Impact of Chemotherapy Treatments on Dietary Intakes of Macro and Micronutrients among Jordanian Women with Breast Cancer

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Abstract: *Background*: Breast cancer (BC) is the leading cause of cancer related deaths among women worldwide. Nutritional factors may account for the large variation in BC incidence around the world. Most studies have shown no link between dietary intakes and increased risk of BC.

Objective: To evaluate the dietary intake of macro and some micronutrients among BC patients with respect to chemotherapy treatment.

Methods: A total of 168 BC patients aged 20-70 years attending BC clinics at the Jordanian Royal Medical Services, Jordan were evaluated for dietary intake. The study design permitted to include 60 newly-diagnosed BC patients who were not exposed to any type of interventions and 108 recently-diagnosed BC patients (up to three months). Recently group member were sub-divided in two sub-groups to control exposure to chemotherapy. The Chemo group (have exposed to chemotherapy) and the non-chemo group (have exposed to other types of treatments interventions). Calculations were based on the computerized nutrient analysis program (the food processor nutrition and fitness analysis software (ESHA), version 10.6/.3, Salem, USA).

Results: Energy, macronutrients and micronutrients intakes were not significantly different considering exposure to chemotherapy. However, they were less than recommended in all BC patients.

Conclusion: The possible risk of dietary undernutrition among BC patients that need a careful monitoring, evaluation and managements care plan.

Keywords: Breast Cancer, Vitamins, Minerals, Dietary intake, Chemotherapy and Jordanian.

CLINICAL RELEVANCY STATEMENT

This study discovers the possible of Macro and Micronutrients undernutrition among breast cancer Jordanian patients that can be beneficial in medical management process. This study will help the researcher to uncover the critical area of dietary intakes of cancer patients that many researchers were not able to explore. Thus, a new theory on dietary intakes and breast cancer related risk, may be arrived at.

1. INTRODUCTION

Breast cancer (BC) is the most frequently occurring and the leading cause of cancer-related deaths among women worldwide [1]. In Jordan, BC ranked first among cancers in females, accounting for about 37% of all female cancers [2,3]. Nutritional risk factors have been largely hypothesized as prominent environmental determinants of BC that account for the large variation in BC incidence around the world [4]. The BC patients are at risk of nutritional problems such as malnutrition due to inadequate nutritional intake or decreased absorption [5]. Nutritional problems may occur before and during or after BC treatment, since about 50% of advanced stage BC patients have been reported to be malnourished [6]. The Morbidity and mortality rate of BC have been shown to increase in malnourished patients [6,7]. Treatment with chemotherapy causes diarrhea, nausea, vomiting and affects the growth of small bowel mucosa; since it targets rapidly dividing cells whether malignant or not. [5,8]. This chemotherapy related side effect, if untreated can result in dehydration, poor appetite and fatigue [8]. In addition, chemotherapy causes inadequate oral food intake, weight loss, electrolyte imbalance, and nutrients malabsorption [9]. Other common side effects of chemotherapy are stomatitis and mucositis that are ulceration or inflammation of the throat and mouth. Chemotherapy can also lead to painful eating therefore, decrease oral food intake [6].

There are no studies that assess dietary intakes in Jordanian or Arab BC patients during first three months

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of diagnosis. Considering that diet is a modifiable risk factors, thus dietary modifications, can be suggested to reduce BC risks and improve its incidence or outcome [10]. Giving that, the objectives of the present study were to:

1. Evaluate the relationships between Dietary intake and BC in accordance to exposure to any chemotherapy regimen in the studied sample.

2. To assess the energy, Macronutrients (carbohydrates, protein, and lipid) and Micronutrients (vitamins and minerals) intake of Jordanian BC patients.

2. SUBJECTS AND METHODS

2.1. Study Sample and Design

In this study, 168 Jordanian BC patients aged 25-65 years attending BC clinics at the Jordanian Royal Medical Services in Amman, Jordan for management and follow-up were screened for the presence of undernutrition according to usual daily dietary intakes without any type of nutritional intervention or counseling. The experimental design permitted to include 60 newly-diagnosed BC patients who were not exposed to any type of interventions and 108 recently-diagnosed BC patients (up to three months). Recently group member were sub-divided in two sub-groups to control exposure to any regimen of chemotherapy as per hospital protocol.

