer is the most common cancer among women over the world. To reduce reoccurrence and mortality rates, adjuvant hormonal therapy (AHT) is used for a long period. The major barrier to the effectiveness of the treatment is adherence. Adherence to medicines among patients is challenging. Patient beliefs in medications can be positively or negatively correlated to adherence**.** The aims of the study were to investigate the extent of adherence and factors affecting adherence, as well as to investigate the association between beliefs and adherence in women with breast cancer taking AHT**.** The method was a cross-sectional study included 124 Iraqi women with breast cancer recruited from Middle Euphrates Cancer Center. Morisky medication adherence scale (MMAS) and beliefs about medication questionnaires (BMQ) are used to assess adherence and beliefs respectively. As a result, 25% of women were fully adherent (MMAS = 8). 83.06% of all women developed side effects from medications received. Side effects and unemployment state were significantly associated with non-adherence. Additionally, there is no significant association between beliefs in medications and adherence. The conclusion of the study was that high percent of poor adherence caused by side effects suggests the need for interventions by educating patients about the importance of their treatment and how to overcome side effects.
Keywords: Adherence, Beliefs, Breast cancer, adjuvant hormonal therapy.

الالتزام والمعتقدات بالعلاج الهرموني المساعد لدى مرضى سرطان الثدي: دراسة مقطعية (بحث مؤتمر)[#]

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الخلاصة

سرطان الثدي هو أكثر أنواع السرطانات شيوعاً بين النساء حول العالم. لتقليل عودة السرطان ومعدل الوفيات، يتم استخدام العلاج الهرموني المساعد لفترة طويلة. العائق الرئيسي لفعالية العلاج هو الالتزام بالعلاج حيث يمثل الالتزام بالأدوية بين المرضى تحديًا. كما يمكن أن ترتبط معتقدات المريض بالأدوية ارتباطًا ايجابياً أو سلبيًا بالالتزام. الهدف من الدراسة هو قياس مدى التزام النساء بالأدوية ومعرفة العوامل المؤثرة على التزامهن، بالإضافة إلى قياس مدى الارتباط بين المعتقدات والالتزام لدى النساء المصابات بسرطان الثدي اللاتي يتلقين العلاج الهرموني المساعد. أقيمت الدراسة في مركز الفرات الأوسط للأورام السرطانية وشملت ١٢٤ امرأة عراقية مصابة بسرطان الثدي حيث استخدم مقياس مورسكي ومقياس المعتقدات حول الدواء لتقييم الالتزام والمعتقدات على التوالي. النتيجة: كان ٢٥ ٪ من النساء ملتزمات تماماً، (٨٣،٠٦%) من جميع النساء ظهرت عليهن آثار جانبية من الأدوية التي تم تلقيها. ارتبطت الآثار الجانبية وحالة انعدام العمل بشكل كبير مع عدم الالتزام بالأدوية بينما لا توجد علاقة ذات دلالة إحصائية بين المعتقدات في الأدوية والالتزام. تشير النسبة العالية من قلة الالتزام الناجم عن الآثار الجانبية إلى الحاجة إلى دراسات تثقيفية للمرضى حول أهمية علاجهم وكيفية التغلب على الآثار الجانبية.
الكلمات المفتاحية: الالتزام، المعتقدات، سرطان الثدي، العلاج الهرموني المساعد.

Introduction

Breast cancer is the most common cancer among women over the world in 2020 and accounting for 24.5% of all cancer cases worldwide while it is accounting 24% of overall malignancies in Iraq [(1)]. Approximately two-thirds of all breast cancer cases have hormone receptor-positive breast cancer [estrogen receptors positive (ER+) or estrogen receptors positive plus progesterone receptors positive (ER+ plus PR+)]. After primary treatment (surgery, radiation, and chemotherapy), adjuvant hormonal therapy (AHT) is a standard therapy prescribed for most hormone receptor-positive breast cancer. The most common two types of AHT used are selective estrogen receptor modulators (SERM) such as tamoxifen and aromatase inhibitors (AI) that inhibit estrogen production such as anastrozole [(2)]. The use of any type depends on the menopause state of the woman. Guidelines recommended the use of tamoxifen for 5 years in premenopausal women while AI is the recommended type in postmenopausal women as

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primary or extended after using tamoxifen for 5 years and sometimes it is recommended to use AI as sequential (a combination with tamoxifen for 3 years followed by 2 years of AI) [3].

