

## Ketogenic Diet: Golden Intervention for Breast Cancer Patients with Type II Diabetes Mellitus an Intervention Study, Mansoura, Egypt

Aml Ahmed Mohammed ELmetwaly<sup>1\*</sup>, Entisar Gaad El moula Shaaban<sup>2</sup>, Ateya Megahed Ibrahim<sup>3</sup>, Safaa Salem Salem Shetawy<sup>4</sup>, Eman Mahmoud Hafez Mohamed<sup>2</sup>

(1) Medical Surgical Nursing, Medical Surgical Nursing Department, Faculty of Nursing, Mansoura University, Egypt.

(2) Medical Surgical Nursing, Medical Surgical Nursing Department, Faculty of Nursing, Aswan University, Egypt.

(3) PhD, Family and Community health Nursing department, Faculty of Nursing, Port Said University, Egypt.

(4) Clinical Nutritionist, Cardiovascular/Respiratory Disorder and Geriatrics Department, Faculty of physical therapy, Cairo University, Egypt.

\*Corresponding author: Aml Ahmed Mohammed ELmetwaly

Email: amlmetwaly86@mans.edu.eg

### Abstract

Ketogenic diets (KDs) have increased popularity among patients and researchers comparable due to their putative anti-tumor mechanisms plus its effect in reducing body weight in obese patients, and improving glycemic & lipid metabolism of diabetic patients. **Aim:** The study aimed to evaluate the effect of ketogenic diet on blood glucose level, body mass index and quality of life among breast cancer patients with type 2 diabetes mellitus. **Design:** A quasi-experimental research design was utilized. **Setting:** The study was conducted at inpatient department at oncology center Mansoura University, and follows those patients at outpatient clinics. **Subjects:** A purposive sample of 26 type 2 diabetes mellitus breast cancer obese patients was enrolled in this study. **Tools:** Two tools were used. Tool I: Structured interview questionnaire. Tool II: SF-8 Questionnaire. **Results:** The mean and SD of body mass index, hemoglobin A1C and fasting blood sugar of females' patients were  $34.78 \pm 7.176$ ,  $8.94 \pm 1.156$  and  $223.50 \pm 41.84$  respectively, before starting Ketogenic diet, which changed with significant difference to become  $32.76 \pm 6.841$ ,  $7.33 \pm 0.686$  and  $135.00 \pm 29.28$  respectively, after applying Ketogenic diet. **Conclusion:** The data presented in the present study showed that a ketogenic diet can help as a natural therapy for significant weight reduction in obese patients, glycemic control and improving quality of life for type 2 diabetic breast cancer patients. **Recommendation:** This study recommended that Ketogenic diet should be incorporated in the dietary regimen for patients suffering from obesity, breast cancer and type 2 diabetes.

**Keywords:** Breast cancer, Glycemic control, Ketogenic diet, Obesity, Quality of life, and Type 2 diabetes mellitus.

### 1. Introduction

Ketogenic diet (KD), well reported to be effective for weight loss and glycemic control. Wilder and Peterman established the term ketogenic diet (KD), and they developed the fat-to-carbohydrate ratio that is still being used today (Wheless, 2008). Ketogenic diet has a minimal carbohydrate content (less than 55 g/d) and relies on fat and protein for energy, causing ketosis and simulating the physiological state of fasting (Saslow, et al., 2017; Joshi, Ostfeld, & McMacken, 2019; Bolla, Caretto, Laurenzi, Scavini, & Piemonti, 2019).

The efficacy and benefits of ketogenic diets (KD) have lately gained popularity around the world, although they are still a

contentious topic in oncology (Erickson, et al., 2017). Several clinical studies argue for the use of the ketogenic diet in combination with standard therapies based on advanced research to enhance the antitumor effects of classic chemo -and radiotherapy. Ketogenic diet is considered to be effective for weight loss and glycemic control (Weber, et al., 2020).

Ketogenic diet is a new metabolic treatment for cancer cells and promising adjuvant as a patient-specific multifactorial therapy. KD considered overall good safety and tolerability and enhance quality of life for obese breast cancer patients (Weber, et al., 2020).

