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A Nonlinear Association of Body Mass Index and Fasting Blood Glucose: A Dose-Response Analysis From Fasa Adults Cohort Study (FACS)

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Keywords: body mass index | diabetes | dose-response analysis | obesity

ABSTRACT

Background and Aims: Obesity is associated with diabetes; however, the dose–response association between body mass index (BMI) and fasting blood glucose (FBG) remains unclear. This study aims to evaluate the dose–response relationship between BMI and the risk of prediabetes and diabetes among adults.

Methods: A total of 10,135 participants were enrolled in this study from the baseline profiles of the Fasa Adults Cohort Study (FACS) conducted between October 2014 and September 2016. Multivariable logistic regression model and restricted cubic spline (RCS) were applied to evaluate the dose–response relationship between BMI and the risk of prediabetes and diabetes. Statistical analyses were performed using the software R (4.3.1), taking the significance level at 0.05.

Results: Findings indicated that after adjusting the confounding variables, the risk of diabetes was increased by increasing BMI (overweight: OR = 1.67, 95% CI = 1.36–2.06; obese: OR = 1.76, 95% CI = 1.37–2.26). The results of dose–response analysis displayed a nonlinear J-shaped association between BMI and the risk of diabetes ($p_{\text{trend}} < 0.001$, nonlinear $p < 0.001$) and prediabetes ($p_{\text{trend}} < 0.001$, nonlinear $p < 0.049$).

Conclusion: Based on our research, a higher BMI is a dose-dependent, independent risk factor for diabetes. As a result, prevention initiatives should think about emphasizing ongoing BMI modifications.

1 | Introduction

Over recent years, the increasing prevalence of diabetes and pre-diabetes become a social health issue that affects people worldwide. The most prevalent kind of diabetes, known as diabetes mellitus, is characterized by persistently high blood sugar levels due to impaired insulin production, elevated insulin resistance, or both. Diabetes is defined as fasting blood glucose (FBG) of 126 (mg/dl) or higher, and Pre-diabetes refers to a condition in which a person has impaired fasting glucose (IFG) (between 100 and 125) [1, 2]. People with IFG are at higher risk of progressing to type 2 DM and its complications, compared to normal population [3]. Based on the WHO reports in 2016, the declared rate of diabetes in the Iranian population

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was 10.3% which has been a notable progressive rate since 1980 [4]. Also, at least 10% of the population of Iran above the age of eighteen have high blood sugar, which is higher than the global average [5].

Several studies during years demonstrated that the incidence of diabetes has a higher rate in people with body mass index (BMI) (kg/m^2) ≥ 25 [4, 6, 7]. A previous research based on the NHANES (from 1988 to 1994 and 1999 to 2014 as a second phase of the study), confirms that obesity accounts for 72% of the increased prevalence of diabetes in the US population [8]. Also, Esteghamati and colleagues concerning the monitoring of non-communicable disease risk factors in 2011 showed that overweight (BMI ≥ 25) is remarkably accompanied by DM after controlling confounding variables (OR: 2.1). Also, the obesity (BMI ≥ 30) was crucialy associated with DM (OR: 2.2) [9].

While a number of studies have demonstrated the role of obesity as a potent predictor of the prevalence of diabetes [10]. and their mutual synergistic effect each other causes wide spectrum microvascular and macro-vascular complications such as diabetic nephropathy, proliferative retinopathy, premature CAD [2, 11–13], and cancer [14]. Recently some studies have investigated the association between FBG and BMI [15, 16], however, the dose–response association between FBG and BMI has not been clarified. Discovering the exact relationship may lead to a decrease in the incidence rate of prediabetes and diabetes in normal populations and pre-diabetics by developing public health education and changing lifestyle and physical activities. The objective of the current investigation is to assess the dose–response relationship between BMI and FBG, with the aim of identifying potential interventions to reduce the incidence rates of prediabetes and diabetes through public health education and lifestyle modifications.