Long-term management by AHT for five years or more is highly effective in reducing recurrence, mortality rates and improve overall survival [4,5]. However, to obtain these benefits, women should take medication as prescribed. Studies found that adherence to AHT was suboptimal, only 50% of women with breast cancer were adherent to AHT and about two-third discontinued AHT before completing recommended period [6,7]. A systematic review of psychosocial motivators and barriers of adherence to oral anticancer used in breast cancer revealed that the barriers of adherence are patients feeling discomfort toward taking AHT, concerns about side effects of AI such as joint pain and gynecological symptoms while good beliefs about medication and good patient-physician relationship are positively correlated with adherence [8]. The non-adherence is also associated with sociodemographic factors such as younger or older age (less than 40 and more than70), ethnicity, unmarried women, and those with lower income [9]. Many studies measured adherence for chronic disease in the Arabic population but few of them focusing on the association between beliefs and adherence in breast cancer survival [10–12]. Therefore, this study aims to investigate the extent of adherence among the breast cancer population, predictors for non-adherence, as well as to investigate the association between beliefs and adherence in women with breast cancer.

Method

Study design and subjects

A cross-sectional study was conducted among 124 women recruited from Middle Euphrates Cancer Center\Najaf governorate\ Iraq from the 15th November 2020 to the 30th April 2021. The study was approved by the Scientific Committee of Researches of Najaf Health Department (reference number 30599). Women were eligible to participate if they were aged ≥ 18, diagnosed with breast cancer, taking tamoxifen or anastrozole for at least one month, and completed all primary treatment (surgery, radiation, and chemotherapy). We excluded women who have metastatic breast cancer and receiving chemotherapy, have a history of recurrence, and women with a psychological problem.

Tools

Sociodemographic and clinical variables were collected from patients including age, marital status, income categorized as following: good income >1,000,000 IQD; medium income 500,000-1,000,000 IQD and; poor income <500,000 IQD [13], smoking, years since diagnosis, type of AHT used, drug side effects, and others summarized in (table 1).

Medication adherence

The assessment of adherence was done by using the Morisky medication adherence scale (MMAS) [14]. It is a validated 8 items scale from previously published 4-items MMAS-4 [15]. MMAS-8 that used in this study was a copy of MMAS-8 used in the previous study [16]. This scale includes 8 items, where the first seven questions are answered by yes or no and the eighth one is a five Likert scale answered either by never/rarely, once in a while, sometimes, usually, and all the time. The score of MMAS ranged from 0 to 8 and in this study scores < 6 were considered to be poor adherence, scores ≥ 6 - < 8 represent medium adherence, and scores = 8 represent high adherence. Women with poor or medium adherence are considered non-adherent [17].

Medication beliefs

Women's beliefs about AHT are measured by the beliefs about medication (BMQ) scale which is widely used in chronic disease [18]. BMQ proven to be used in women taking AHT [19]. The validated Arabic version with proven validity and reliability is used in a previous study [20]. The scale consists of 18 items included in two sections which are either general or specific. Specific-BMQ (questions specific for AHT medications) has two 5-item subscales, the specific-necessity subscale to assess the necessity of the prescribed AHT medication and the specific-concern subscale to assess concern about the negative effect of prescribed AHT medication. General-BMQ (questions about medicines in general) has 8 items also subdivided into two 4-item subscales, general-harm that to assess the beliefs about the harmful effect of the any medication and general-overuse to assess beliefs of medication overuse by doctors. Each item is a five-point Likert scale (strongly disagree, disagree, uncertain, agree, and strongly agree to have a score of 1, 2, 3, 4, and 5 respectively). Answers are recorded and a high score (agree and strongly agree answers) indicates stronger beliefs in the concepts of each subscale.