2.1.1. Inclusion and Exclusion Criteria

The median age of BC females in Jordan is 51 years, and about 80% of the diagnosed cases lied between the ages 35 and 65 years [3].Women aged 25-65 years, with newly and recently diagnosed BC were included in the study. The patients were excluded if she had any clinical or laboratory evidence of congestive heart failure, coronary disease, chronic renal failure, polycystic ovary syndrome hyper- or hypo-thyroidisim, pregnancy and lactation. Any subject did not fit the inclusion criteria were excluded.

Informed consent was obtained from each participant at the start of the study. The Royal Medical Services Ethical Committee approved this study (1/2013).

2.2. Data Collection

A questionnaire which included personal information, health and nutritional data, was used for data collection. For both quantitative and qualitative dietary assessment, patients were requested to submit a 3-day weighed food intake record “three non-consecutive days; two week days and one weekend” Instructions for dietary intake recording were given to each patient. Instructions included information about food measures and portion sizes, food ingredients and descriptions of dishes, meal frequency, and snacking and food groupings. Food intakes were converted to daily energy and nutrient intakes including: energy, proteins, carbohydrates, fats, cholesterol, saturated, monounsaturated and polyunsaturated fatty acids, dietary fibers, animal and plant proteins, in addition to some micronutrients namely, vitamins A, C, E, B12, B6, folate, thiamin, niacin and riboflavin, and the minerals iron, copper, iodine, zinc, calcium, phosphorous and selenium. Calculations were based on the computerized nutrient analysis program (the food processor nutrition and fitness analysis software (ESHA), version 10.6/.3, Salem, USA).

2.3. Data Analysis

Calculations were based on the computerized nutrient analysis program (the food processor nutrition and fitness analysis software (ESHA), version 10.6/.3, Salem, USA). Statistical analyses were performed using Statistical Program for Social Studies (SPSS), version 10.0 (SPSS Inc., Chicago, USA).

3. RESULTS

Intakes of macronutrients and their energetic contributions (%) of breast cancer patients according to treatment exposure are shown in Table **1**. Intakes of macronutrients and their energetic contributions of BC patients were not significantly different ($p \geq 0.05$) among study groups. In the whole sample, energy intake was (1373 ± 54.7 Kcal/day). About (17.0 ± 0.5%), (58.9 ± 1.8%) and (24.5 ± 0.9%) of energetic intakes respectively came from protein (57.3 ± 2.4 g/day), carbohydrates (201.0 ± 9.5 g/day) and fat (36.4 ± 1.9 g/day). The intakes and energetic contribution of saturated fatty acid (SFA), mono unsaturated fatty acid (MUFA), poly unsaturated fatty acid (PUFA) and trans fat were respectively (10.7 ± 0.7 g/day vs. 7 ± 0.1%), (12.0 ± 0.9 g/day vs. 7.9 ± 0.2%), (8.5 ± 0.6 g/day vs. 5.6 ± 0.2%) and (0.5 ± 0.0 g/day vs. 0.32 ± 0.0%). The intakes of cholesterol and dietary fiber were (144.2 ± 8.3 mg/day) and (16.2 ± 1.0 g/day) respectively (Table **1**).