Breast cancer is the most common neoplastic tumour in women all over the world. Type 2 diabetes is a secondary serious health

problem in industrialised countries. Additionally, up to 16 %of the breast cancer patients suffer from diabetes .advanced research and epidemiologic research imply that type 2 diabetes increases the risk of breast cancer and mortality, although there is minimal experimental evidence metabolic treatment supporting this association (Schott, Schneeweiss, & Sohn, 2010).

Obesity can increased blood levels of insulin and insulin-like growth factor-1 (IGF-1) (ading tole hyperinsulinemia or insulin resistance, development of type 2 diabetes and help promote the development of many types of cancers (Gallagher, LeRoith, 2015). Furthermore, some studies reported that, women with a higher BMI is associated with a modest increase their risk of breast cancer (Renehan, et al., 2008).

Breast cancer clinical trials interventions reported that, weight loss that resulted from intervention by KD may lead to beneficial changes in biomarkers that have been linked to the association between obesity and prognosis of cancer (Goodwin, et al., 2014; Harrigan,et al., 2016).

Ketogenic diet requires collaborates with the multidisciplinary team therapy as physicians, nurses, dietitians, and social workers to assess dietary preferences, aversions, intolerances, and allergies .The nurse practitioner and dietitian then determine which diet therapy to begin as inpatient initiation, and should make daily patient interviewing to assess tolerance of the diet, address complications, institute medical interventions as necessary (Zupec-Kania, et al., 2013).

### Significance of the study

Obesity is a significant chronic condition that affects both industrialised and developing nations. Furthermore, it is associated with a variety of chronic diseases .Annually, about 4.7 million premature deaths occur due to obesity . It was ranked fifth among the leading preventable causes of death (Mehrzaad, 2020), making up 8.4 %of deaths worldwide in 2017 (Our World in Data, 2017).

According to the World Health Organization (WHO), Egypt ranks 18th with

the highest prevalence of obesity worldwide (ProCon.org, 2020). Breast cancers are the most frequent cancers among Egyptian females accounting for 32.04 %of all incident cancers that affecting Egyptian females with crude incidence rate about 35.8 /100,000 females (Ibrahim, Khaled, Mikhail, Baraka, & Kamel, 2014). Approximately 16 %of patients with breast cancers are suffering from type II diabetes mellitus (Wolf, Sadetzki, Catane, Karasik, & Kaufman, 2005)

Ketogenic diet has gained popularity among patients and researchers alike due to their putative anti-tumor mechanisms .Use of the KD as an adjuvant to cancer therapy also began to emerge .Therefore, this study was conducted to evaluate the effect of ketogenic diet on blood glucose level, BMI and quality of life among breast cancer patients with type 2 DM.

## 2. Aim of the Study

To evaluate the effect of ketogenic diet on blood glucose level, body mass index and quality of life among breast cancer patients with type 2 DM.

### 2.1. Research Hypothesis

- H1** .A ketogenic diet will enhance blood glucose level among type 2 DM breast cancer patients after following the ketogenic diet.
- H2** .A ketogenic diet will enhance body mass index among type 2 DM breast cancer patients after following the ketogenic diet.
- H3** .A ketogenic diet will improve quality of life among type 2 DM breast cancer patients after following the ketogenic diet.

## 3. Method

### 3.1. Study Design

This study was conducted using a quasi-experimental research design.

### 3.2. Settings

The research was conducted at the inpatient department of Mansoura University's oncology centre, with patients being followed up on in outpatient clinics.

### 3.3. Subjects

A purposive sample of 26 type 2 DM breast cancer obese patients was enrolled in this study using pre and posttest based on the following criteria :

**Inclusion criteria:** Adult female patients, ranged from 20 to 60 years, patients with 2 DM breast cancer patients and BMI more than 25.

**Exclusion criteria:** Have already completed a formal education programme on any specific diet, other types of cancer, type 1 diabetes, dementia patients, mental retardation, apparent physical problems, and a history of serious psychiatric disorder.