Procedure

Face-to-face interview was chosen because it is the most effective way of capturing a wide range of perspectives and allow interviewers to explore deeply for responses and clarify any ambiguity. Furthermore, during the interview, patients' sensitive topics concerning their daily and social lives can be discussed, making participants feel more comfortable providing this information privately in a one-to-one setting and when compared to telephone interviews or self-reporting questionnaires, face-to-face interviews are known to have a greater response rate [21]. Women who visited Middle Euphrates Cancer Center to refill the prescription were asked to participate in the study.

After informed consent was taken from women, face-to-face interview by the researcher with each woman for about 20 min. Firstly, sociodemographic data and clinical information were taken from patients. Accordingly, MMAS and BMQ questionnaires were filled.

Data analysis

The results were analyzed by using a statistical package for social sciences (SPSS) version 23. Descriptive analysis was expressed as mean ± standard deviation (SD) and median (lower-upper quartiles [Q1-Q3]). Categorical variables were represented as numbers and percentages. Correlation between adherence levels and demographic and clinical data was analyzed by Chi-square test for categorical variables, while unpaired *t*-test for continuous normally distributed variables and Mann Whitney test for continuous non-normal distributed variables were used to compare between groups. Mann-Whitney test and Wilcoxon Z score were used for an association between BMQ and adherence levels. Logistic regression was performed to investigate predictors of non-adherence. The level of significance was set as a p-value < 0.05 using the adherent group as reference.

Results

Characteristic of study participants and adherence

A total of 165 women interviewed to participate in the study, 124 women met the inclusion criteria and completed the questionnaires. The mean age was 50.00±9.383 years (range 30 - 78). Most of them were married (83.06%), unemployed (79.84%), medium-income (48.39%), and (79.84%) women with primary school education. The median of AHT duration was 18 months (6-36). 41.94% of women could not buy their medications from private sectors if they are unavailable in the Oncology center, since they may stop their treatment until being available in the center. 54.84% of women had chronic diseases, where hypertension (41.94%) and diabetes mellitus (25.81%) were the most frequently reported among the study sample. There is a significant association between non-adherence and unemployed (p = 0.002), retired women (p = 0.002) and the presence of side effects (p = 0.04). Sociodemographic and clinical characteristics are summarized in table 1.

Table 1. Sociodemographic and clinical characteristics of participants

Variables	Overall Number (N)=124	Adherence level		P value
		Adherers (N =31)	Non-adherers (N =93)	
Age (years), mean ± SD	50.00±9.383	52.74±11.04	49.09±8.638	0.06
Residency, N (%) Urban Rural	 100(80.65) 24(19.35)	 25(80.65) 6(19.35)	 75(80.65) 18(19.35)	 >0.9
Employment status, N (%) Employee Unemployed Retired	 20(16.13) 99(79.84) 5(4.03)	 5(16.13) 24(77.42) 2(6.45)	 15(3.22) 75(80.65) 3(16.13)	 0.02* 0.02*
marital status, N (%) married single widow divorced	 103(83.06) 6(4.84) 14(11.29) 1(0.85)	 26(83.87) 1(3.23) 4(12.90) 0(0)	 77(82.79) 5(5.37) 10(10.75) 1(1.07)	 0.64 0.79
Income, N (%) Good >1,000,000 IQD Medium 500,000-1,000,000 IQD Poor <500,000 IQD	 13(10.48) 60(48.39) 51(41.13)	 1(3.23) 20(64.52) 10(32.26)	 12(12.90) 40(43.01) 41(44.09)	 0.06 0.31
Smoking, N (%) No Yes	 121(97.58) 3(2.42)	 30(96.77) 1(3.23)	 91(97.85) 2(2.15)	 0.66
Educational level, N (%) <Secondary school ≥Secondary school	 99(79.84) 25(20.16)	 24(77.42) 7(22.58)	 75(80.65) 18(19.35)	 0.69
Type of AHT Tamoxifen Anastrozole	 69 (55.65) 55 (44.35)	 13 (41.94) 18 (58.06)	 56 (60.22) 37 (39.78)	

Continued table 1.