Macronutrients intakes as percentages of recommendations of breast cancer patients are given

Table 1: Intake of Macronutrients and their Energetic Contributions (%) of Breast Cancer Patients According to Treatment Exposure[1-3]

Macronutrients	Newly- diagnosed (N=60)		Recently– diagnosed (N=108)						Whole sample (N=168)	
			Non- chemo (N=42)		Chemo (N=66)		Total (N=108)			
	Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM
Energy (Kcal/day)	1395	103	1381	153	1351	60.0	1361	63.7	1373	54.7
Protein (g/day)	60.3	4.7	57.1	5.7	58.0	2.6	55.0	2.5	57.3	2.4
Protein (%E)	17.3	0.8	16.4	1.2	17.3	0.8	17.0	0.6	17.0	0.5
Carbohydrates (g/day)	206.9	13.2	208.2	30.4	193.6	12.7	198.0	12.9	201.0	9.5
Carbohydrates (%E)	59.5	3.6	60.2	2.5	57.4	2.7	58.1	2.0	58.9	1.8
Fat (g/day)	35.6	3.6	36.1	3.5	38.1	2.8	37.4	2.2	36.4	1.9
Fat (%E)	23.2	1.5	23.4	2.0	25.3	1.3	24.9	1.1	24.5	0.9
SFA (g/day)	11.1	1.0	11.0	1.1	10.2	0.8	10.5	0.8	10.7	0.7
SFA (%E)	7.2	0.8	7.2	0.8	6.8	0.5	6.9	0.3	7.0	0.1
MUFA (g/day)	10.1	1.1	11.8	1.6	13.7	1.5	13.1	1.1	12.0	0.9
MUFA (%E)	6.5	0.9	7.7	0.8	9.1	0.7	8.9	0.5	7.9	0.2
PUFA (g/day)	7.4	0.9	8.3	0.8	9.6	1.0	9.2	0.7	8.5	0.6
PUFA (%E)	4.8	0.4	5.4	0.5	6.4	0.6	6.1	0.3	5.6	0.2
Trans fat (g/day)	0.6	0.1	1.1	0.2	0.2	0.0	0.5	0.0	0.5	0.0
Trans fat (%E)	0.4	0.0	0.7	0.1	0.13	0.0	0.33	0.0	0.32	0.0
Cholesterol (mg/day)	153.2	15.3	159.3	26.3	129.3	12.3	139.3	10.6	144.2	8.3
Dietary fiber (g/day)	18.1	1.8	14.0	1.8	15.7	1.4	15.1	1.1	16.2	1.0

[1]Values are given as mean ± SEM.
[2]No significant different in macronutrient intakes and their energetic (%) among treatment exposure groups ($p \geq 0.05$).
[3]Abbreviations and definitions: newly diagnosed: breast cancer patients who are not exposed to any type of interventions; recently- diagnosed: breast cancer patients within 3 months of diagnosis who are either exposed (chemo) or not exposed (non- chemo) to chemical therapy; E: energy; MUFA: mono unsaturated fatty acid; PUFA: poly unsaturated fatty acid; SFA: saturated fatty acid; SEM: stander error of means.

Table 2: Macronutrients Intake as Percentages of Recommendations of Breast Cancer Patients[1-3]

Macronutrients	Actual intake		Recommended intake		Percent of recommendations
	Mean	±SEM	Mean	±SEM	
Energy (Kcal/day)	1373	54.7[a]	2392	95.3[b]	57.4%
Protein (g/day)	57.3	2.4[a]	64.7	2.5[a]	88.5%
Carbohydrates (g/day)	205.0	9.5[a]	325.5	15.6[b]	63%
Fat (g/day)	36.4	1.9[a]	74.1	3.8[b]	49.1%
SFA (g/day)	10.7	0.7[a]	24.3	1.4[b]	44.1%
MUFA (g/day)	12.0	0.9[a]	27.0	1.9[b]	44.5%
PUFA (g/day)	8.5	0.6[a]	29.6	1.4[b]	28.7%
Trans fat (g/day)	0.5	0.0[a]	1.1	0.4[b]	45.4%
Cholesterol (mg/day)	144.2	8.3[a]	268.0	14.7[b]	53.8%
Dietary fiber (g/day)	16.2	1.0[a]	24.4	1.1[b]	66.4%

[1]Values are given as mean ± SEM.
[2]Values in rows with different superscripts are significantly different ($p<0.05$).
[3]Abbreviations and definitions: MUFA: mono unsaturated fatty acid; PUFA: poly unsaturated fatty acid; SFA: saturated fatty acid SEM: stander error of mean.