**Sample size:** Sample size was calculated according to the following equation:

$$n = \left( \frac{Z_{1-\alpha/2} + Z_{1-\beta}}{ES} \right)^2$$

The standard normal deviate for  $\alpha = Z_{\alpha} = 1.960$

The standard normal deviate for  $\beta = Z_{\beta} = 0.842$

A = 8

B) =  $Z_{\alpha} + Z_{\beta} = 7.8489$

C) =  $E/S \Delta((^2) = 0.3906$

AB/C = 20.0931

n = 21

$n = \left( \frac{1.96+0.84}{0.3906} \right)^2 = 20.0931 \approx 21$  patients

Sample size is 26 patients to achieve a power of 95 % and a level of significance of 5 % (two sided), assuming the standard deviation of the differences to be 8 between pairs )Rosner ,2016.(

### 3.4. Tools of Data Collection

Two tools were used for collection of data and achieve the aim of the study as the following:

**Tool I:** Structured interview questionnaire

This tool was developed by researchers after extensive literature review to collect baseline and personal data (Tokuda, et al, 2009; Cohen, et al, 2018; Weber, et al., 2020). It consisted of two parts as follows :

**Part I:** Demographic data: such as name, age, level of education, occupation, marital status, residence and body mass index (BMI) .

**Part II:** Health relevant data such: as disease stage, diagnosis time of cancer, diagnosis time of DM, chemotherapy cure numbers, comorbid diseases, Adherence to treatment of DM and clinical findings as Hb A1C and fasting blood glucose .

### Tool II :SF-8 Questionnaire

SF-8 is a generic multipurpose short-form health-related quality of life instrument and was developed by the RAND Corporation and the Medical Outcomes Study (MOS) in the 1980s, which was originally a short-form health survey with 36 questions (Roberts, Browne, Ocaka, Oyok, & Sondorp, 2008; Valles, et al., 2010; Campolina, Pinheiro, Ciconelli, & Ferraz, 2011).

#### Scoring system:

The questionnaire contained the 8 items of the SF-8, with a 4-week recall period .Each item has a 5 -or 6-point response range . Physical )PCS (and mental (MCS )component addressing eight domains of general health, physical functioning, role limitations due to physical health problems, bodily pain, vitality )energy/fatigue(, social functioning, mental health, and role limitations due to emotional problems .SF-8 measures can be scored on the same metrics as the SF-36 scales .SF-8 scales are scored using norm-based scoring methods )NBS “50/10” referring to means of 50 and standard deviations of 10) (Ware, Kosinski, Dewey, & Gandek, 2001).

Note that all items are scored so that a high score defines a more favorable health state .In addition, Scores represent the percentage of total possible score achieved.

#### Validity of the SF-8 Questionnaire:

It has been reported to be quite high in various settings; among the US population, test-retest reliability for the eight scales ranged from 0.59 to 0.70, and test-retest reliability for PCS-8 and MCS-8 was 0.73 and 0.74, respectively (Ware, Kosinski, Dewey, & Gandek, 2001).

The Spanish version of the SF-8 was tested ( $n = 2,991$ ), and Cronbach's alpha of 0.92 was reported (Valles, et al., 2010).

### 3.5. Pilot Study

A pilot study was conducted on 10 patients (10%) representing the study sample to test the feasibility and clarity of the used tools; modifications were done based on the results. The sample included in the pilot study was excluded from the final study sample and modifications were made as a result of the findings.

### 3.6. Field Work

Data collection was extended over a period of 3 months starting from the beginning of June 2020 till September 2020; the researchers were attended to the previously mentioned settings three days/ week from 9:00 Am to 1:30 Pm. The study was conducted in three phases namely: assessment, implementation and evaluation.

#### 3.6.1. The interviewing and assessment phase:

The researchers conveyed the study's aim, tool components, and ketogenic diet component instructions throughout this phase. The time it took each patient to complete the questionnaire ranged from 10 to 15 minutes.

