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# Macronutrient Intake and Association with the Risk Factors of Diabetic Complications among People with Type 2 Diabetes Mellitus in Al-Madinah Al-Munawara

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**Abstract**

**BACKGROUND:** Worldwide, Type 2 diabetes mellitus (T2DM) is a leading cause of morbidity and mortality. There is little research on the relationship between T2DM problems and daily macronutrient intake in Saudi Arabia, particularly in Al-Madina Al-Munawara.

**AIM:** This study aimed to investigate the relationship between T2DM complications and daily carbohydrate, protein, and fat intake in T2DM patients.

**MATERIALS AND METHODS:** A cross-sectional study was conducted on 138 T2DM patients in Al-Madina Al-Munawara City, Saudi Arabia. The data were collected using a questionnaire that was published on social media. The macronutrient data were collected by a 24-h dietary recall questionnaire on 2 non-consecutive days. Appropriate statistical tests were done, and univariate and multivariate logistic regression were used to examine the association of macronutrient intake with diabetes complications among the studied patients.

**RESULTS:** The mean age of patients was 53.8 ± 11.3 years, and 55.8% were females. The prevalence of T2DM complications was 55.8% for diabetic retinopathy, 30.4% for cardiovascular diseases (CVD), 26.1% for diabetic foot, 19.6% for stroke, and 5.3% for kidney diseases with no significant difference by patients' sex. Daily carbohydrates intake >65% was associated with an increased risk of CVD, retinopathy, and diabetic foot with odds ratio (OR) of 4.75, 4.35, and 65.5, respectively. Daily proteins intake >20% and daily fat intake ≥30% were associated with a significant increased risk of stroke and CVD, respectively.

**CONCLUSION:** The study findings suggest that high daily calorie intake from carbohydrate protein and fat plays an important role in the risk of T2DM complications. Patients with diabetes who understand the value of consuming calories from macronutrients and how to distribute their daily intake of these calories may reduce their risk of developing diabetic complications.

## Introduction

Diabetes mellitus (DM) is characterized as an abnormal metabolic state with glucose intolerance brought on by insufficient insulin activity. Moreover, it is diagnosed when FPG level >126 mg/dL (7.0 mmol/L) or a random plasma glucose >200 mg/dL (11.1 mmol/L) or HBA1C (≥6.5%) [1]. Long-term elevated glucose levels are linked to cellular damage and organ and tissue failure [2].

Type 2 DM (T2DM) is more prevalent than Type 1 and most frequently affects obese people. It typically manifests in middle life. Patients rarely have a non-ketotic coma with high plasma osmolarity [3], [4]. Nowadays, 90% of adults worldwide have T2DM [5]. T2DM prevalence in the Saudi population increased from 8.5% in 1992 to 39.5% in 2022. If the prevalence of obesity decreased, the incidence of diabetes was predicted to decline by 10% by 2022 [6].

The primary goal of the management of diabetes is to achieve normal or near-normal blood glucose levels and if requires weight loss. Dietary carbohydrates are the major determinant of postprandial glucose levels. The quantity and quality of carbohydrates play a major role in the postprandial glycemic response. Carbohydrates are classified into three primary categories: Starch (complex carbs), sugar (simple carbs), and fiber. These types can be found alone or in combination in a variety of dietary groups, including cereal, pasta, fruits, legumes, starchy vegetables, milk, yogurt, and desserts. All carbohydrate-rich foods affect blood glucose levels postprandial. Consuming foods with a low glycemic index, high in fiber, and low in sugar is advised [7], [8].

Adults should consume between 10 and 35% of their daily calories from digestible proteins, or a minimum of 0.8 g/kg of body weight, based on the European Food Safety Authority in 2010 [9].

To lower the risk of cardiovascular diseases (CVD), health professionals' main objective was to reduce total lipids in patients with diabetes by 30% and to restrict their intake of saturated fatty acids, and dietary cholesterol. Saturated fat was thought to be the main factors affecting plasma LDL. Changes in the fatty acid content of cell membranes, which are strongly dependent on dietary fat consumption, have been linked to impaired insulin binding or glucose transport [10], [11].

Over time, diabetes can cause severe complications and affect a wide range of organ systems. Neuropathy, nephropathy, and retinopathy are examples of microvascular complications. CVD, stroke, and peripheral vascular disease are examples of macrovascular complications. Peripheral vascular disease can result in gangrene, amputation, and bruises or injuries that do not heal [12], [13], [14].

Genetic, metabolic, and environmental influences interact with one another to increase the chance of developing T2DM. Although ethnicity and family history/genetic predisposition, which are non-modifiable risk factors for T2DM, have a strong genetic base, epidemiological studies have shown that many cases of T2DM can be averted by addressing the major modifiable risk variables (obesity, low physical activity, and an unhealthy diet). The largest risk factor for T2DM is obesity (body mass index [BMI] more than 30 kg/m$^2$), which is linked to metabolic abnormalities that lead to insulin resistance [15], [16]. Therefore, the goals of our study are to evaluate the macronutrient intake of T2DM patients, identify the health issues, and investigate the relationship between patients' macronutrient intake and diabetes complications, in Al-Madinah Al-Munawara, Saudi Arabia.

## Materials and Methods

### *Ethical consideration*

We obtained ethical approval to start this study from the ethical committee of the College of Applied Medical Sciences at Taibah University and the ethical approval number is number 2023/160/205 CLN. We clarified that participation is optional and that all participants are informed, they have the right to withdraw from the study at any time before they fill out the questionnaire. The participants' privacy is protected by not mentioning any private information in the study.

