JNFS
Journal of Nutrition and Food Security
Shahid Sadoughi University of Medical Sciences
School of Public Health
Department of Nutrition
Shahid Sadoughi University of Medical Sciences School of Public Health Nutrition Department

eISSN: 2476-7425 pISSN: 2476-7417 JNFS 2025; 10(3): 413-422 Website: jnfs.ssu.ac.ir

Nutritional Assessment and Estimation of the Attributable Risk of Diabetes Mellitus to Simple Sugar Intake in Northern Iran: The PERSIAN Guilan Cohort Study

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ARTICLE INFO

ORIGINAL ARTICLE

Article history:
Received: 8 Oct 2024
Revised: 21 Mar 2025
Accepted: 21 Mar 2025

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Keywords:
Demography; Dietary pattern; Diabetes mellitus; Non-communicable diseases; Nutritional assessment.

ABSTRACT

Background: Diabetes Mellitus (DM) is a non-communicable disease with an increasing rate across all age groups worldwide. It makes the body vulnerable to other chronic diseases. Besides medication therapy, DM can be controlled by following a healthy lifestyle. In this study, the dietary patterns of diabetic individuals assessed in the Prospective Epidemiological Research Studies of the Iranian Adults (PERSIAN) Guilan Cohort Study (PGCS) population. **Methods:** A comprehensive survey was conducted over three years among 10,276 individuals aged 35 to 70 in the PGCS population. Socio-demographic and food intake information of 2,531 diabetic patients was collected using a food frequency questionnaire (FFQ). Data analysis was conducted with SPSS software. The estimation of the attributable risk of DM related to the intake of simple sugars was performed using the population attributable risk (PAR) equation. **Results:** The intake of dietary fibers was lower than the recommended 25-38 g/day in these patients, while they consumed high carbohydrates (more than 65% of total calories/day) and simple sugars (more than 10% of total calories/day). More than 15% of total energy was provided by simple sugars in these patients. The average population attributable risk of DM (PAR_{DM}) in the total population was 17.84% based on the intake of fructose and glucose, which was close to the proportion of diabetic patients in this survey by considering the proportion of pre-diabetic patients. **Conclusions:** Regarding the significant effect of dietary patterns on the development of DM, the authors suggest developing educational programs to help individuals maintain a balanced diet to decrease the rate of DM in the coming years.

Introduction

Diabetes mellitus (DM) is one of the most common non-communicable diseases (NCDs) in Iran, which may lead to death in the population under uncontrolled conditions (Moslemi *et al.*, 2020), although it has a smaller share in annual deaths compared to cardiovascular

This paper should be cited as: Moslemi M, Mahdavi-Roshan M, Joukar F, Mansour-Ghanaei F. ***Nutritional Assessment and Estimation of the Attributable Risk of Diabetes Mellitus to Simple Sugar Intake in Northern Iran: The PERSIAN Guilan Cohort Study.*** *Journal of Nutrition and Food Security (JNFS)*, 2025; 10(3): 413-422.

[DOI: 10.18502/jnfs.v10i3.19240]

diseases, cancers, and respiratory diseases (Ryan-Harshman and Aldoori, 2006). Several studies have shown the impact of food habits and daily diet on the incidence or prevention of Non-communicable diseases (NCDs) (Alkhatib *et al.*, 2017, Aune *et al.*, 2013, Curioni *et al.*, 2022, Kopčeková *et al.*, 2020, Soltanipour *et al.*, 2019, Tariq *et al.*, 2022). Unfortunately, the modernization of communities toward a higher intake of low-nutrition foods and high-sugar snacks is a noticeable risk factor in the prevalence of DM. The hunger rate has gradually decreased in Iran, while people commonly eat unhealthy foods, especially in industrial cities (Faramarzi *et al.*, 2019). Interestingly, improving food knowledge toward healthy eating behavior at early age helps decrease the rate of NCDs in adulthood and reduces burdens on governments (Albuquerque *et al.*, 2023, Lunze *et al.*, 2015). Therefore, the development of educational programs following national surveys presenting dietary habits is of great importance. In this regard, governments are recommended to adhere to the global action plan developed by the World Health Organization (WHO) in 2013 to decrease the rate of NCDs in countries (Moslemi *et al.*, 2020).