in Table **2**. Actual intakes of macronutrients was significantly lower ($p<0.05$) compared with recommended intakes. The percentages (actual intake vs. recommended intake) of recommendations were

Table 3: Vitamins Intake of Breast Cancer Patients According to Treatment Exposure[1-2]

Vitamins	Newly-diagnosed (N=60)		Recently-diagnosed (N=108)						Whole sample (N=168)	
			Non-chemo (N=42)		Chemo (N=66)		Total (N=108)			
	Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM
A(RAE)	103.4	6.8	98.4	8.5	94	7.8	95.4	6.5	99.1	5.8
C(mg)	74.6	10.1	42.2	9.0	70	8.1	60.6	9.2	67.6	9.1
E(mg)	1.6	0.1	1.5	0.2	2.1	0.2	1.9	0.1	1.81	0.15
B1(mg)	1.7	0.4	2.2	0.8	2.2	0.5	2.2	0.6	1.96	0.3
B2(mg)	1.1	0.1	0.9	0.1	0.9	0.1	0.9	0.0	1.0	0.09
B3(mg)	19.9	1.1	18.4	1.5	15.3	1.2	16.3	1.1	18.2	1.3
B6(mg)	1.0	0.0	0.9	0.1	0.9	0.5	0.9	0.0	1.0	0.1
B9 (mcg)	296	19.8	301	15.3	352	21.4	335	12.7	318	19.8
B12 (mcg)	2.0	0.7	0.5	0.2	3.6	0.4	2.5	0.6	2.2	0.7

[1]Results are expressed as Mean ± SEM.
[2]Abbreviations and definitions: newly diagnosed: breast cancer patients who are not exposed to any type of interventions; recently- diagnosed: breast cancer patients within 3 months of diagnosis who are either exposed (chemo) or not exposed (non- chemo) to chemical therapy; REA: retinol activity equivalences = mcg retinol + (mcg beta-carotene equivalents/12); SEM: stander error of mean.
[3]No significant different in vitamins intake among treatment exposure groups ($p \geq 0.05$).

57.4% of energy intakes (1373 ± 54.7 vs. 2392 ± 95.3 kcal/day), 63.0% of carbohydrates (205.0 vs. 325.5 ± 15.6 g/day), 49.1% of fat (36.4 ± 1.9 vs. 74.1 ± 3.8 g/day), 44.1% of SFA (10.7 ± 0.7 vs. 24.3 ± 1.4 g/day), 44.5% of MUFA (12.0 ± 0.9 vs. 27.0 ± 1.9 g/day), 28.7% of PUFA (8.5 ± 0.6 vs. 29.6 ± 1.4 g/day) and 45.4% of Trans fat (0.5 ± 0.0 vs. 1.1 ± 0.4 g/day). While, they were 88.5% of protein (57.3 vs. 65 g/day), (53.8%) and (66.4%) for cholesterol (144.2 ± 8.3 vs. 268.0 ± 14.7 mg/day) and dietary fiber (16.2 ± 1.0 vs. 24.4 ± 1.1 g/day) respectively (Table **2**).

Vitamin intakes of breast cancer patients according to treatment exposure are indicated in Table **3**. Vitamins intake were not significantly different ($p \geq 0.05$) among study groups. The intakes of vitamin A, C and E were respectively (99.1 ± 5.8 retinol activity equivalent), (67.6 ± 9.1 mg) and (1.815 ± 0.1 mg). They were (1.96 ± 0.4mg), (1.0 ± 0.09 mg), (18.2 ± 1.3 mg), (1.0 ± 0.1 mg), (318 ± 19.8 mcg) and (2.2 ± 0.7 mcg) for B1, B2, B3, B6, B9 and B12 respectively.