### *Research design*

In an observational, descriptive, and cross-sectional study, a questionnaire was shared on social media and in a real interview to assess diabetic complications and their association with macronutrient intake among T2DM patients in Al-Madinah Al-Munawara.

### *Sample size calculations*

The minimum sample size for this study was 138 T2DM patients (61 male participants and 77 female participants), as estimated by the equation suggested by Charan and Biswas for cross-sectional studies (REF), Z 1−9/2 = 1.96, p = 0.10, and D = 0.05 with alpha 0.05 and beta 0.10, determined based on a two-sided test [17].

### *Study setting and population*

In the study conducted from December 2022 to May 2023, 138 patients with T2DM participated either through an online questionnaire that was shared through social media between people who have or know someone with diabetes or through a real interview in Al-Madinah Al-Munawara, Saudi Arabia. Forms were filled out for illiterate patients by us or their families. We studied the prevalence of diabetes complications (CVD, stroke, nephropathy, retinopathy, and diabetic foot) and their association with macronutrient intake in T2DM patients through a detailed questionnaire that assessed information about their blood pressure, duration of illness, macronutrient intake, physical activity, and laboratory investigations such as HBA1C, fasting blood glucose (FBG), and lipid profile.

Inclusion criteria include T2DM patients living in Al-Madinah Al-Munawara, Saudi Arabia. Incomplete data, patients suffering from chest infections, cancer, and pregnant women were excluded from the study.

### *The questionnaire*

The tool used for data collection was a questionnaire. It was designed by us, and it was designed to preserve the privacy of the participants. None of the participants' names or home addresses was asked. It is important to ask about the phone number to call them on need. A 24-h dietary recall is conducted to collect data about their dietary intake on 2 non-consecutive days: The previous day and a weekend day. The questionnaire consisted of 29 questions. We used a detailed questionnaire to assess information about anthropometric measurements (weight, and height), and then BMI was calculated, socioeconomic data such as age and gender, educational status, occupation, physical activity, knowledge level, diabetic complications, blood pressure, laboratory investigations, and medications taken to control BP.

### *Statistical analysis*

The collected data were analyzed using SPSS version 24. Data were normally distributed and presented using frequencies, means, and standard deviation as appropriate. The sociodemographic, clinical, and anthropometric data were compared by the patients' sex using the independent t-test for continuous variables and the Chi-square test or Fischer's exact test for categorical variables, as appropriate. The mean percentage of daily macronutrient intake was compared by the studied patient's characteristics using the t-test and the one-way ANOVA analysis as appropriate. Pearson's correlation was done for normally contributed continuous data to calculate the correlation coefficient between macronutrient calorie intake and some of the studied patient's clinical variables. Finally, univariate and multivariate logistic regression analyses were used to examine the association between complications due to T2DM and high intake of macronutrients with the calculation of the odds ratio and their 95% confidence intervals. p = 0.05 was used as a level of statistical significance.

## Results

The data from 138 T2DM patients (61 males and 77 females) were analyzed to investigate the association between macronutrient intake and diabetic complications among T2DM patients in Al-Madinah Al-Munawara, Saudi Arabia.

Table 1 presents the sociodemographic characteristics of the 138 T2DM patients studied by their sex. The mean age of the studied patients was 53.8 ± 11.3 years; 63.8% of them aged 40–60 years, with no significant difference found between male and female patients. About 60% of the studied patients had higher secondary (29.7%) and graduate degrees' education (29%), with no significant difference between males and females. Most of the studied patients were not working (72.5%), and the highest percent of them were found in female patients (83.1%), with a statistically significant difference compared with male patients. The percentage of smokers in the sample was 14.5%, and all of them were male patients. Most patients were reported to practice light physical activity (79%), with no statistically significant difference between male and female patients.

**Table 1: Sociodemographic characteristics of the studied patients with Type 2 diabetes mellitus by their sex**

| Variables | Total (n = 138) | Male patients (n = 61) | Female patients (n = 77) | p |
|---|---|---|---|---|
| Age (years), mean ± SD | 53.8 ± 11.3 | 54.5 ± 11.4 | 53.2 ± 11.2 | 0.49 |
| Age (years), category | | | | |
| <50 | 50 (36.2) | 19 (31.1) | 31 (40.3) | 0.29 |
| ≥50 | 88 (63.8) | 42 (68.9) | 46 (59.7) | |
| Education | | | | |
| Illiterate | 24 (17.4) | 6 (9.8) | 18 (23.4 | 0.10 |
| Primary | 20 (14.5) | 6 (9.80 | 14 (18.2) | |
| Secondary | 13 (9.4) | 6 (9.8) | 7 (9.1) | |
| Higher Secondary | 41 (29.7) | 22 (36.1) | 19 (24.7) | |
| Graduate degrees | 40 (29.0) | 21 (34.4) | 19 (24.7) | |
| Occupation | | | | |
| Not working | 100 (72.5) | 36 (59.0) | 64 (83.1) | 0.002** |
| Working | 38 (27.5) | 25 (41.0) | 13 (16.9) | |
| Smoking status | | | | |
| No | 98 (71.0) | 21 (34.4) | 77 (100.0) | <0.0001*** |
| Ex-smoker | 20 (14.5) | 20 (32.8) | 0 | |
| Current smoker | 20 (14.5) | 20 (2.8) | 0 | |
| Physical activity level | | | | |
| Light | 109 (79.0) | 46 (75.4) | 63 (81.8) | 0.23 |
| Moderate | 24 (17.40 | 11 (18.0) | 13 (16.9) | |
| Active | 5 (3.6) | 4 (6.1) | 1 (1.3) | |

Data are presented by mean ± SD or by n (%). **p-values were calculated by Chi-square test, ***p-value was calculated by Fischer's exact test. SD: Standard deviation.