2 | Methods & Materials

The baseline database of the Fasa Adults Cohort Study was used in this study. The Fasa Adults Cohort Study, which ran from October 2014 to September 2016, is a population-based longitudinal study with a 15-year follow-up phase. The rural health care workers called “behvarz” gathered information during a health house meeting by the census. The sample includes community residents aged 35–70 years from a rural district “sheshdeh” and its 24 surrounding satellite villages. Previous publications have included more details about the FACS. All information and questionnaires were gathered by the cohort center with individual consent, and this survey was authorized by the deputy for research and technology of the Iranian Ministry of Health (MOH) [17].

2.1 | Inclusion and Exclusion Criteria

We included the study participants based on the following criteria: (1) participants must be aged between 35 and 70 years; (2) residence should be reside in the study area (the Sheshdeh region and its 24 surrounding satellite villages); (3) participants must provide written informed consent to participate in the study; absence of medical conditions that would impede participation in the study. However, pregnant women, individuals with data that lies outside the other values in the set were excluded.

2.2 | Clinical Evaluation, Lab Measurement, and Medical History

In addition to valid and standard questionnaires, digital data acquisition sheets were used to gather demographic characteristics such as age, gender, marital status, education, and chronic illness. Age, and lifestyle factors including smoking and alcohol consumption divided into nonsmoker and smoker, non-drinker, and drinker, respectively. Height and weight were measured by using bioelectrical impedance analysis. Weight in kilograms divided by height in meters squared yielded the BMI [18]. Following standard procedures, the fasting blood glucose was measured and divided into three subgroups based on threshold values: normal, pre-diabetes, and diabetes [2].

2.3 | Questionnaire and Definitions

Diabetes mellitus is defined as the presence of at least one of the following conditions: Have you been diagnosed as diabetic by a doctor? Are you taking medication for diabetes? Have you ever had a fasting blood glucose ≥ 126? According to the international BMI cutoff points (16), overweight and obesity were classified as BMI ≥ 25 and BMI ≥ 30, respectively [18].

2.4 | Statistical Analysis

The categorical variables were described using percentage and frequency. To evaluate the relationship between BMI and the risk of prediabetes and diabetes, logistic regression analysis was employed. In multivariable logistic regression, to adjust the effect of age, gender, marital status and education, Model 1 was used and Model 2 was fitted to further adjust for chronic disease, drinking, smoking, LDL, HDL, Triglycerides (TG), physical activity (MET) and hypertension. Moreover, to evaluate the relationship between BMI and the likelihood of developing prediabetes and diabetes, the restricted cubic spline (RCS) method was utilized. To determine the difference between males and females in terms of dose–response relationship, gender stratification analysis was used the variation in the dose–response relationship between age groups was taken into account using the age stratification analysis. All statistical analyses were performed using R (4.3.1) software by considering the significance level as 0.05.

2.5 | Ethical Approval

Our study protocol has been approved by the Ethics Committee and Research Council of the Fasa University of Medical Sciences (approval code: IR. FUMS. REC.1401.175), and each participant provided written informed consent.

TABLE 1 | The descriptive statistics of the research subjects.

Variables	Category	
Age (years) *N* (%)		
	< 40	2550 (25.2)
	40–60	6213 (61.3)
	> 60	1371 (13.5)
Gender *N* (%)		
	Male	4577 (45.2)
	Female	5557 (54.8)
Marital status *N* (%)		
	Single	374 (3.7)
	Married	9014 (88.9)
	Widowed	644 (6.4)
	Divorced	102 (1)
Education *N* (%)		
	Elementary school	3292 (32.5)
	Middle school	1358 (13.4)
	High school diploma	604 (6)
	Associate degree	61 (0.6)
	Bachelor's degree	149 (1.5)
	Master's degree	23 (0.2)
	PhD	1 (0.0)
	Illiterate	4642 (45.8)
Chronic disease *N* (%)		
	Yes	4564 (45)
	No	5570 (55)
Alcohol consumption *N* (%)		
	Yes	485 (4.8)
	No	9645 (95.2)
Smoke *N* (%)		
	Yes	2758 (27.2)
	No	7372 (72.7)
BMI *N* (%)		
	Underweight	584 (5.8)
	Normal	4133 (40.8)
	Overweight	3624 (35.8)
	Obese	1776 (17.5)
LDL *N* (%)		
	Normal	6809 (67.2)
	High	3287 (32.4)
Hypertension *N* (%)		
	Yes	2029 (20)
	No	8100 (79.9)
Glucose *N* (%)		
	Normal	8612 (85)