DM is characterized by hyperglycemia when the body is deficient in insulin due to insufficient insulin secretion and/or resistance of body cells to insulin. DM is mainly classified into type 1 (insulin deficiency), type 2 (predominantly insulin resistance), and gestational diabetes (Ballali and Lanciai, 2012, Fernandes *et al.*, 2022). In general, glucose enters the cells from the bloodstream to supply energy through its metabolism by the tricarboxylic acid cycle in the mitochondria (Gasmi *et al.*, 2021). In diabetic patients, glucose levels exceed the normal range in blood, putting the body at risk of several complications, such as cardiovascular diseases and kidney failure, due to oxidative stress (Charlton *et al.*, 2020).

It was estimated that 9.5% of Iranians suffered from DM in 2021 (Najafi *et al.*, 2024). Currently, there are about 420 million patients worldwide (World Health Organization, 2023). There is strong evidence addressing the adverse impact of a high-fat and carbohydrate diet and low intake of dietary fibers on the development of DM. A high fat level in blood may impair the function of β-cells responsible for insulin secretion in the pancreas, leading to hyperglycemia. In addition, some dietary fats, such as omega-6 fatty acids, may alter the expression of insulin signaling genes, and oxidative stress developed under dyslipidemia may block insulin signaling, leading to insulin resistance (Młynarska *et al.*, 2025, Prasad *et al.*, 2022). Furthermore, dietary fibers influence the secretion of incretin hormones and the degradation and absorption of nutrients in the lumen (Xie *et al.*, 2021). In the study by Lindström *et al.* on 522 prediabetic patients, a high-fat, low-fiber diet significantly affected the incidence of type 2 DM, with a hazard ratio of 1.89 compared to the group consuming a low-fat, high-fiber diet (Lindström *et al.*, 2006). Moreover, Breen *et al.* compared 248 adults in two groups: healthy individuals and patients with type 2 DM. They found that the healthy group consumed less fat and more fiber than the diabetic patients (Breen *et al.*, 2014). On the other hand, Joshi *et al.* reported that the intake of carbohydrates in 796 Indian patients with type 2 DM exceeded the national recommendation in India (Joshi *et al.*, 2014). Although results from a prospective cohort study by AlEssa *et al.* on 70,025 American women showed that carbohydrate content is not associated with DM (relative risk of 0.98), starch content directly contributes to the development of DM (relative risk of 1.23). In their study, total fiber, cereal fiber, and fruit fiber were found to reduce the risk of type 2 DM with relative risks of 0.8, 0.71, and 0.79, respectively (AlEssa *et al.*, 2015).

According to the evidence, one feasible approach in the prevention and control of DM is following a healthy eating habit that includes the recommended amounts of dietary fibers (21-38 g/day), carbohydrates (45-65% of total calories/day), and fat (up to 20-35% of total calories/day) (Mahan and Escott-Stump, 2004). To determine the association of eating behaviors with DM types 1 and 2, the authors investigated 2,531 diabetic residents of Guilan (North of Iran) over three years (2014-2017). In this study, the

[DOI: 10.18502/jnfs.v10i3.19240]

amounts of the main dietary components affecting blood sugar levels were considered. This work is the first study to monitor the association of DM with dietary habits, especially simple sugars, in the Prospective Epidemiological Research Studies of the Iranian Adults (PERSIAN) Guilan Cohort Study (PGCS) population. The results provide a potent baseline for developing national strategies to control DM in the country.

Materials and Methods

Participants and experimental design

This was a cross-sectional study conducted within the framework of the Prospective Epidemiological Research Studies in Iran (PGCS) (Mansour-Ghanaei *et al.*, 2019, Poustchi *et al.*, 2018). Over three years (8 October 2014 to 20 January 2017), 10,276 individuals from Sowme'eh Sara, a county in northern Iran, aged between 35 and 70, were assessed. Of these, 2,531 diabetic patients (989 men and 1,542 women) were further evaluated for the dietary habits study. After excluding outliers based on dietary energy intakes (individuals with energy intake lower than 900 kcal and more than 4500 kcal were excluded), 2,467 diabetic individuals were included in the analysis.