Table 2 shows the clinical and anthropometric measurements of the studied T2DM patients. About two-thirds of patients had DM durations of >5 years (68.8%), with no significant difference between male and female patients. One-third of the sample were obese (34.1%), and two-thirds were on oral hypoglycemic treatment (69.6%). Periodic medical follow-up was higher among female patients (79.2% vs. 67.2%), although not statistically significant. There was no statistically significant difference between male and female patient's mean FBG or their mean HbA1c and cholesterol levels. Furthermore, the mean saturated fatty acid intake was higher among male patients, although no statistically significant difference was detected. The mean daily intake of carbohydrate and fat did not show any statistically significant difference between male and female patients. The mean daily fat intake in grams, however, showed a statistically significant difference where the mean intake was higher in male (103 ± 73.5) compared to female (76.6 ± 56.1) patients. The rate complications due to DM were higher among male patients regarding CVD, kidney diseases, and stroke; a statistically significant difference was detected for stroke only (29.5% vs. 10.4%, p = 0.01). Retinopathy and diabetic foot were higher, however, among female patients, with no statistically significant difference.

**Table 2: Clinical and anthropometric measurements of the studied patients with Type 2 diabetes mellitus**

| Parameter* | Total (n = 138) | Male patients (n = 61) | Female patients (n = 77) | p |
|---|---|---|---|---|
| Duration of diabetes (years) | | | | |
| ≤5 | 43 (31.2) | 18 (29.5) | 25 (32.5) | 0.70 |
| >5 | 95 (68.8) | 43 (70.5) | 52 (67.5) | |
| BMI | | | | |
| Normal | 30 (21.7) | 14 (23.0) | 16 (20.8) | 0.21 |
| Overweight | 61 (44.2) | 31 (50.8) | 30 (39.0) | |
| Obese | 47 (34.1) | 16 (26.2) | 31 (40.2) | |
| Medication of DM | | | | |
| Insulin | 15 (10.9) | 5 (8.2) | 10 (13.0) | 0.10 |
| OHA | 96 (69.6) | 39 (64.0) | 57 (74.0) | |
| OHA + insulin | 27 (19.5) | 17 (27.8) | 10 (13.0) | |
| Medication of HTN | 45 (32.6) | 22 (36.1) | 23 (30.0) | 0.44 |
| Medical follow-up | | | | |
| Always | 102 (73.9) | 41 (67.2) | 61 (79.2) | 0.11 |
| Sometimes | 36 (27.1) | 20 (32.8) | 16 (20.8) | |
| Laboratory tests, mean ± SD | | | | |
| FBG (mg/dL) | 193.2 ± 69.7 | 203.1 ± 78.2 | 185.3 ± 61.7 | 0.13 |
| HbA1c (%) | 8.3 ± 1.4 | 8.1 ± 1.2 | 8.5 ± 1.5 | 0.13 |
| Cholesterol | 244.3 ± 162.2 | 237.2 ± 147.8 | 250.1 ± 173.5 | 0.64 |
| Macronutrients (g/day) | | | | |
| CHO | 230.4 ± 99.2 | 242.6 ± 97.6 | 220.6 ± 99.9 | 0.19 |
| Protein | 88.5 ± 65.5 | 103.6 ± 73.6 | 76.6 ± 56.1 | 0.01* |
| Fat | 73.1 ± 22.3 | 70.1 ± 19.0 | 75.3 ± 24.6 | 0.17 |
| Complications due to DM (%) | | | | |
| Cardiovascular | 42 (30.4) | 20 (32.8) | 22 (28.6) | 0.71 |
| Kidney disease | 8 (5.3) | 4 (6.5) | 4 (5.2) | 0.75 |
| Retinopathy | 78 (55.8) | 30 (49.0) | 46 (61.0) | 0.12 |
| Stroke | 26 (19.6) | 17 (29.5) | 9 (11.4) | 0.01** |
| Diabetic foot | 36 (26.1) | 14 (23.0) | 22 (28.6) | 0.45 |

*Data are presented by mean ± SD or by n (%). **p-values were calculated by Chi-square and t-test as appropriate. SD: Standard deviation, CHO: Carbohydrate, OHA: Oral hypoglycemic agents, BMI: Body mass index, DM: Diabetes mellitus, FBG: Fasting blood glucose.

Table 3 shows the association of daily caloric intake of macronutrients with patients' characteristics (sex, age, education level, occupation, smoking status, and physical activity). The daily calorie intake showed a significant difference between male and female patients regarding protein and fat, with a high intake of protein for males (p = 0.01) and a high intake of fat for female patients (p = 0.02). Statistically significant differences were also found between patients by their levels of FBG and cholesterol, where the percentage of fat and protein calories was significantly higher in patients with FBG levels ≥200 mg/dL and cholesterol levels ≥200 mg/dL. Although not significant, high daily fat calorie intake was higher in patients aged <50 years, illiterate, not working, never smokers, duration of DM ≤5 years, with HbA1c >7, and on oral hypoglycemic agents. High-calorie protein intake was higher among smokers and patients with blood glucose levels ≥200 mg/dL, although not significantly.