(Continues)

TABLE 1 | (Continued)

Variables	Category	
	Pre-diabetic	926 (9.1)
	Diabetic	544 (5.4)
HDL (Mean ± SD)		51.0 ± 15.9
TG (Mean ± SD)		131.8 ± 82.4
Cholesterol (Mean ± SD)		185.1 ± 39.1
LDL (Mean ± SD)		107.9 ± 32.9
Physical activity (METs) (Mean ± SD)		41.4 ± 11.3

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; METs, metabolic equivalent of task; TG, triglycerides.

3 | Results

A total of 10135 participants were enrolled in this study, more than half of them were 40–60 years (61.3%); most of them were women (54.8%); the majority were married (88.9%), and were illiterate (45.8%). About 45% of the sample had one or more diseases. Also, the majority of the study participants did not smoke (72.7%), nor drink alcohol (95.2%). In terms of BMI classification, 5.8% of people were underweight, 35.8% were overweight, 17.5% were obese and the rest were normal. Of our participants, 5.4% suffered from diabetes, 20% from hypertension, and 32.4% suffered from higher low-density lipoprotein. The mean cholesterol of the study participants was 185.1 ± 39.17, triglycerides (TG) was 131.8 ± 82.46, LDL was 107.9 ± 32.9, and HDL was 51.0 ± 15.9. Moreover, the mean of physical activity in terms of metabolic equivalent of task (METs) was 41.4 ± 11.3 (Table 1).

The results of multiple logistic regression models for assessing the association between diabetes and prediabetes with various BMI levels was presented in Table 2. Model 1(M1) in Table 2 which is adjusted for age, gender, marital status and education illustrated that compared to the group with normal BMI, the risk of prediabetes is increased with increasing body mass index. The increased risk of prediabetes was higher in the obese group (OR = 2.38, 95% CI = 1.96–2.87) than in the overweight individuals (OR = 1.63, 95% CI = 1.38–1.93). The same results were found for increasing the risk of diabetes, based on the increase in BMI categories in model 1. Compared to the normal weight group, the increased risk of diabetes was higher in the obese group (OR = 1.76, 95% CI = 1.37–2.25) than in the overweight individuals (OR = 1.67, 95% CI = 1.36–2.06), while the inverse association was seen in underweight groups (OR = 0.19, 95% CI = 0.07–0.51) (Table 2, model 1).

By adjusting more variables, for example, chronic disease, drinking, smoking, LDL, HDL, TG, physical activity, and hypertension in model 2 (M2), the risk of having prediabetes in overweight and obese groups of participants was still higher than in normal group (OR = 2.07, 95% CI = 1.69–2.52; OR = 1.47, 95% CI = 1.24–1.75, respectively) (Table 2). Moreover, the risk of having diabetes in obese and overweight groups of participants was still higher than normal group (OR = 1.50, 95% CI = 1.16–1.93; OR = 1.46, 95% CI = 1.18–1.81, respectively) and the inverse association was identified in underweight groups (OR = 0.21, 95% CI = 0.80–0.59) (Table 2, Model 2).

Tables 3 and 4 investigates the association between prediabetes and diabetes with various BMI levels, considering gender and age groups.

3.1 | Gender Subgroups

The findings suggest a strong association between overweight and obesity and the risk of prediabetes and diabetes, regardless of gender. In both models (M1 and M2), overweight (OR = 1.71, 95% CI: 1.32–2.20 and OR = 1.46, 95% CI: 1.13–1.90, respectively) and obese (OR = 2.77, 95% CI: 1.99–3.87 and OR = 2.34, 95% CI: 1.66–3.30, respectively) males had significantly increased odds of prediabetes compared to normal-weight males. In female subgroups in both models (M1 and M2), overweight (OR = 1.59, 95% CI: 1.27–1.98 and OR = 1.51, 95% CI: 1.20–1.90, respectively) and obese (OR = 2.23, 95% CI: 1.77–2.83 and OR = 2.06, 95% CI: 1.62–2.62, respectively) females also had significantly higher odds of prediabetes compared to normal-weight females (Table 3).