Vitamins intake as percentages of recommendations of breast cancer patients are shown in Table **4**. The actual intakes of vitamin A, C, E and B6 were significantly lower ($p<0.05$) compared to recommended intakes. They were respectively (63.6%), (66.6%), (16.9%) and (64.7%). The intakes of

Table 4: Vitamins Intake as Percentages of Recommendations of Breast Cancer Patients[1-3]

Vitamin	Actual intake		Recommended intake		Percent of recommendation
	Mean	±SEM	Mean	±SEM	
A(RAE)	99.1	5.8[a]	155.7	6.11[b]	63.6%
C(mg)	67.6	9.1[a]	101.5	10.6[b]	66.6%
E(mg)	1.81	0.15[a]	10.7	0.8[b]	16.9%
B1(mg)	1.96	0.4[a]	1.65	0.41[a]	118.8%
B2(mg)	1.0	0.09[a]	1.08	0.1[a]	92.6%
B3(mg)	18.2	1.3[a]	18.09	0.92[a]	100.6%
B6(mg)	1.0	0.05[a]	1.54	0.1[b]	64.7%
B9 (mcg)	318	19.8[a]	358.7	20.9[a]	88.7%
B12(mcg)	2.2	0.7[a]	2.6	0.5[a]	84.6%

[1]Values are given as mean ± SEM.
[2]Values in rows with different superscripts are significantly different ($p< 0.05$).
[3]Abbreviations:RAE: retinol activity equivalent (= mcg retinol + (mcg beta-carotene equivalents/12), SEM: stander error of mean.

Table 5: Mineral Elements Intake of Breast Cancer Patients According to Treatment Exposure[1-3]

Mineral	Newly-diagnosed (N=60)		Recently-diagnosed (N=108)						Whole sample (N=168)	
			Non-chemo (N=42)		Chemo (N=66)		Total(N=108			
	Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM
Fe (mg)	12.1	0.7	11.6	0.9	13.1	1.0	12.6	0.7	12.4	0.5
Cu (mg)	1.0	0.1	0.7	0.0	0.9	0.1	0.8	0.0	0.9	0.1
I (mcg)	24.9	1.2	27.7	1.3	30.6	1.8	29.6	1.7	27.9	1.4
Zn (mg)	6.1	0.1	5.5	0.1	5.9	0.1	5.8	0.09	5.9	0.1
Ca (mg)	580.6	19.0	578.7	17.9	552	14.6	561	13.2	568	10.2
P(mg)	667	13.6	6213	16.5	638	18.9	633	15.3	645	14.8
Se (mcg)	76.8	1.3	81.3	1.9	77.8	2.0	79.0	1.7	78.2	1.5

[1]Results are expressed as Mean ± SEM.
[2]Abbreviations and definitions: newly diagnosed: breast cancer patients who are not exposed to any type of interventions; recently- diagnosed: breast cancer patients within 3 months of diagnosis who are either exposed (chemo) or not exposed (non- chemo) to chemical therapy; SEM: stander error of mean.
[3]No significant different in minerals intake among treatment exposure groups ($p \geq 0.05$).

B1 (118.8%), B2 (92.6%), B3 (100.6%) B9 (88.7%) and B12 (84.6%) were not significantly different ($p \geq 0.05$) than recommended intakes.

Mineral intakes of breast cancer patients according to treatment exposure are shown in Table **5**. Mineral intakes were not significantly different ($p \geq 0.05$) among study groups. The intakes of Fe, Cu, I, Zn, Ca, P and Se were respectively (12.4 ± 0.5 mg), (0.9 ± 0.1 mg), (27.9 ± 1.4 mg), (5.9 ± 0.1 mg), (568.0 ± 10.2 mg), (645 ± 14.8mg) and (78.2 ± 1.5 mcg).

Minerals intake as percentages of recommendations of breast cancer patients are given in Table **6**. Actual mineral intakes were significantly lower ($p<0.05$) compared to recommended intakes. The percentages of recommendations were respectively (88.7%), (78.9%), (71.7%), (50.3%) and (88.6%) for Fe, Cu, Zn, Ca and P. The actual Se intake (95.6%) was almost as recommended ($p \geq 0.05$), whereas the actual I intake (20.8%) was much lower ($p<0.05$) than recommended intake.