Duration of AHT (month), median (Q1-Q3)	18 (6 - 36)	24(10-38)	15(5.5 - 36)	0.2
Years since diagnosis, mean ± SD	3.589±2.346	3.79±2.78	3.52±2.197	0.58
Can buy medication Yes No/by finance help	 72(58.06) 52(41.94)	 16(51.61) 15(48.39)	 56(60.22) 37(39.78)	 0.4
Family remind you to take medication? N (%) Yes No	 27(21.78) 97(78.22)	 4(12.90) 27(87.10)	 23(24.73) 70(75.27)	 0.17
Do medication affect your daily activity? N (%) Yes No	 116(93.55) 8(6.45)	 29(93.55) 2(6.45)	 87(93.55) 6(6.45)	 >0.9
Side effects, N (%) No Yes	 21(16.94) 103(83.06)	 9(29.03) 22(70.97)	 12(12.91) 81(87.09)	 0.04*
Chronic disease, N (%) No Yes	 58(46.77) 66(53.23)	 13(41.94) 18(58.06)	 45(48.39) 48(51.61)	 0.53
Number of chronic illness, N (%) 1 ≥2	 39(59.09) 27(40.91)	 9(50) 9(50)	 30(62.50) 18(37.50)	 0.36
Diabetes mellitus, N (%) No Yes	 92(74.19) 32(25.81)	 22(70.97) 9(29.03)	 70(75.26) 23(24.74)	 0.64
Hypertension, N (%) No Yes	 72(58.06) 52(41.94)	 14(45.16) 17(54.84)	 56(61.54) 35(38.46)	 0.11
Ischemic heart disease, N (%) No Yes	 120(96.77) 4(3.23)	 30(96.77) 1(3.23)	 90(96.77) 3(3.23)	 >0.9
Number of other medication, N (%) No 1 ≥2	 63 29 32	 14 8 9	 49 21 23	 0.58 0.53

* =p< 0.05 indicate statistically significant differences.

Adherence of the study participants

Overall, MMAS score in patients was 6.55 ± 1.35. Only 31 (25%) study individuals were high adherent, whereas 93 (75%) women were non-adherent. 40.32% of women forgot to take their medication. 24.19% of them did not take their medication at least once in the last 2 weeks. 5.65% of women stopped taking their medications because they felt worse when taking them. 9.68% of women forgot to take their AHT medication when they have a trip. Most of them (93.55 %) answered that they take their medication yesterday. 0.81% (one individual) of women answered yes as she stopped taking her medication when became in a good health. 35.48% of women were hassled about the treatment plan. About half of women (46.77%) did not forget to take their medication (see table 2).

Table 2. Self-reported medication adherence behavior of study participants as determined by the MMAS-8.

Item	Number and percentage (%) of female patients who answered yes
Do you sometimes forget to take your breast cancer oral medication?	50 (40.32)
People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your breast cancer oral medication?	30 (24.19)
Have you ever cut back or stopped taking your breast cancer oral medication without telling your doctor because you felt worse when you took it?	7 (5.65)
When you travel or leave home, do you sometimes forget to bring along your breast cancer oral medication?	12 (9.68)
Did you take your breast cancer oral medication yesterday?	116 (93.55)
When you feel like your breast cancer is under control, do you sometimes stop taking your medication?	1 (0.81)
Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your breast cancer treatment plan?	44 (35.48)
How often do you have difficulty remembering to take all your medications?	
Never/rarely	58 (46.77)
Once in a while	43 (34.68)
Sometimes	15 (12.09)
Usually	7 (5.65)
Always	1 (0.81)

MMAS-8: morisky medication adherence scale -8 items.