The same results in both models were found for the risk of diabetes for both genders. In both models (M1 and M2), overweight (OR = 1.71, 95% CI: 1.32–2.20 and OR = 1.46, 95% CI: 1.13–1.90, respectively) and obese (OR = 2.77, 95% CI: 1.99–3.87 and OR = 2.34, 95% CI: 1.66–3.30, respectively) males had significantly increased odds of diabetes compared to normal-weight males (Table 4). In female subgroups in both models (M1 and M2), overweight (OR = 1.59, 95% CI:1.27–1.98 and OR = 1.51, 95% CI: 1.20–1.90, respectively) and obese (OR = 2.23, 95% CI: 1.77–2.83 and OR = 2.06, 95% CI:1.62–2.62, respectively) females also had significantly higher odds of diabetes compared to normal-weight females (Table 4).

3.2 | Age Subgroups

In the age < 40 subgroup, model M1 indicated that overweight and obese individuals showed a trend towards increased odds of prediabetes and diabetes compared to normal-weight individuals. However, in the adjusted model (model M2) after conducting further adjustments of potentially confounding variables, no significant association was found for overweight or obese individuals with increased risk of prediabetes and diabetes (Tables 3 and 4).

TABLE 2 | Multiple logistic regression models for assessing the association between diabetes and prediabetes with various BMI levels.

		Overweight OR (95% CI)	Underweight OR (95% CI)	Normal OR (95% CI)	Overweight OR (95% CI)	Obese OR (95% CI)	*p* for Trend
Prediabetes	M1		0.79 (0.53, 1.17)	Reference	1.63 (1.38, 1.93)***	2.38 (1.96, 2.87)***	< 0.001
	M2		0.93 (0.62, 1.39)	Reference	1.47 (1.24, 1.75)***	2.07 (1.69, 2.52)***	< 0.001
Diabetes	M1		0.19 (0.07, 0.51)**	Reference	1.67 (1.36, 2.06)***	1.76 (1.37, 2.25)***	< 0.001
	M2		0.21 (0.80, 0.59)**	Reference	1.46 (1.18, 1.81)***	1.5 (1.16, 1.93)**	< 0.001

Note: Model M1: adjusted for age, gender, marital status and education; Model M2: further adjusted for chronic disease, drink, smoke, LDL, HDL, TG, METs and hypertension.
*$p < 0.01$; **$p < 0.001$; ***$p < 0.0001$ a $p < 0.05$.

The association between overweight and obesity and the risk of prediabetes and diabetes appears to be more pronounced in older age groups. In the 40–60 and > 60 age subgroups, in both models (M1 and M2), overweight and obese individuals had significantly increased odds of prediabetes and diabetes compared to normal-weight individuals (Tables 3 and 4). In the adjusted model (M2), overweight (OR = 1.53, 95% CI: 1.24–1.90) and obese (OR = 2.16, 95% CI:1.70–2.74) individuals had significantly increased odds of prediabetes compared to normal-weight individuals (Table 3). However, after adjusting for potential confounding variables, only the obese (OR = 2.16, 95% CI:1.70–2.74) individuals have a significant association with increased odds of diabetes (Table 4). In the > 60 age subgroups, after adjusting for potentially confounding variables (model M2), overweight (OR = 1.58, 95% CI: 1.13–2.22 and, OR = 1.52, 95% CI: 1.03–2.59, respectively) and obese (OR = 1.91, 95% CI: 1.24–2.94 and, OR = 1.14, 95% CI:1.09–1.97, respectively) individuals had significantly increased the odds of both prediabetes and diabetes compared to normal-weight individuals, respectively (Tables 3 and 4).