Socio-demographic information of patients with type 1 and type 2 DM, including age, body mass index (BMI), education, marital status, socio-economic status, habitat, and smoking is reported in **Table 1**. The socio-economic status was based on the monthly income of the family head and other variables, including access to a washing machine, freezer, computer, Internet, automobile, color TV, mobile phone, laptop, etc., across different price ranges, as well as international travel.

Daily food intake of the patients, including the main dietary groups and simple sugars, is presented in **Table 2**. Diabetic patients were those diagnosed with DM by a doctor, having fasting blood sugar equal to or higher than 126 mg/dl, or taking insulin or antidiabetic medicine (Mansour-Ghanaei *et al.*, 2019, Poustchi *et al.*, 2018).

The participants completed a 125-item semi-quantitative food frequency questionnaire (FFQ) adapted for Iranians (Mirmiran *et al.*, 2010). They reported the average frequency of consumption for each food over the past year per day, week, month, and year, or indicated if they never consumed it. The portion size was converted to grams using household measures. Data were categorized based on nutrients and food groups. Energy intake was calculated using the Food Composition Table (FCT) of the US Department of Agriculture (USDA) because the Iranian FCT was incomplete. However, the Iranian FCT was used as an alternative for traditional foods not listed in the USDA FCT (Ahuja *et al.*, 2012, Azar and Sarkisian, 1980).

Ethical considerations

This project was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1402.594), and was in accordance with the ethical principles in the Declaration of Helsinki.

Data analysis

Initial assessment and analysis of the nutritional result was done by N4 software, and statistical analysis was done by IBM SPSS Statistics 26 (SPSS Inc., Chicago, IL, USA). Differences were significant at P-value≤0.05. Moreover, numeric and qualitative variables were compared between two groups of men and women by Independent Sample t-test and Chi-square test, respectively. Food intake data are reported as g/day by quartile and tertile other than mean±SD. To anticipate the risk of type 2 DM arising from daily intake of simple sugars in individuals, the average intake of simple sugars (especially glucose and fructose) in the total population (n=10,276) was calculated based on information provided by the participants through questionnaires. Simple sugars' intake included amounts directly consumed by the participants or as ingredients in their homemade meals; sugar from ready-to-eat or processed foods was not considered. The population attributable risk (PAR) of DM due to the intake of simple sugars in the total population was calculated according to Equation 1 (Moslemi *et al.*, 2021):

$$\text{PAR (\%)} = \frac{P_e \times (RR-1)}{P_e \times (RR-1) + 1}$$

[DOI: 10.18502/jnfs.v10i3.19240]

Equation 1

where, Pe is the proportion of population exposed to the risk factor (i.e., fructose + glucose intake more than 56.2 g/day), and RR is the relative risk of risk factor with respect to DM, which was reported in a comprehensive study done by other scientists (Montonen et al., 2007, Moslemi et al., 2021).

Results

Socio-demographic information of the diabetic individuals is presented in **Table 1**. As seen, most patients of both genders were overweight or obese. A low percentage of diabetic patients had a college degree, and most were married. Despite the higher number of diabetic women, socio-economic status was slightly better among women, and a higher rate of smoking was observed in men.

Table 1. Socio-demographic information of the individuals with diabetes mellitus among PGCS population.