#### 3.6.2. The implementation phase:

- Based on the findings of assessment phase, goals and expected outcomes were formulated.
- In this phase a ketogenic diet instruction for patients who undergoing chemotherapy was provided and their relatives by an oral instruction as a method of teaching supported by data show presentation and simulated booklet contains diagrams and pictures which designed by researchers in simple Arabic language.
- Ketogenic menu was made after consulting a nutritionist to ensure their effectiveness and optimal application and avoid any possible harm to those patients.
- The selected patients who were recruited were interviewed individually by the

researchers two times throughout the study.

- ✚ **The first interview time** for pretest, which implemented through two sections:

- **First section;** was carried out by the researchers for each participant at inpatient departments for collecting baseline data about their demographic, clinical finding and measurement the quality-of-life scale. The interview carried out at the previously mentioned departments in the hospital during the morning and afternoon shifts. It took about 10 -15 minute using tool (I, and II).

- **Second section;** was carried out individually and addressed ketogenic diet-related behaviors. Audiovisual and written instructions about the importance of healthy nutrition, effect on daily activities were used, and the consequences of poor nutritional habits. These materials were introduced to the patients within 30 minutes, then researchers allowed 10 minutes to participants to ask their enquiries. Ketogenic diet instructions as the following:

- Definition of Ketogenic diet.
- Allowed foods.
- Forbidden foods.
- How to apply it?
- Bread alternatives.
- Examples of breakfast, lunch, dinner menu and some alternatives.
- Participants received weekly phone calls from the study researchers for the remainder of the intervention to review food records and discuss strategies to enhance participants' adherence and enjoyment of their assigned diets.
- Two women withdrew during the study. One was died during the study and one experienced A cancer recurrence and no longer want to continue in the study.

- ✚ **The second interview time** was carried out by the researchers for each patient in outpatient clinic after implementing the

instructions by three months using the clinical finding's part from tool I and II as a posttest, the researchers were interviewed each patient individually .

### 3.6.3. The evaluation phase:

The goal of this phase was to estimate the effect of the intervention in order to establish if the study's goal had been met or not, by comparing pre and post implementation of diet instructions on BMI, blood glucose level, and quality of life.

### 3.7. Ethical Considerations and Human Rights:

- After clarifying the study's purpose to the responsible administrative personnel, an official approval for conducting the study was acquired.
- Participants were advised that participation in the study is entirely voluntary, and that they have the opportunity to quit at any moment without incurring any consequences.
- After discussing the study's goal, benefits, and protocol, each patient gave their informed oral consent to participate.
- Anonymity and confidentiality of data was assured and was used only for research purposes.

### 3.8. Statistical Analysis

Data were presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, and means and standard deviations for quantitative variables .Shapiro-Wilk Test and Kolmogorov-Smirnov Test were used to determine whether or not a variable follows a normal distribution, when normal distribution of the data could not be assumed, the non-parametric Wilcoxon test and Spearman correlation coefficient were used instead .

Qualitative variables were compared using chi-square test .In larger than 2x2 cross-tables, Mont Carlo test was applied whenever the expected value in 2 or more of the cells was less than 5 .Statistical significance was considered at p-value <0.05.

## 4. Results

**Table (1);** Illustrates that 50 %of females' participant have breast cancer with third degree, while 84.6 %and 46.2 %of them discover breast cancer and diabetes from one year respectively .On the other hand, 69.2 %of patients taken 8 – 10 chemotherapy cures .In addition to 65.4 %of them have comorbidity diseases .

**Table (2);** Shows that 76.9 %of the participants are obese with BMI  $\geq 30$  before starting ketogenic diet while their number decrease to 62.5 %after applying ketogenic diet .On the other hand, 57.7 %of them not adhere to treatment of diabetes before starting ketogenic diet while 95.8 %of patients adheres to their diabetic treatment after applying ketogenic diet.

**Table (3);** Displays that the mean and SD of BMI, HbA1C and fasting BI .Sugar of females' patients are  $34.78 \pm 7.176$ ,  $8.94 \pm 1.156$  and  $223.50 \pm 41.84$  respectively, before starting ketogenic diet which changed with significant difference to become  $32.76 \pm 6.841$ ,  $7.33 \pm 0.686$  and  $135.00 \pm 29.28$  respectively, after applying ketogenic diet .In addition to the mean and SD of total QoL of the participant before starting ketogenic diet is  $36.89 \pm 10.52$  and improved significantly after applying ketogenic diet by  $55.28 \pm 7.29$  .