A dose–response relationship was assessed between BMI and the risk of prediabetes. As shown in Figure 1A, with adjusting for gender, education, age, LDL, hypertension, chronic diseases, and marital status; the odds ratio of prediabetes and BMI demonstrated a nonlinear relationship ($p_{trend} < 0.001$, nonlinear $p = 0.049$). The trend of the odds ratio is progressively increased with an increase of 1 kg/m2 in BMI. The ORs for prediabetes were about 0.82 for 16 kg/m2, the ORs were about 1.2 for BMI at 20 kg/m2; and 2 for BMI at 27.5 kg/m2 which illustrated there is an increasing risk of prediabetes with BMI increases. As shown in Figure 1A, when BMI was between 18 and 25 kg/m2, the risk of prediabetes increased with a relatively low slope. Between 25 and 30 kg/m2, the slope became steeper and after 30 kg/m2, the risk quickly increased, as shown in Figure 1A.

According to the findings, there was an increasing trend in the risk of diabetes with rising BMI and a nonlinear relationship ($p_{trend} < 0.001$, nonlinear $p < 0.001$). As the BMI increased, the risk of diabetes increased gradually when the BMI was less than 25 kg/m2, but it increased quickly when the BMI exceeded 25 kg/m2, as Figure 1D illustrates.

The dose–response relationship was explained in detail using a subgroup analysis. The logistic regression model grouped by gender illustrated that in both males and females, the risk of prediabetes in overweight and obese individuals was increased, while no statistically significant correlation was found between underweight and BMI in males and females (Table 4). The results of the restricted cubic spline model by gender indicated a nonlinear relationship between BMI and the increase in the risk of prediabetes and diabetes so that up to BMI values less than 25, this slope increases gradually. In BMI values of 25 and above, the risk of developing prediabetes and diabetes increases suddenly with similar trends in both sexes (Figure 1B–E). However, in general, women have higher risk values than men for developing diabetes and prediabetes with the same dose–response trend of increasing risk with increasing BMI levels (Figure 1B–E).

The results of the restricted cubic spline model by age groups indicated a same nonlinear relationship between BMI and the

TABLE 3 | Multiple logistic regression models for assessing the association between prediabetes with various BMI levels separately by gender and age groups.

Variables		Model	Underweight OR (95% CI)	Normal OR (95%CI)	Overweight OR (95% CI)	Obese OR (95% CI)
Gender	Male	M1	0.78 (0.47, 1.27)	Reference	1.71 (1.32, 2.20)***	2.77 (1.99, 3.87)***
		M2	0.88 (0.54, 1.50)	Reference	1.46 (1.13, 1.90)***	2.34 (1.66, 3.30)**
	Female	M1	0.86 (0.43, 1.66)	Reference	1.59 (1.27, 1.98)***	2.23 (1.77, 2.83)***
		M2	0.97 (0.49, 1.90)	Reference	1.51 (1.20, 1.90)***	2.06 (1.62, 2.62)**
Age	< 40	M1	0.77 (0.27, 2.20)	Reference	1.05 (0.65, 1.71)	1.71 (0.99, 2.95)
		M2	0.88 (0.30, 2.55)	Reference	0.92 (0.56, 1.52)	1.47 (0.83, 2.59)
	40–60	M1	0.79 (0.48, 1.29)	Reference	1.71 (1.38, 2.10)***	2.45 (1.94, 3.09)*
		M2	0.90 (0.55, 1.48)	Reference	1.53 (1.24, 1.90)***	2.16 (1.70, 2.74)***
	> 60	M1	0.69 (0.29, 1.66)	Reference	1.73 (1.25, 2.40)**	2.14 (1.4, 3.27)***
		M2	0.81 (0.33, 1.96)	Reference	1.58 (1.13, 2.22)*	1.91 (1.24, 2.94)*

Note: M1 adjusted for age, gender, marital status and education; M2 further adjusted for chronic disease, drink, smoke, LDL, HDL, TG, physical activity (MET) and hypertension.
*$p < 0.01$; **$p < 0.001$; ***$p < 0.0001$, a $p < 0.05$.

TABLE 4 | Multiple logistic regression models for assessing the association between diabetes with various BMI levels separately by gender and age groups.