**Table 3: Association of daily macronutrients intake calories with patient's characteristics**

| Characteristic | Percentage of calorie intake (CHO) | | Percentage of calorie intake (protein) | | Percentage of calorie intake (fat) | |
|---|---|---|---|---|---|---|
| | Mean ± SD | p | Mean ± SD | p | Mean ± SD | p |
| Gender | | | | | | |
| Male | 47.5 ± 10.1 | 0.48 | 19.1 ± 9.6 | 0.01* | 33.3 ± 10.9 | 0.02* |
| Female | 46.2 ± 12.0 | | 15.3 ± 7.1 | | 38.5 ± 14.1 | |
| Age (years) | | | | | | |
| <50 | 46.0 ± 10 | 0.81 | 15.4 ± 6.8 | 0.11 | 38.0 ± 10.6 | 0.18 |
| ≥50 | 47.1 ± 12 | | 17.8 ± 9.3 | | 35.1 ± 14.2 | |
| Education | | | | | | |
| Illiterate | 45.5 ± 11.1 | 0.35 | 17.1 ± 6.7 | 0.94 | 37.7 ± 14.5 | 0.48 |
| Primary | 48.5 ± 15.3 | | 16.4 ± 9.3 | | 35.3 ± 18.5 | |
| Secondary | 42.3 ± 10.6 | | 15.8 ± 9.7 | | 41.7 ± 8.1 | |
| Higher secondary | 46.1 ± 11.5 | | 17.8 ± 9.7 | | 36.1 ± 12.2 | |
| Graduate degrees | 48.9 ± 8.5 | | 16.7 ± 7.5 | | 34.4 ± 11.0 | |
| Occupation | | | | | | |
| Not working | 46.5 ± 12.1 | 0.69 | 16.5 ± 8.1 | 0.35 | 36.9 ± 13.9 | 0.25 |
| Working | 47.4 ± 8.6 | | 18.2 ± 9.7 | | 34.3 ± 10.3 | |
| Smoking status | | | | | | |
| No | 46.6 ± 11.8 | 0.81 | 16.4 ± 8.2 | 0.02* | 36.9 ± 14.1 | 0.29 |
| Ex-smoker | 48.2 ± 8.5 | | 15.2 ± 8.7 | | 36.5 ± 9.4 | |
| Current smoker | 46.5 ± 11.1 | | 21.5 ± 8.7 | | 31.9 ± 10.2 | |
| Physical activity | | | | | | |
| Light | 46.7 ± 11.2 | 0.83 | 16.6 ± 8.1 | 0.30 | 36.5 ± 12.7 | 0.54 |
| Moderate | 46.8 ± 11.0 | | 18.4 ± 9.9 | | 34.8 ± 13.5 | |
| Active | 47.9 ± 10.0 | | 17.4 ± 10.1 | | 34.6 ± 20.7 | |
| BMI | | | | | | |
| Normal | 50.8 ± 10.7 | 0.35 | 15.3 ± 5.4 | 0.17 | 40.1 ± 14.5 | 0.17 |
| Overweight | 46.1 ± 11.7 | | 16.5 ± 8.8 | | 35.4 ± 11.5 | |
| Obese | 46.9 ± 9.4 | | 18.8 ± 9.6 | | 34.7 ± 13.8 | |
| Medication of DM | | | | | | |
| Insulin | 50.8 ± 10.7 | 0.32 | 13.1 ± 5.6 | 0.10 | 35.9 ± 12.1 | 0.86 |
| OHA | 46.1 ± 11.7 | | 17.3 ± 8.8 | | 36.5 ± 13.5 | |
| OHA + insulin | 46.9 ± 9.4 | | 18.0 ± 8.5 | | 35.0 ± 12.2 | |
| HBA1c | | | | | | |
| ≤7 | 47.0 ± 9.6 | 0.89 | 15.2 ± 7.7 | 0.16 | 37.3 ± 12.8 | 0.45 |
| >7 | 46.9 ± 11.7 | | 17.5 ± 8.7 | | 35.7 ± 13.1 | |
| FBG (mg/dL) | | | | | | |
| <200 | 45.7 ± 11.7 | 0.20 | 14.7 ± 6.3 | 0.001* | 29.5 ± 13.5 | 0.001* |
| ≥200 | 48.2 ± 10.4 | | 20.1 ± 10.1 | | 31.7 ± 11.2 | |
| Cholesterol level (mg/dL) | | | | | | |
| <200 | 45.3 ± 10.5 | 0.19 | 14.0 ± 6.3 | 0.001* | 32.9 ± 12.4 | 0.001* |
| ≥200 | 47.8 ± 11.6 | | 19.1 ± 9.2 | | 40.6 ± 12.6 | |

*Significant. p-values were calculated by t-test and one-way ANOVA as appropriate. SD: Standard deviation, CHO: Carbohydrate, OHA: Oral hypoglycemic agents, BMI: Body mass index, DM: Diabetes mellitus, FBG: Fasting blood glucose.

Table 4 presents the distribution of patients by complications due to T2DM and daily macronutrient calorie intake. The prevalence of CVD was higher among patients with daily calorie CHO intake >65% (67.7% vs. 29.6%; p = 0.016) and daily calorie fat intake ≥30% (35.9% vs. 19.6; p = 0.03). A significant high prevalence of retinopathy and diabetic foot was found among patients with daily calorie intakes of CHO >65%. A significant high prevalence of stroke was observed in patients with daily calorie and protein intake >20%. A significant low prevalence of stroke (14.5% vs. 26.1%) and diabetic foot (20.7% vs. 37.0%; p = 0.04), however, was found among patients with a daily calorie intake of fat below 30%.