Side effects of AHT and the impact on adherence

The total number of women who had side effects was 103 participated women (83.06%) with a significant proportion in non-adherent women (87.09%) when compared with adherent women (70.97%). The most frequent side effects reported were hot flush (79.61%), joint pain (76.70%), night sweating (39.81%), vaginal discharge (22.33%), fatigue (11.65%) and depression (10.69%) (see Table 3).

Table 3. Number (N) and percentage (%) reporting side effects, for total patients as well as for adheres and non-adheres patients.

Side effect	Total, *N* (%)	Adherence level	
		Adheres, *N* (%)	Non-adheres, *N* (%)
Any	103/124(83.06)	22/103(21.36)	81/103(78.64)
Hot flush	82/103(79.61)	17/22(77.27)	65/81(80.25)
Night sweating	41/103(39.81)	8/22(36.36)	33/81(40.74)
Joint pain	79/103(76.70)	17/22(77.27)	62/81(76.54)
Fatigue	12/103(11.65)	1/22(4.55)	12/81(14.81)
Vaginal discharge\dryness	23/103(22.33)	7/22(31.82)	16/81(19.75)
Depression	11/103(10.69)	2/22(9.09)	9/81(11.11)

BMQ and impact on adherence

The majority of women supported the necessity of AHT by answering agree or strongly agree that their medications have protected them from being worse and their state improved by their medications. The concerns about AHT were also reported. Many women answered agree or strongly agree that they were not familiar with their medications and they were worried from a long term effect of their medication. Approximately, all women answered that the doctors are reliable on medicines and if doctors had more time with their patients they would prescribe fewer medicines. The

mean rank of total belief scores of each section showed that adherent women had non-significant high specific-necessity belief, low specific-concern belief, high general-harm belief and low general-overuse belief. In terms of BMQ items, there were no significant differences between adherent or non-adherent women. (Table 4)

Table 4.Response to BMQ items and participants' scores for each item by adherence level

Item	Total, Agree/strongly, Agree answers N (%)	Adherence level		Wilcoxon Z scores	P-value
		Adherers	Non-adherers		
		Mean rank			
Specific-necessity					
BMQ necessity score, as a total		65.13	61.62	-0.476	0.634
1-My life would be impossible without medicine	76(61.29)	42.61	37.13	-0.974	0.330
2-Without medicine I'll be very ill	81(65.32)	43.57	40.10	-0.602	0.547
3-My health, at present, depending on my medicine	87(70.16)	49.29	42.32	-1.131	0.258
4-My medicine protected me from becoming worse	89(71.77)	50.45	43.32	-1.133	0.257
5-My health in the future depends on my medicine	86(69.35)	50.97	41.52	-1.468	0.142
Specific-concern					
BMQ concerns score, as a total		58.16	63.95	-0.779	0.436
6-I sometimes worry about the long term effect of my medicine	73(58.87)	43.47	35.18	-1.396	0.163
7-Having to take medicine scares me	75(60.48)	43.44	36.53	-1.137	0.256
8-I sometimes worry about becoming too dependent on my medicine	43(34.67)	25.85	20.83	-1.123	0.262
9-My medicine disrupt my life	17(13.71)	8.25	9.41	-0.467	0.641
10-My medicines are mystery to me	79(63.70)	46.39	38.62	-1.156	0.248
General-harm					
BMQ harms score, as a total		62.38	61.88	-0.068	0.946
11-People who take medicines should stop their treatment for a while every now and again	7(5.65)	3.50	4.08	-0.255	0.799
12-Most medicines are addictive	39(31.45)	19.40	20.21	-0.197	0.844
13-Medicines do more harm than good	49(39.52)	23.91	25.32	-0.295	0.768
14-All medicines are poison	68(54.84)	32.26	35.25	-0.547	0.585
General-overuse					
BMQ overuse score, as a total		59.68	63.44	-0.512	0.609
15-Doctors use too many medicines	15(12.09)	9.83	7.54	-0.808	0.419
16-Doctors place too much trust on medicines	117(94.35)	60.04	58.67	-0.188	0.851
17-If doctors had more time with their patients they would prescribe fewer medicines	122(98.38)	58.42	62.55	-0.569	0.569
18-Natural remedies are safer than medicines	32(25.80)	16.63	16.46	-0.044	0.965

BMQ: beliefs about medication scale**.**

Multivariate analysis of factors predicting non-adherence

The factors included in this test were age, education, side effects, and BMQ sections (specific-necessity, specific-concerns, general-harm, and general-overuse). No one of these variables was a significant predictor of non-adherence (Table 5).