Variables		Model	Underweight OR (95% CI)	Underweight OR (95% CI)	Overweight OR (95% CI)	Overweight OR (95% CI)
Gender	Male	M1	0.17 (0.04, 0.61)*	Reference	2.24 (1.60, 3.21)***	3.08 (1.91, 4.85)***
		M2	0.18 (0.04, 0.76)*	Reference	1.89 (1.32, 2.72)***	2.39 (1.49, 3.83)**
	Female	M1	0.20 (0.05, 0.82)*	Reference	1.31 (1.02, 1.68)***	1.42 (1.06, 1.89)***
		M2	0.24 (0.6, 1.01)	Reference	1.15 (0.89, 1.48)	0.99 (0.75, 1.34)
Age	< 40	M1	0.001 (0.0, 4.8)	Reference	2.54 (1.09, 5.90)*	1.24 (0.39, 3.19)
		M2	0.001 (0.00, 5.52)	Reference	1.91 (0.8, 4.56)*	0.74 (0.22, 2.46)
	40–60	M1	0.25 (0.09, 0.69)**	Reference	1.48 (1.15, 1.92)**	1.74 (1.3, 2.34)***
		M2	0.31 (0.112, 0.84)*	Reference	1.23 (0.94, 1.60)	1.41 (1.04, 1.90)*
	> 60	M1	—	Reference	1.80 (1.30, 2.64)**	1.36 (1.17, 2.31)**
		M2	—	Reference	1.52 (1.03, 2.59)**	1.14 (1.09, 1.97)**

Note: M1 adjusted for age/gender, marital status and education; M2 further adjusted for chronic disease, drink, smoke, LDL, HDL, TG, physical activity (MET) and hypertension.
*$p < 0.01$; **$p < 0.001$; ***$p < 0.0001$, a $p < 0.05$.

increase in the risk of prediabetes and diabetes so that up to BMI values less than 25, this slope increases gradually for all age groups. In BMI values of 25 and above, the risk of developing prediabetes and diabetes increases suddenly with similar trends in both age groups of 60–40 years old and over 60 years old (Figure 1C–F). However, in general, women have higher risk values than men for developing diabetes and prediabetes with the same dose–response trend of increasing risk with increasing BMI levels (Figure 1B–E). However, this increasing dose–response trend was not significant for the age group of less than 40 years for diabetes and pre-diabetes (Figure 1C–F).

4 | Discussion

Our study aimed to evaluate the dose–response relationship between body mass index (BMI) and fasting blood glucose in rural adults aged 35 to 70 years from the Fasa adult cohort study (FACS). We found that the risk of pre-diabetes and diabetes increases significantly among overweight and obese individuals as BMI rises. Specifically, the odds ratios for both pre-diabetes and diabetes exhibited a nonlinear relationship, escalating sharply for BMI values exceeding 25 and 30, respectively. Notably, individuals aged over 40 from both the overweight and obese categories showed a heightened risk of pre-diabetes, while there was no significant difference in pre-diabetes risk between normal and underweight groups.

These findings may suggest a critical threshold in BMI, beyond which the risk of developing diabetes increases markedly. Our results contribute to the growing evidence that being overweight or obese poses a substantial risk for diabetes, aligning with previous research indicating that obesity is a significant risk factor for type 2 diabetes mellitus (T2DM) compared to individuals in a