**Table 4: Distribution of patients by Type 2 diabetes mellitus complications and daily macronutrients calorie intake**

| Complications | Carbohydrate calories | | Protein calories | | Fat calories | |
|---|---|---|---|---|---|---|
| | 45%–65% | >65% | ≤20% | >20% | <30% | ≥30% |
| Cardiovascular | | | | | | |
| Yes (n = 42) | 40 (29.6) | 2 (67.7) | 31 (32.0) | 11 (26.8) | 9 (19.6) | 33 (35.9) |
| No (n = 96) | 95 (70.4) | 1 (33.3) | 66 (68.0) | 30 (73.2) | 37 (80.4) | 59 (64.1) |
| P | 0.16 | | 0.41 | | 0.04* | |
| Kidney disease | | | | | | |
| Yes (n = 8) | 8 (5.9) | 0 | 5 (5.2) | 3 (7.3) | 2 (4.3) | 6 (6.5) |
| No (n = 130) | 127 (94.1) | 3 (100.0) | 92 (94.8) | 38 (92.7) | 44 (95.7) | 86 (93.5) |
| P | 0.03* | | 0.62 | | 0.60 | |
| Retinopathy | | | | | | |
| Yes (n = 78) | 75 (55.6) | 3 (100.0) | 57 (58.8) | 21 (51.2) | 25 (54.3) | 53 (57.6) |
| No (n = 60) | 60 (44.4) | 0 | 40 (41.2) | 20 (49.8) | 21 (45.7) | 39 (42.4) |
| P | 0.04* | | 0.18 | | 0.71 | |
| Stroke | | | | | | |
| Yes (n = 26) | 26 (19.3) | 0 | 14 (14.4) | 12 (30.5) | 12 (26.1) | 14 (16.5) |
| No (n = 112) | 109 (80.7) | 3 (100.0) | 83 (85.6) | 29 (69.5) | 34 (73.9) | 78 (83.5) |
| P | 0.26 | | 0.02* | | 0.01* | |
| Diabetic foot | | | | | | |
| Yes (n = 36) | 33 (24.2) | 3 (67.7) | 26 (26.8) | 10 (24.4) | 17 (37.0) | 19 (20.7) |
| No (n = 102) | 102 (75.8) | 0 (33.3) | 71 (73.2) | 31 (75.6) | 29 (73.0) | 75 (79.3) |
| P | 0.003* | | 0.76 | | 0.04* | |

*Significant. p-values were calculated by Chi-square and Fischer's exact test as appropriate.

Table 5 presents the correlation of macronutrient intake calories with patients' clinical data. Apart from BMI, there has been a significant positive correlation between daily CHO intake and the studied clinical variables. Daily calorie protein intake showed a significant positive correlation with almost all studied variables, with the highest positive relationship being with FBG (r = 0.45, p = 0.0001). A negative correlation was detected between daily calorie fat intake and BMI, FBG, and HBA1c, which was significant with BMI (r = 0.19, and p = 0.03).

**Table 5: Correlation of macronutrients calories intake with patient's clinical variables**

| Variables | Percentage of CHO intake | | Percentage of protein intake | | Percentage of fat intake | |
|---|---|---|---|---|---|---|
| | Correlation coefficient | p | Correlation coefficient | p | Correlation coefficient | p |
| Age (years) | 0.18 | 0.03* | 0.16 | 0.04* | 0.07 | 0.40 |
| BMI ($kg/m^2$) | –0.04 | 0.68 | 0.05 | 0.52 | –0.19 | 0.03* |
| FBG (mg/dL) | 0.26 | 0.004* | 0.45 | <0.0001* | –0.02 | 0.84 |
| HbA1c (%) | 0.18 | 0.03* | 0.19 | 0.03* | –0.01 | 0.93 |

*Significant. BMI: Body mass index, FBG: Fasting blood glucose, CHO: Carbohydrate.

Table 6 displays the association of T2DM complications with daily calories of carbohydrate intake among the studied patients in the univariate and multivariate logistic regression analyses. The risk of CVD was significantly increased among patients with daily calorie CHO intake >65% in the univariate model (OR = 4.75; 95% CI = 1.42–53.8), but the significance disappeared in the multivariate model. Furthermore, the risk of retinopathy and diabetic foot was highly increased, with ORs of 4.35 and 65.5, respectively, although not significant. On the other hand, however, the risk of stroke and kidney disease was decreased, with risk reductions of 65% and 90%, respectively, in the multivariate model, although not significant. The adjusted OR was 0.35 (95% CI = 0.01–22.2) for stroke and 0.10 (95% CI = 0.01–19.3) for kidney diseases.

**Table 6: Association of Type 2 diabetes mellitus complications with daily calories of carbohydrate intake in logistic regression univariate and multivariate analysis**

| Variables | OR (95% CI) | p | OR adjusted* (95% CI) | p |
|---|---|---|---|---|
| Cardiovascular complications | | | | |
| Calories of carbohydrate (%) | | | | |
| 45–65 | 1.00 (Reference) | 0.02** | 1.00 (Reference) | 0.29 |
| >65 | 4.75 (1.42–53.8) | | 3.85 (0.31–47.5) | |
| Retinopathy | | | | |
| Calories of carbohydrate** | 4.35 (0.25–88.4) | 0.33 | 4.90 (0.20–154.1) | 0.37 |
| Stroke | | | | |
| Calories of carbohydrate** | 0.80 (0.10–34.9) | 0.90 | 0.35 (0.01–22.2) | 0.61 |
| Diabetic foot | | | | |
| Calories of carbohydrate** | 65.3 (1.50–290.9) | 0.03*** | 102 (17.4–567.7) | 0.02* |
| Kidney diseases | | | | |
| Calories of carbohydrate** | 0.09 (0.01–7.2) | 0.19 | 0.10 (0.01–19.3) | 0.30 |

*OR adjusted by patients age, sex, education, occupation, DM duration, BMI, HBA1c, total cholesterol, and blood glucose level, **Carbohydrate intake was entered in the regression models as continuous variables due to absence of cases in some of its categories, ***Significant. OR: Odds ratio, BMI: Body mass index, DM: Diabetes mellitus, CI: Confidence interval.