Variable	Men (n=974)	Women (n=1493)	Total (n=2467)	P-value[c]
Age (year)	54.41±8.55[a]	54.64±8.68	54.55±8.62	0.641
Body mass index (kg/m^2)				
< 18.5	19 (1.95)[b]	3 (0.20)	22 (0.89)	< 0.001
18.5-25	339 (34.80)	197 (13.20)	536 (21.73)	
25-30	438 (44.97)	549 (36.77)	987 (40.01)	
30 <	178 (18.28)	744 (49.83)	922 (37.37)	
Education (years)				
0 (illiterate)	121 (12.42)	481 (32.22)	602 (24.40)	< 0.001
≤ 5	285 (29.26)	507 (33.96)	792 (32.10)	
6-12	482 (49.49)	479 (32.08)	961 (38.95)	
12 <	86 (8.83)	26 (1.74)	112 (4.54)	
Marital status				
Single	7 (0.72)	38 (2.54)	45 (1.82)	< 0.001
Married	953 (97.84)	1242 (83.19)	2195 (88.97)	
Widow	12 (1.23)	193 (12.93)	205 (8.31)	
Divorced	2 (0.20)	20 (1.34)	22 (0.89)	
Socio-economic status				
Low	358 (36.76)	384 (25.72)	742 (30.08)	< 0.001
Moderate	320 (32.85)	540 (36.17)	860 (34.86)	
High	296 (30.39)	569 (38.11)	865 (35.06)	
Habitat				
Urban	438 (44.97)	699 (46.82)	1137 (46.09)	0.39
Rural	536 (55.03)	794 (53.18)	1330 (53.91)	
Smoking				
Yes	516 (52.98)	22 (1.47)	538 (21.81)	< 0.001
No	458 (47.02)	1471 (98.53)	1929 (78.19)	

[a]: Mean±SD; [b]: n(%); [c]: It obtained from an independent sample t-test for quantitative variables and from chi-square test for qualitative variables

The dietary intake of patients with diabetes is reported in **Table 2**. Accordingly, 65.84% and 66.27% of daily energy was supplied by carbohydrates in men and women, respectively. As expected, men had a higher energy intake than women. In particular, men had a higher intake than women in all food groups. In both genders, the intake of dietary fibers and carbohydrates was outside the recommended range (i.e., 25-38 g/day for dietary fibers and 45-65% of total calories/day for carbohydrates). Besides, the high intake of total carbohydrates, more than 15% of total energy was provided by simple sugars in both men and women. The share of each macronutrient and food group in the daily food intake of DM patients is illustrated in **Figure 1**.

To predict the incidence of DM in the total population (n=10,276), the relative risk of DM considering the intake of fructose and glucose was extracted from the study by Montonen *et al.*

[DOI: 10.18502/jnfs.v10i3.19240]

(Montonen *et al.*, 2007). **Table 3** shows that the intake of simple sugars significantly affects DM based on quartiles of consumption. The number of individuals with fructose + glucose intake of more than Q3 was calculated for the PAR formula.

Table 2. Total energy and dietary intake of the diabetic individuals among PGCS population.

Variable	Men (n=974)	Women (n=1493)	Total (n=2467)	Q_1	Q_2	Q_3
Energy (kcal/day)	2060.54±630.35	1890.12±623.99	1957.40±631.90	1494.85	1854.97	2306.85
Dietary fibers	23.23±8.72	21.16±8.02	21.98±8.36	15.98	20.46	26.58
Total carbohydrate	339.15±107.46	313.13±106.92	323.40±107.86	244.32	304.71	381.17
Protein	69.45±24.04	62.21±22.89	65.07±23.62	48.06	60.71	77.47
Fat	51.25±20.45	46.82±19.60	48.57±20.06	34.35	44.48	58.49
Food group (g/day)						
Bread and cereals	482.27±186.82	448.13±191.16	461.61±190.15	329.82	434.07	557.77
Dairies	220.12±154.35	207.08±161.25	212.23±158.66	115.98	177.75	266.46
Fruits	296.29±171.85	277.66±164.84	285.01±167.85	171.09	251.87	355.20
Vegetables	608.10±294.96	573.03±271.79	586.87±281.63	391.86	530.33	712.98
Simple sugars (g/day)						
Fructose	25.99±13.50	23.98±13.10	24.77±13.30	15.74	22.10	31.06
Glucose	20.21±9.84	18.64±9.67	19.26±9.77	12.52	17.27	23.85
Fructose + Glucose	46.20±23.20	42.62±22.64	44.03±22.92	28.29	39.32	54.89
Sucrose	30.20±23.02	28.83±25.29	29.37±24.42	13.38	22.37	37.93
Lactose	3.19±3.49	2.92±3.59	3.03±3.55	0.98	1.90	3.92
Total of simple sugars	79.59 ±38.74	74.37 ±40.47	76.43 ±39.87	48.94	68.07	94.71

Q_1: First quartile; Q_2: Second quartile; Q_3: Third quartile.