**Table (4);** Illustrates that females' participant aging is a positive indicator of increasing body mass index, cancer stage, chemotherapy cure number, comorbidity disorder, HbA1c baseline, and fasting blood glucose level, on the other hand the aging of them is a negative indicator on the quality of life and diabetes medication adherence before applying ketogenic diet with no statistically significant difference While .,there was a negative effect of marital status on fasting blood sugar with a statistically significant difference at p value 0.026.

In addition, the same table shows that the educational level of patients has a negative effect on body mass index and HbA1c baseline . While the occupational status of them has a negative indicator on the quality of life and diabetes medication adherence before applying

ketogenic diet and has a statistically significant relation with p value 0.034.

**Table (5);** Illustrates that females' participant aging is a positive indicator of increasing body mass index, HbA1c baseline, and diabetes medication adherence after applying ketogenic diet .In addition, the same table shows that the educational level of patients has a negative effect on body mass index, HbA1c baseline, and fasting blood glucose level .While the occupational status of them has a negative indicator on body mass index, and fasting blood glucose level after applying ketogenic diet with no statistically significant difference between .variables

**Table (6);** Demonstrates that, comorbidity diseases of the participants have a negative effect on quality of life with presence of statistically significant difference at P value  $\leq 0.05$  after applying ketogenic diet .On the other hand, there aren't statistically significant difference among HbA1c baseline, BMI, DM treatment adherence and quality of life at P value  $>0.05$ , but the same table find that HbA1c baseline and diabetic treatment adherence have a negative effect on females' participants quality of life before applying ketogenic diet while after applying ketogenic diet on them, it finds that a positive relation between HbA1c baseline, diabetic treatment adherence and quality of life.

**Table 1: Number and percent distribution of patients according to their health relevant data.**

Parameter	N=26	%
<b><u>Breast cancer stage</u></b>		
II	9	34.6
III	13	50
IV	4	15.4
<b><u>Time since initial diagnosis)cancer(</u></b>		
<b><u>Mean in months</u></b>	8.00±8.988	
<one year	22	84.6
≥ one year	4	15.4
<b><u>Time since initial diagnosis) DM(</u></b>		
<b><u>Mean in months</u></b>	35.76±56.19	
<one year	12	46.2
1-3 year	7	26.9
>3 year	7	26.9
<b><u>The number of chemotherapy cure</u></b>		
2-4 cure	3	11.5
5-7 cure	5	19.2
8-10 cure	18	69.2
<b><u>Comorbidity</u></b>		
Yes	17	65.4
No	9	34.6
<b>Hypertension )n=17(</b>		
Heart	5	29.4
Asthmatic	5	29.4
Thyroid	4	23.5

**Table 2:** Number and percent distribution of patients according to their BMI and adherence to treatment of DM pre and post applying ketogenic diet.

Parameter	Pre		post		X <sup>2</sup>	P value
	N=26	%	N=24	%		
<b>BMI</b>						
Overweight (25:29.9)	6	23.1	9	37.5	Mc	0.615
Obese (≥30)	20	76.9	15	62.5		
<b>Adherence to treatment of DM</b>						
Yes	11	42.3	23	95.8	16.432	0.000
No	15	57.7	1	4.2		

MC: Monte Carlo test: 2 cells have expected cell count <5.  $\chi^2$ : Chi-square test. P: Significance. \* Significant ( $p \leq 0.05$ ).

**Table 3:** Mean and SD distribution of patients according to their clinical parameters and quality of life pre and post applying ketogenic diet.

Parameter	pre	Post	Wilcoxon Signed Ranks Test	
			Z	P value
BMI	34.78±7.176	32.76±6.841	-4.286	0.000
HbA1C	8.94±1.156	7.33±0.686	-4.288	0.000
Fasting Bl .sugar	223.50±41.84	135.00±29.28	-4.060	0.000
Total QoL	36.89± 10.52	55.28±7.29	-4.217	0.000

Wilcoxon Signed Ranks Test P: Significance. \* Significant ( $p \leq 0.05$ ).