Table 7 shows the association of T2DM complications with daily calories of protein intake among the studied patients in the univariate and multivariate logistic regression analyses. The risk was significantly increased in association with stroke (OR = 2.45; 95% CI = 1.02–4.91) among patients reporting >20% calories of protein intake in the univariate model, and this was insignificantly increased in association with kidney diseases with an OR of 1.50 in the univariate and 1.40 in the multivariate model. The risk, however, was decreased in the association of calories from protein intake >20% with CVD, retinopathy, and diabetic foot in both regression models, with ORs of 0.65, 0.80, and 0.47 in the multivariate model, respectively, although not significant.

**Table 7: Association of Type 2 diabetes mellitus complications with daily calories of protein intake in logistic regression univariate and multivariate analysis**

| Variables | OR (95% CI) | p | OR adjusted* (95% CI) | p |
|---|---|---|---|---|
| Cardiovascular complications | | | | |
| Calories of protein intake (%) | | | | |
| ≤20 | 1.00 (Reference) | 0.55 | 1.00 (Reference) | 0.32 |
| >20 | 0.80 (0.38–1.75) | | 0.65 (0.24–1.60) | |
| Retinopathy | | | | |
| Calories of protein intake (%) | | | | |
| ≤20 | 1.00 (Reference) | 0.41 | 1.00 (Reference) | 0.38 |
| >20 | 0.75 (0.35–1.53) | | 0.80 (0.30–1.87) | |
| Stroke | | | | |
| Calories of protein intake (%) | | | | |
| ≤20 | 1.00 | 0.04** | 1.00 (Reference) | 0.49 |
| >20 | 2.45 (1.02–5.91) | | 1.45 (0.51–3.91) | |
| Diabetic foot | | | | |
| Calories of protein intake (%) | | | | |
| ≤20 | 1.00 | 0.76 | 1.00 | 0.16 |
| >20 | 0.90 (0.39–2.01) | | 0.47 (0.16–1.35) | |
| Kidney diseases | | | | |
| Calories of protein intake (%) | | | | |
| ≤20 | 1.00 | 0.62 | 1.00 | 0.20 |
| >20 | 1.50 (0.73–6.38) | | 1.40 (0.85–5.91) | |

*OR adjusted by patient's age, sex, education, occupation, DM duration, BMI, HBA1c, total cholesterol, and blood glucose level, **Significant. OR: Odds ratio, BMI: Body mass index, DM: Diabetes mellitus, CI: Confidence interval.

Table 8 presents the association of T2DM complications with daily calorie intake among the studied patients in the univariate and multivariate logistic regression analyses. Patients reporting ≥30% of daily calories related to fat intake showed a significant high risk of CVD in both regression models, and an OR of 3.25 (95% CI = 1.22–8.68) was the result of the multivariate model. The risk was also increased in association with kidney diseases, with an OR of 3.30 (95% CI = 0.45–24.3) in the multivariate model, although not significant. The risk, however, was decreased in association of ≥30% of daily calories of fat intake with stroke and diabetic foot. Although not significant, the risk reduction was 50% in stroke in the univariate model and 50% in diabetic foot in the univariate model.

**Table 8: Association of Type 2 diabetes mellitus complications with daily calories of fat intake in logistic regression univariate and multivariate analysis**

| Variables | OR (95% CI) | p | OR adjusted* (95% CI) | p |
|---|---|---|---|---|
| Cardiovascular complications | | | | |
| Calories of fat intake (%) | | | | |
| <30 | 1.00 | 0.04** | 1.00 | 0.02** |
| ≥30 | 2.30 (1.01–5.34) | | 3.25 (1.22–8.68) | |
| Retinopathy | | | | |
| Calories of fat intake (%) | | | | |
| <30 | 1.00 | 0.71 | 1.00 | 0.83 |
| ≥30 | 1.15 (0.56–2.32) | | 1.20 (0.43–3.12) | |
| Stroke | | | | |
| Calories of fat intake (%) | | | | |
| <30 | 1.00 | 0.12 | 1.00 | 0.08 |
| ≥30 | 0.50 (021–1.21) | | 1.02 (0.99–1.05) | |
| Diabetic foot | | | | |
| Calories of fat intake (%) | | | | |
| <30 | 1.00 | 0.04** | 1.00 | 0.15 |
| ≥30 | 0.45 (0.20–0.97) | | 0.50 (0.18–1.30) | |
| Kidney diseases | | | | |
| Calories of fat intake (%) | | | | |
| <30 | 1.00 | 0.60 | 1.00 | 0.20 |
| ≥30 | 1.55 (0.30–7.92) | | 3.30 (0.45–24.3) | |

*OR adjusted by patient's age, sex, education, occupation, DM duration, BMI, HBA1c, total cholesterol, and blood glucose level, **Significant. OR: Odds ratio, BMI: Body mass index, DM: Diabetes mellitus, CI: Confidence interval.