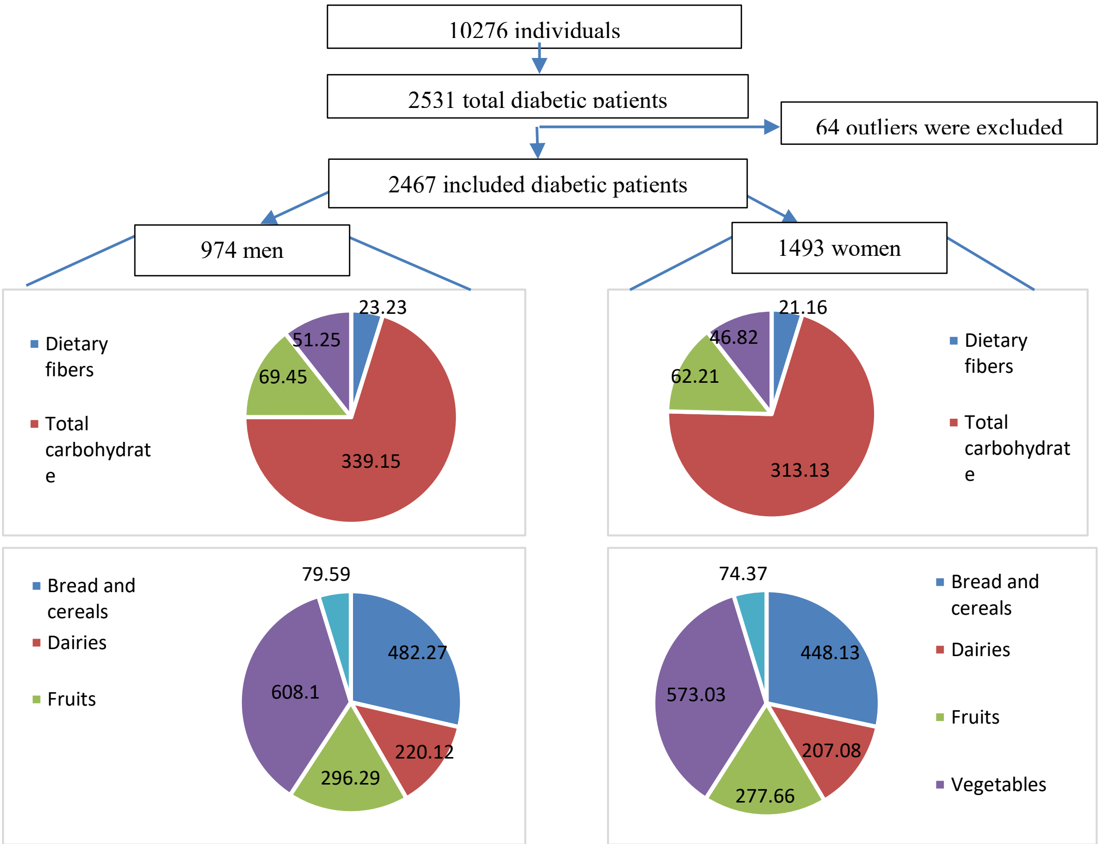

Figure 1. Share of each dietary component in the diet of diabetic individuals.

[DOI: 10.18502/jnfs.v10i3.19240]

Table 3. Intake of simple sugars of the total participants among PGCS population.

Intake (g/day)	Q_1	Q_2	Q_3
Fructose	16.31	22.92	31.62
Glucose	13.08	17.96	24.46
Fructose + Glucose	29.45	40.93	56.16
Sucrose	17.59	28.68	46.02
Lactose	0.94	1.88	3.94

Q_1: First quartile; Q_2: Second quartile; Q_3: Third quartile.