**Table 4:** Correlation among personal characteristics, cancer stage, chemotherapy cure, comorbidity, clinical parameters and QOL pre-applying ketogenic diet.

Parameter	BMI	Cancer stage	Chemo.no	Comorbidity	HbA1c baseline	Fasting BG	QOL	Adherence to diabetic treatment
Age	R	0.204	0.216	0.010	0.065	0.023	0.177	-0.079
	P value	0.318	0.289	0.962	0.753	0.911	0.387	0.702
Residence	R	-0.328	-0.090	-0.221	0.243	-0.169	0.293	0.283
	P value	0.102	0.662	0.278	0.233	0.408	0.146	0.161
Marital status	R	-0.096	-0.127	-0.083	0.093	-0.058	-0.435*	-0.106
	P value	0.640	0.538	0.687	0.650	0.779	0.026	0.606
Education	R	-0.164	0.153	0.014	0.057	-0.116	-0.221	0.259
	P value	0.425	0.456	0.947	0.782	0.573	0.279	0.202
Occupation	R	0.020	-0.143	0.048	-0.055	0.280	0.072	-0.085
	P value	0.925	0.487	0.816	0.789	0.166	0.727	0.680

Spearman correlation P: Significance. \* Significant ( $p \leq 0.05$ ).

**Table 5:** Correlation among personal characteristics, clinical parameters and QOL post applying ketogenic diet:

Parameter	BMI	HbA1c	Fasting BG	QOL	Adherence to diabetic treatment
Age	R	0.258	0.085	-0.145	-0.144
	P value	0.223	0.693	0.498	0.502
Residence	R	-0.349	-0.262	-0.225	0.134
	P value	0.095	0.217	0.290	0.533
Marital status	R	-0.065	0.000	0.121	-0.220
	P value	0.762	1.000	0.573	0.301
Education	R	-0.160	-0.126	-0.004	0.265
	P value	0.456	0.556	0.985	0.211
Occupation	R	-0.007	0.195	-0.022	0.007
	P value	0.973	0.361	0.917	0.972

Spearman correlation P: Significance. \* Significant ( $p \leq 0.05$ ).

**Table 6** :Correlation among QoL with clinical parameters Pre and post applying ketogenic diet.

Items	QoL		
		Pre	Post
Comorbidity	r	-0.364	-0.521
	P value	0.067	0.009*
HbA1c baseline	r	-0.071	0.246
	P value	0.731	0.247
BMI	r	-0.304	-0.286
	P value	0.131	0.176
DM treatment adherence	R	-0.167	0.228
	P value	0.416	0.283

Spearman correlation P: Significance. \* Significant ( $p \leq 0.05$ )

## 5. Discussion

Diabetes mellitus (DM) is a growing public health concern around the world (Roglic, 2016; Al-Lawati, 2017). Type 2 Diabetes is a major health issue that affects more than 7% of adults in affluent countries. Diabetes affects up to 16% of breast cancer patients, and two key risk factors for type 2 diabetes, old age and obesity, are both linked to breast cancer (Wolf, Sadetzki, Catane, Karasik, & Kaufman, 2005).

According to case reports and clinical research, KD is safe and acceptable for cancer patients (Tan-Shalaby, 2017). Thus, the current study evaluated the effect of ketogenic diet on blood glucose level and quality of life on patients with type 2 DM obese breast cancer patients.

To our knowledge, the effects of glycemic control on the prognosis of BC have not been thoroughly evaluated. so, this is the first study to investigate the relationship of blood glucose level control and BC with ketogenic diet intervention by setting a cut-off point of the HbA1C level fasting blood glucose and body mass index in stage 1–3 breast cancer patients in Egypt.