Table 5. Factors predicting non-adherence

Variable	OR (95% CI)	P value
Age	1.037 (0.989-1.088)	0.135
Education	1.523 (0.381-6.084)	0.551
Employment	1.011 (0.209- 4.895)	0.989
Side effect	0.423 (0.143-1.252)	0.120
BMQ-specific-necessity	1.009 (0.926-1.101)	0.833
BMQ-Specific-concerns	0.935 (0.853-1.023)	0.144
BMQ general-harm	1.051 (0.904-1.221)	0.518
BMQ-general- overuse	0.930 (0.738-1.172)	0.541

OR: Odd Ratio, CI: Confidence Interval (lower-upper), BMQ: beliefs about medication scale**.**

Discussion:

In the current study, the adherence was suboptimal and the majority of women (75%) were non-adherent to AHT. The results of this study were in agreement with those of previous studies that examined adherence to AHT [17,22,23]. The level of adherence to AHT is greatly below the level investigated in the study conducted by Karbala/Iraq who found that (62.38%) of postmenopausal women are highly adherent to AIs [16]. Another study in Sudan found revealed that high percent of patients (93%) were adherent to AHT [24]. This confliction may be attributed to the type of method used to measure adherence such as face to face interviews, self-reported questionnaires, pill count, electronic monitoring devices, and medical records. There is no standard method to measure medication adherence precisely [25]. Non-adherence is a multifactorial problem that affects therapy outcomes and lead to disease recurrence, re-hospitalization, and decrease survival rate [26]. Several studies found that socioeconomic status and clinical data including older age, single, low income and out-of-pocket cost of AHT [26–31], comorbidity, treatment side effects, depression [32–34] are associated with non-adherence. In this study, non-adherence is significantly associated with side effects of AHT and the employment state of women. This finding was supported by several studies investigated the factors associated with non-adherence indicating that side effects are a potential contributing factor [35]. Unemployed and retired women were significantly non-adherent. In contrast, a previous study in the UK found that in-paid employment was more likely to be non-adherent to AHT [32]. These differences imply that these results needed further investigation. Patients' beliefs about their medications were observed to correlate with medication adherence. A positive association between high score specific-necessity and adherence while a high score of specific-concern showed significantly in patients with poor adherence. Many studies of chronic diseases and cancer revealed these associations [10,12,17,36] but in our study, binary logistic regression test found no positive or negative significant association between each part of BMQ and adherence. This is similar to previous studies that investigated no effects of beliefs on adherence [37–39]. This may be due to our small sample size and may have insufficient strength to find a significant effect. The limitations of this study, are limited to one center and does not represent all Iraq population, many variables are related to the adherence were not included in this study such as self-efficacy, perceived social support, patient-physician communication, and severity of symptoms, the data presented here reflects only the AHT adherence using a questionnaire through face to face interview. In our opinion, this method is more accurate than obtaining data from self-reported questionnaires, prescription and pharmacy records and medical claims methods. Still, all those observational methods remain limited [40]. A confirmation method that measures the medications or related markers in blood is more accurate [41] and recommended in future studies.

Conclusion

This study provides important information about the adherence extent of Iraqi women with breast cancer to their AHT and factors leading to poor adherence. A majority of women were non-adherent to their treatment. Side effects and unemployment women were the only factors investigated to be associated with non-adherence. There was no positive or negative association between beliefs and adherence.

Competing interests

The authors confirm that there is no conflict of interest.

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Availability of data and materials:

The databases used and/or analyzed for the present study are accessible from the corresponding author on reasonable request.

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