To better determine the impact of sugar intake on the incidence of diabetes, the risk of DM in the total population was assessed using PAR formula. In the study by Montonen *et al*., the relative risk of type 2 DM incidence for individuals with fructose and glucose intake exceeding 56.2 g/day was 1.87. According to **Table 3**, Q3 of fructose and glucose intake was 56.16 g/day, which is close to the cut-off point reported in Montonen *et al*.'s study. Therefore, the authors conducted two scenarios to calculate PART2DM in the population.

First scenario: The analysis revealed that 25% of the population had more than 56.16 g/day fructose and glucose intake. Accordingly, 17.86% of the total population is at risk of type 2 DM incidence.

Second scenario: Evaluation of the data revealed that 24.92% of the total population consumed more than 56.2 g/day of fructose and glucose (the cut-off point of Montonen *et al*. (Montonen *et al.*, 2007). Therefore, 17.82% of the total population is at risk of type 2 DM incidence.

Discussion

Socio-demographic and food intake information of the diabetic patients showed a high correlation between food habits and the development of DM. Food intake evaluation revealed a relatively high intake of carbohydrates and a low intake of fiber in this study (**Table 2**). This is likely attributed to the low proportion of patients with high socio-economic status and the low number of academically educated patients, especially among women. Inadequate knowledge is a significant factor affecting body health. According to **Table 1**, most patients had no academic degree, and likely, were not educated enough to follow a balanced diet. The role of socio-economic status in dietary patterns was confirmed in a study by Casari *et al.*, where the rural population of Burkina Faso with lower socio-economic status consumed more carbohydrates than urban inhabitants (Casari *et al.*, 2022). Additionally, rural Polish adolescents with low socio-economic status followed a low-fiber diet in a study by Krusinska *et al*. (Krusinska *et al.*, 2017). Similarly, Egyptian mothers with low socio-economic status believed that a healthy diet is expensive and preferred to spend less to simply keep their children full. In comparison, those with high socio-economic status spent more money on their food (Ismail *et al.*, 2022). Therefore, it would be expected that people with low to moderate socio-economic status tend to choose low-cost foods, such as carbohydrate-based rather than protein-based meals.

Fruits and vegetables are the main sources of dietary fiber in daily diet. The World Health Organization recommends at least 400 g/day of fruits and vegetables combined to maintain health (World Health Organization, 2022) . Moreover, a consumption of 200 g/day of fruits is recommended to prevent type 2 DM (Park, 2021). However, fruit consumption is controversial, and its effect on diabetes prevention is dose-dependent. It is reported that fruit intake exceeding the recommendation does not show a positive effect and might lead to an increased prevalence of type 2 DM (Park, 2021). According to **Table 2**, the consumption of fruits by patients exceeded the recommended amount, supplying high levels of simple sugars to the body. It was reported that the type of fruit is a deterministic factor in the development of DM, with some fruits potentially increasing the risk of type 2 DM (e.g., cantaloupe), while others have a protective effect (e.g., pear and apple). The authors suggested that phytochemicals such as flavonoids and chlorogenic acid present in fruits play different roles concerning DM development (Park, 2021, Seino *et al.*, 2021). Flavonoids are associated with β-cell proliferation and insulin secretion. Furthermore, the consumption of lower glycemic index fruits is of

[DOI: 10.18502/jnfs.v10i3.19240]

interest in the control of DM. Importantly, the concentration of fructose and fiber in fruits is a deterministic factor in this regard. After ingestion, fibers are consumed by the intestinal microflora, leading to the production of short-chain fatty acids and the satiety hormone GLP-1. Moreover, both fructose and sucrose stimulate the secretion of GLP-1 and FGF-21 satiety hormones (Seino *et al.*, 2021). As mentioned above, the effect of fructose (the main sugar in fruits) is dose-dependent. Chronic high intake of fructose may lead to insulin resistance, hyperglycemia, and fatty liver by depleting ATP stores and causing uric acid accumulation in the body, which increases the risk of oxidative stress. However, moderate fruit intake results in lower food consumption and a low glycemic index, which supports diabetes prevention and control (Ang and Yu, 2018, Mai and Yan, 2019). In addition, the consumption of sweetened foods appears to be high among diabetic patients, with the intake of simple sugars (**Table 3**) exceeding the maximum recommended range by health agencies (Cozma and Sievenpiper, 2014).