4. DISCUSSION

In the present study, dietary intakes of energy macro-and micronutrients were insignificantly different among study groups, but these intakes were lower than recommendations; this may indicate an alarming situation of malnutrition risk in this vulnerable BC patients. According to WHO (2016) "malnutrition refers to deficiencies, excesses or imbalances in a person's intake of energy and/or nutrients. The term malnutrition covers 2 broad groups of conditions. One is 'undernutrition'—which includes stunting (low height for age), wasting (low weight for height), underweight (low weight for age) and micronutrient deficiencies or insufficiencies (a lack of important vitamins and

Table 6: Minerals Intakes as Percentages of Recommendations of Breast Cancer Patients[1-3]

Minerals	Actual intake		Recommended intake		Percent of recommended
	Mean	±SEM	Mean	±SEM	
Fe (mg)	12.4	0.5[a]	14.0	0.9[b]	88.7%
Cu (mg)	0.9	0.1[a]	1.14	0.1[b]	78.9%
I (mcg)	27.9	1.4[a]	134	9.4[b]	20.8%
Zn (mg)	5.9	0.1[a]	8.2	0.19[b]	71.7%
Ca (mg)	568	10.2[a]	1130	18.4[b]	50.3%
P (mg)	645	14.8[a]	728	17.6[b]	88.6%
Se (mcg)	78.2	1.5[a]	81.6	1.6[a]	95.9%

[1]Results are expressed as Mean ± SEM.
[2]Values in rows with different superscripts are significantly different ($p<0.05$).
[3]Abbreviations: SEM: stander error of mea.

minerals)" [11]. Similar results have been observed [12,13]. The reason behind these inadequate dietary intakes may be due to psychological and clinical side effect [14,15]. The BC patients in current study, showed decreased interest in food intake in term of quality and quantity. It has been shown in a study by Amirkalali *et al*., that loss of interest in dietary intakes may be related in part to adverse effects of BC treatment like alterations in taste and smell, nausea, vomiting, anorexia, diarrhea, constipation, stomatitis, mucositis, pain, depression and anxiety [14]. Another study by Wojtaszek *et al*., has suggested the role of psychological issue as a possible cause of lower dietary intakes in BC patients. In this study, the dietary record of BC patients was at time of diagnosis or within three months of diagnosis, this critical period plays important role in the alteration of nutritional statues [15]. In a study, Demark-Wahnefried *et al*., have reported that the observed weight gain of BC patients was related to lack of exercise and increased fat mass but not related to overeating [13]. In a study based on Patient-Generated Subjective global assessment method to assess nutritional status among BC Indonesian patients it has been found that 68.2 % of patient were at risk of malnutrition, and 13.6% were moderately malnourished while severe malnourished not identified in this study [16]. On other hand, higher rate of mild and moderately malnourished (24%) was reported in Brazil [17]. These results may indicate the need for interventions aimed to assess the nutritional status of BC patient considering hormonal status as biomarker. To best of our knowledge, this study is the first in Jordan and perhaps in the Middle East that assessing the dietary intake of Jordanian BC patients within three months of diagnosis highlighting the risk of malnutrition among BC patients. The study is limited by assessing BC patients at diagnosis or no more than three months later, therefore, it cannot estimate the lifestyle factors before and after that period, in addition to problems of reliability in self-reported lifestyle factors, in particular the estimation of dietary intake by questionnaire.

CONCLUSIONS

In the whole sample, the actual intakes of macronutrients was significantly lower (p<0.05) compared with recommended intakes for the following energy intake, carbohydrates and fat. The actual intake of vitamins A, C, E and B6 in the whole sample, were significantly lower (p<0.05) compared to recommended intakes. Actual minerals intake were significantly lower (p<0.05) compared to recommended intakes. The percentages of recommendations in the whole sample for Cu, Zn and, Ca. furthermore, the actual I intake (20.8%) was much lower (p<0.05) than recommended intake**.** Dietary intakes of macro and micronutrients were not significantly different among treatment exposure study groups. A careful monitoring, evaluation and managements care plan must be adapted to insure that sufficient requirements are met in such critical conditions.

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