The present study illustrated that more than half of females' participant have breast cancer with third degree, this finding could be due to the difficulty in early detection of BC in its earlier stages and lack of access to treatment, besides the rapid spread and development of breast cancer, frighteningly, if not treated early. This contradicted the result of Chang, Sheu, Lin, & Liou, (2018), who examined the association between glycemic control and mortality in BC patients and found

most of the participants who have diabetes are in the second stage, then the third stage follows those.

Furthermore, majority of them discovered breast cancer and diabetes since less than one year. This finding could support the fact that women with type 2 diabetes had a modestly elevated incidence of breast cancer and vice versa. This in agreement with the American study by Westman, Yancy, Mavropoulos, Marquart, & McDuffie, (2008), who apply his study in less than one-year type 2 diabetes mellitus patients.

This result is contradicting the result of Cohn, et al., (2018), who conducted his study at Birmingham Participants on women with ovarian or endometrial cancer to estimate the effect of KD in improving body composition and lower serum insulin and insulin-like growth factor-I (IGF-I), the participants of this study reported that the time since initial diagnose was  $2.4 \pm 3.0$ .

On the other hand, nearly two thirds of patients took 8 – 10 chemotherapy cures. This result is fully consistent with a previous result in the present research, which found that more than half of the sample were in the third degree of disease, and it is known that the number of treatment cures is determined previously before starting treatment, based on the type and stage of cancer.

In addition to nearly two thirds of the present study participants had comorbidity diseases. Hypertension (HTN) was the most prevalent with more than half of the participant followed by heart diseases.

This could be explained by the fact that hypertension may raise the risk of breast cancer by preventing and then changing apoptosis, so

affecting cell turnover regulation (Han, et al., 2017). Concerning, the association between diabetes mellitus and hypertension, it is explained as, Diabetes affects arteries, making them vulnerable to atherosclerosis (hardening of the arteries). This can result in high blood pressure, which, if left untreated, can cause problems such as blood vessel damage, heart attack, and renal failure (Boer, et al., 2017).

This gone in the same line with Shao, et al., (2018) and Tsimihodimos, Gonzalez-Villalpando, Meigs, & Ferrannini, (2018), who examined the association between DM-2 diagnosed pre and post breast cancer diagnosis and overall survival and found most of the female participants with DM suffering from HNT and less than one third of them had coronary heart disease.

Regarding BMI, the present study showed that more than three quarter of the participants were obese with BMI  $\geq 30$  before starting ketogenic diet while their number decreased to become less than half of overweight patients with BMI (25:29.9) after applying ketogenic diet by three months. This result corresponds with Dashti and his colleagues, who apply Low-carbohydrate, ketogenic diet (LCKD):  $< 20$  g/day carbohydrates, on adult Kuwait citizen with BMI equals  $\geq 30$  and noticed a severe weight loss after 12 weeks from application of Low-carbohydrate, ketogenic diet (Dashti, et al., 2007).

This could be owing to a lack of carbohydrate in the diet, which suggested inducing fatty acid mobilisation from adipose tissue as a way to deliver energy to the body via ketone bodies, resulting in an ancient technique of weight loss promotion (Paoli, 2014).

In references to clinical parameters of the participants, this study clears that the mean and SD of BMI, HbA1C and fasting Blood Sugar of females' patients are  $34.78 \pm 7.176$ ,  $8.94 \pm 1.156$  and  $223.50 \pm 41.84$  respectively, before starting ketogenic diet which changed with significant difference to become  $32.76 \pm 6.841$ ,  $7.33 \pm 0.686$  and  $135.00 \pm 29.28$  respectively, after applying ketogenic diet.

These results to some extent similar to the study done to evaluate whether type-2 diabetes mellitus has an effect on the clinicopathological stage of breast cancer at diagnosis at Benha university, Egypt which

stated that, type-2 diabetic breast cancer women, their mean BMI was  $34.7 \pm 4.5$  kg/m<sup>2</sup>, FBS was  $145.4 \pm 18.1$  mg/dL, and of HbA1c was  $9.1 \pm 1.4\%$  without any intrusive procedure (Ali, Mohamed, Khattab, Tabl, & Emam, 2020). So, this is a point that counts in favor of our study because it evaluates clinical parameters pre and post an interventional procedure and there is a clear difference and variation in the results of ketogenic diet, and this indicates its effectiveness.