The average of two PAR_{T2DM} predictions based on the Q_3 and the cut-off point reported by Montonen *et al*. was 17.84% (Montonen *et al.*, 2007). This predicted average differed slightly from the proportion of diabetic patients in the total population (24.01%). However, 17.46% of the total population were prediabetic individuals (fasting blood sugar 100-125 mg/dl), who may develop DM if they do not modify their dietary patterns toward lower intake of simple sugars and carbohydrates and increase their intake of dietary fibers. Accordingly, Tabak *et al*. reported that up to 70% of prediabetic individuals might eventually develop DM (Tabák *et al.*, 2012). Nonetheless, a comparison of predictive data and observed results confirmed the association of an imbalanced diet with the incidence of type 2 DM in the population. The findings of this study are a breakthrough for the development of educational programs for both virtual and in-person education.

This study benefits from its large, population-based design within the PGCS, which enhances generalizability and leverages standardized protocols to ensure methodological rigor. The use of a validated, culturally adapted FFQ and the exclusion of implausible energy intakes strengthened the reliability of dietary assessments, while the integration of USDA and Iranian food composition databases improved nutrient estimation accuracy. Furthermore, calculating population attributable risk provided actionable insights into the preventable diabetes burden linked to simple sugars. However, the cross-sectional design precludes causal inference, and reliance on self-reported dietary data introduces potential recall bias, particularly as processed/ready-to-eat food sugars were excluded, possibly underestimating total intake. The use of external relative risk values for PAR calculations, though methodologically sound, may not fully reflect regional biological or behavioral contexts. Future longitudinal studies with repeated dietary measures and biomarkers (e.g., HbA1c) are warranted to establish causality, and expanding the Iranian Food Composition Table could refine nutrient assessments. Replication in diverse geographic and ethnic populations would improve generalizability, and inclusion of processed food sugar data would provide a more comprehensive risk profile.

Conclusion

This study revealed that an imbalanced diet was significantly associated with the development of DM in individuals. The calculation of PAR_{T2DM}, as a predictive tool, confirmed that a high intake of simple sugars (especially fructose and glucose) affected DM incidence. It is expected that fruits play a major role, as they are considered the main source of dietary fiber and fructose (one of the dominant simple sugars in the diet) simultaneously. Fruits have a preventive role in DM development up to the recommended level (200 g/day), while they could be deleterious if consumed at higher levels. The type of fruit, considering its glycemic index and inclusion of phytochemicals, is a determining factor. Moreover, it is established that dietary patterns are affected by socio-economic status. In this study, a high proportion of the patients were those with low to moderate socio-economic status, low daily fiber, and high carbohydrate intake. It is assumed that

[DOI: 10.18502/jnfs.v10i3.19240]

changing food intake habits is difficult for individuals with low socio-economic status because they have limited options in selecting food items for their food basket. However, promoting their knowledge about the outcomes of an imbalanced and unhealthy diet may help them follow a cost-effective healthy dietary pattern. For example, using inexpensive and valuable proteinaceous meals such as herbal proteins instead of high carbohydrate-based foods to overcome hunger would be greatly important. On the other hand, changing preferences towards low-sugar foods and/or using alternative sweeteners with a low glycemic index will significantly affect the control of diabetes in the general population and diabetic patients.

Acknowledgments

This article is derived from a research project approved at Guilan University of Medical Sciences, Rasht, Iran. We would like to thank the staff of Guilan University of Medical Sciences for their efforts in data collection.

Authors' contributions

Mansour-Ghanaei F, Moslemi M, Joukar F, and Mahdavi-Roshan M participated in the research design. Moslemi M, Joukar F, and Mahdavi-Roshan participated in writing the first draft. Mansour-Ghanaei F, Moslem M, Joukar F, and Mahdavi-Roshan M participated in the performance of the research and analytic tools. Moslem M, and Joukar F participated in data analysis. All authors reviewed and confirmed the final manuscript.

Conflict of interest

The authors declared no conflict of interest.

Funding

No funding.

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