## Discussion

One of the most common chronic diseases in the world is DM. The prevalence of Type 2 diabetes, which is an increasingly serious health issue in the Gulf States, was highest (31.6%) in Saudi Arabia [18]. With an estimated population of 7 million people with DM and more than 3 million people with pre-diabetes, Saudi Arabia, is ranked by the World Health Organization as having the second-highest rate of DM in the Middle East and the seventh-highest rate in the world [19].

Several regional and international epidemiologic studies have reported many macrovascular and microvascular complications of T2DM [20], [21], [22], [23], [24]. Most of these studies examined the risk of T2DM complications, such as CVD, retinopathy, neuropathy, nephropathy, and foot complications, in association with sociodemographic and clinical factors related to DM, such as duration of the disease and HBA1c [22], [23], [24].

The DM literature, however, is still lacking data about the role of daily macronutrients and calorie intake on the risk of T2DM complications. The present cross-sectional study has investigated the risk of T2DM complications in association with the daily consumption of calories from carbohydrate, protein, and fat in a cohort of T2DM patients in Al-Madinah Al-Munawara City, Saudi Arabia.

The present study showed a considerable prevalence of T2DM complications, reaching up to

55.8% for diabetic retinopathy among the studied patients. Furthermore, the prevalence of other complications was as high as 30.4% for CVD, 26.1% for diabetic foot, 19.6% for stroke, and only 5.3% for kidney diseases. The prevalence of these complications showed no statistically significant differences in the studied male and female patients except for stroke, whose prevalence was higher among males (29.5% vs. 11.4%). These reported rates appeared high compared with a recent study conducted on 505 Moroccan patients with T2DM, where retinopathy disease was the most frequent diabetic complication (29.5%), followed by CVD (22.4%), diabetic kidney disease (9.8%), diabetes foot (2.8%), and neuropathy (1.8%) [25]. Most patients in that study, however, were women (85%), and in our study, the rate of complications was lower in the female patients studied, although not significant.

The present study's rate of complications was in line with other studies conducted in Saudi Arabia, where the rate of diabetic foot was 19% in a cohort of 86 T2DM patients [26]. The rate of retinopathy was as high as 44.7% in a Saudi study conducted in Riyadh district between 2014 and 2017 on 890 diabetic patients [27]. Furthermore, the rate of cardiovascular complications due to T2DM was high in Saudi Arabia, and a recent report of the Saudi Scientific Diabetes Society indicates that more than 50% of patients with T2DM die due to CVD [28].

The low prevalence rate, however, observed in this study for kidney diseases (5.4%) did not match the results obtained from other Arabic countries where the prevalence of kidney diseases in T2DM patients was 9.8% in Morocco [25], 25.2% in Libya [29], and 33.2% in Egypt [30]. The observed differences in the prevalence of kidney disease in the current and other studies could be attributed to the nature of our e-mailed sample, whereas other studies might include hospitalized patients who receive more advanced cases addressed to the nephrology department.

The daily macronutrient calorie intake in the present study did not differ according to socioeconomic and clinical data except for sex, FBG level, and cholesterol level. The significant high percentage of protein calories intake was among males, and the significant high percentage of fat calories intake was among female patients. The percentages of fat and protein calories intake were significantly higher in patients with FBG levels ≥200 mg/dL and cholesterol levels ≥200 mg/dL. Similarly, a recent Malaysian study on 453 newly diagnosed diabetic patients reported that male patients consumed a high proportion of carbohydrate (>65%) and protein (>20%), while female patients were found to consume fat (>30%) more than the studied male patients [31].

Diabetic patients with high blood glucose and cholesterol levels tend to lower their carbohydrate intake in their diet [32], and hence they increase their caloric intake from protein and fat. It is known that a very low-carbohydrate diet reduces cholesterol significantly but increases HDL cholesterol [33].

The associations of T2DM complications with daily calories of macronutrient intake among the studied patients were examined in the univariate and multivariate logistic regression analyses. The use of a multivariate model was important to get the adjusted risk, as many factors other than the studied macronutrient factors are known to be associated with T2DM complications [20], [21], [22], [23], [24]. In this study, the obtained risk was adjusted for age, sex, education, occupation, DM duration, BMI, HBA1c, total cholesterol, and blood glucose level.

Daily calories of carbohydrate intake >65% were associated with a significant increased risk of cardiovascular complications among the studied patients (OR = 4.75; 95% CI = 1.42–53.8). A clinical study discovered that reducing the amount of carbohydrates consumed daily reduces the risk of CVD. This can also improve serum lipid levels and lower blood pressure, which are known risk factors for CVD [34]. Moreover, decreasing carbohydrates can also decrease other cardiovascular risk factors, particularly cholesterol and glucose intolerance [35].

Findings of a systematic review on the effects of different dietary approaches on T2DM patients revealed that with lower carbohydrate diets, the levels of the risk factors for CVDs improved [36]. Another intervention study on 100 poorly controlled diabetic patients showed that a low glycemic load diet (low carbohydrate 41%, high fat 36% from good fats, and high protein 22%) is appropriate for diabetic patients who manage their diabetes poorly and can improve their CVD risk [37].

Increasing carbohydrate intake was found to be associated with the risk of retinopathy and diabetic foot. The higher the carbohydrate diet, the higher the glucose, the greater the glycemic effect [38], and the greater the insulinogenic effect [39].