Also, Hussain et al., 2012 and Saslow et al., (2017) found an improvement in HbA1c had positive effects on glycemic control with very low carbohydrates diet on patients with type 2 DM.

This is explained by the physiology and biochemistry of ketogenic diet which depends on very low carbohydrates. After that, insulin secretion is reduced then the body enters a catabolic state causing metabolic changes (gluconeogenesis and ketogenesis) which in turn sharply reduces the stimulus for fat and glucose storage (Jagadish, et al., 2019 and Mohorko, et al., 2019).

Also, an American study by Westman, Yancy, Mavropoulos, Marquart, & McDuffie, (2008), who evaluated the effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in less than one year type 2 diabetes mellitus and found BMI of the study sample was  $36.3 \pm 1.4$ .

On the other hand, more than half of them not adhere to treatment of diabetes before starting ketogenic diet while majority of patients adheres to their diabetic treatment after applying ketogenic diet. In addition to the mean and SD of total QoL of the participant before starting ketogenic diet is  $36.89 \pm 10.52$  and improved significantly after applying ketogenic diet to become  $55.28 \pm 7.29$ .

A study conducted in Iran to explore the effect of a randomly assigned KD on quality of life, physical activity, and biomarkers in breast cancer patients found that the KD group had superior global QoL at week 6 ( $P = 0.02$ ) than the control group (Khodabakhshi, Seyfried, Kalamian, Beheshti, & Davoodi, 2020).

According to the present study, the level of adherence to the KD intervention and treatment suggests that the diet is a feasible option for women with breast cancer type 2 DM who are receiving chemotherapy.

The present study data pre applying the KD illustrates that females' participant aging is a positive indicator of increasing body mass index, cancer stage, chemotherapy cure number, comorbidity disorder, HbA1c baseline, and fasting blood glucose level, on the other hand the aging of them is a negative indicator on the quality of life and diabetes medication adherence before applying ketogenic diet with no statistically significant difference. This result may be logical, since half of the study participate aged  $\geq 50$  years and physiological changes that occur with aging process leading to decrease quality of life in noncompliant patients. While, there was a statistically significant difference between marital status and fasting blood sugar.

Furthermore, the educational level of patients has a negative effect on body mass index and HbA1c baseline. While the occupational status of them has a negative indicator on the quality of life and diabetes medication adherence before applying ketogenic diet with a statistically significant difference. This may be due to majority of the study sample are unemployed and more than third are illiterate so, this leads to a lack of health awareness of treatment and their adherence to it, and thus will affect the laboratory results and their quality of life.

Post intervention of ketogenic diet, the researchers excluded three variables from associations (cancer stage, chemotherapy cure number and co morbidity) because they are constants variables that do not change with time.

It has been observed that adherence to treatment has changed after applying ketogenic diet from a negative to positive association with age. This result attributed to effect of the intervention of our study and increasing awareness among women.

Finally, the current study investigates the association between QoL with clinical parameters and adherence to DM treatment pre and post applying ketogenic diet and found, comorbidity have a negative effect pre and post application of intervention with a statistically significant difference post intervention only as comorbidity is a constant variable that not changed with period. While, HbA1c and DM treatment adherence have positive effect with QoL post application of ketogenic diet and this

is a good indicator and prove the efficacy of our study.

## 6. Conclusion

The current study concluded that, a ketogenic diets help as a natural therapy for significant weight reduction in obese patients, glycemic control and enhance quality of life for type 2 diabetic breast cancer patients. This is a unique study that followed participants for three months to see how they responde to a ketogenic diet.

## 7. Recommendation

The present study recommended:

- Patients with breast cancer and type 2 diabetes mellitus should incorporate a ketogenic diet in their nutritional regimen since it improves BMI, HbA1c, and quality of life.
- Further studies are needed to determine the ketogenic diet's long-term viability and consequences on clinically important endpoints such as obesity-related morbidity and mortality.

## Conflict of interest

The authors declared there is no conflict of interest

## 8. References

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