Hyperglycemia is an important predictor of diabetic complications, particularly diabetic retinopathy [40], [41] and diabetic foot [42]. Hyperglycemia-induced biochemical and molecular alterations, systemic metabolic factors, and aberrant activation of signaling cascades ultimately lead to the activation of several transcription factors, causing functional and structural damage to retinal cells [41]. In this respect, according to the Food and Drug Administration and United States Department of Agriculture guidelines, at least 45% and not exceeding 65% of calories should be consumed from dietary carbohydrate by a healthy adult in a day [43].

On the other hand, however, the risk of stroke and kidney disease decreased in association with increased macronutrient intake. The risk of microalbuminuria and nephropathy is known to depend on the presence of hypertension, higher Hb A1c serum blood urea nitrogen, and creatinine [44].

The reduced risk of stroke obtained in the present study coincides with the results of previous dietary studies reporting that simple sugars with a high glycemic index can decrease the risk of stroke and can prevent cognitive functional impairment [45], [46].

The present study found daily protein calorie intake >20% to be associated with a significant increased risk of stroke (OR = 2.45; 95% CI = 1.02–4.91) and an insignificant increased risk of kidney diseases (OR = 1.50; 95% CI = 0.73–6.38) among the studied T2DM patients. Increasing the risk of stroke with an increasing intake of protein was supplemented by dietary studies that have shown that a diet that emphasizes the intake of certain fat ingredients, fruits, and vegetables but less protein can reduce the risk of stroke [47].

High protein intake was known in the literature to increase the risk of diabetic kidney disease with a worsening of kidney function and increased albuminuria among diabetic patients [48]. Although the literature includes several studies that have investigated the role of dietary protein restriction in reducing the risk of kidney diseases among T2DM patients, the findings are still inconclusive [48], [49], [50], [51].

Daily fat calorie intake ≥30% showed a significantly high risk of CVD (OR = 3.25; 95% CI = 1.22–8.68) and kidney diseases (OR = 3.3; 95% CI = 0.45–24.3) in the present study. A meta-analysis of randomized control trials found a 10% reduction in chronic heart disease for each 5% of energy from fat and saturated fatty acids substituted for polyunsaturated fatty acids [52]. In the present study, the prevalence of CVD was lower among female patients (20 out of 62 cases), and the mean polyunsaturated fatty acid intake was found to be higher among them compared with that in male patients. Moreover, evidence from prospective studies has also shown that a high intake of saturated fatty acids can increase the risk of T2DM complications, including CVD and diabetic nephropathy, while a high intake of polyunsaturated fatty acids reduces the risk of the condition [53]

A risk reduction of diabetic foot was found in the present study in association with increasing daily intake of protein and fat. Vitamins A and D are fat-soluble vitamins that have numerous bodily functions. Dietary Vitamin A is absorbed as retinol from either preformed retinoids or provitamin A carotenoid. Retinoids play an important role in wound healing as they are involved in cell mitosis, angiogenesis, increasing epithelial thickness, and collagen synthesis [54]. Furthermore, proteins have roles in collagen synthesis and cell replication [55], which play an important role in wound healing in diabetic ulcers.

The present study has several strengths, including the fact that the study results add to the limited Saudi literature regarding this issue. According to the best available knowledge, assessing the association of daily calorie intake of macronutrients with several T2DM complications is the first study to address the effect of macronutrient calories on the risk of T2DM complications among diabetic patients in Al-Madina Al-Munawara.

The studied problem was also analyzed by different statistical methods, including comparison and univariate and multivariate regression analysis, in relation to many sociodemographic, clinical, laboratory, and diabetes-related factors, as well as the main study factor, daily macronutrient calorie intake.

The questionnaire used in data collection was validated and structured. The macronutrient data were collected using a sensitive, valid, and reliable 24-h dietary recall questionnaire on 2 non-consecutive days: the previous day and a weekend day. The macronutrient data were collected over the phone by the researchers themselves with the e-mail questionnaire respondents. Using validated tools and data collection by researchers is known to increase confidence in obtaining sound and standard information.

Although the study provides useful information, it may have some limitations. The design was cross-sectional, in which both cause and effect are measured at the same time; therefore, the causality of the association could not be confirmed. Self-selection bias may have been a limitation factor in this study due to the method of data collection through an email questionnaire, and so the patients who chose to participate and fill out the questionnaire may be more familiar than those who refused to be contacted.

Furthermore, the study included T2DM patients from only one Saudi city, Madinah. It is therefore difficult to generalize the study findings to all diabetic patients in the Kingdom. However, the main scope of this study was to probe the effect of daily macronutrient and calorie intake on T2DM complications and to add to the Saudi literature. Furthermore, the use of structured and valid questionnaires has facilitated confidence in obtaining sound information in a standardized manner.

## Conclusion

High daily calories of carbohydrate intake play an important role in the risk of T2DM patients, particularly those related to cardiovascular complications, retinopathy, nephropathy, diabetic foot ulcers, and diabetic foot. High daily calorie intakes of protein and fat were also found to increase the risk of cardiovascular complications and diabetic nephropathy, but this intake was found to be a protective factor for diabetic retinopathy and diabetic foot ulcers and damage. The observed risk reduction of diabetic retinopathy and diabetic foot in association with high fat intake may suggest the role of polyunsaturated fatty acids and fat-soluble Vitamins (A and D) in the prevention of such complications and enhance their daily use as dietary supplements.

### *Recommendations*

Awareness among diabetic physicians as well as diabetic patients regarding the role of calories from macronutrient intake in the complications of T2DM and how to distribute the daily calories of these macronutrients may play a significant role in preventing or at least reducing the rate of diabetic complications, particularly cardiovascular complications, retinopathy, nephropathy, and diabetic foot.

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