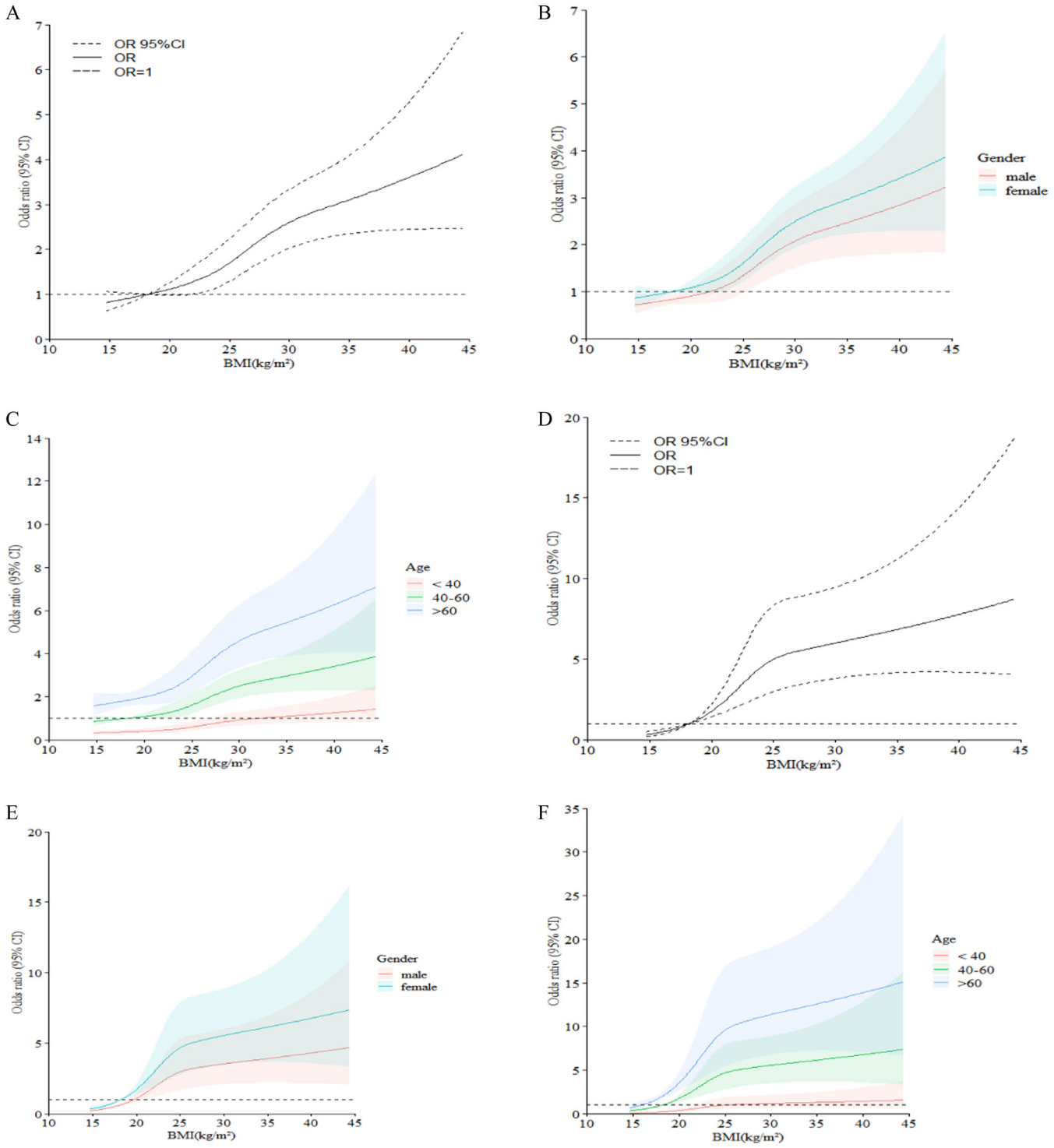

FIGURE 1 | A. Association between BMI and prediabetes risk based on restricted cubic spline model in total population. B. Association between BMI and prediabetes risk based on restricted cubic spline model in total population. C. Association between BMI and prediabetes risk based on restricted cubic spline by gender. D. Association between BMI and diabetes risk based on restricted cubic spline by gender. E. Association between BMI and prediabetes risk based on restricted cubic spline by age. F. Association between BMI and diabetes risk based on restricted cubic spline by gender.

healthy weight range. A large body of studies showed that people with obesity have a higher risk of developing type 2 DM and pre-diabetes, compared with individuals in the healthy weight range [19–21]. Based on the study conducted in 2014, weight loss has been shown to delay or decrease the risk of developing T2DM in prediabetes, while in established T2DM, weight loss has been shown to improve blood sugar control [22]. Also, T. Nagaya et al. showed that, the increasing in BMI, even in nonobese levels, results in an increase in the risk of type 2 DM [23].

Several mechanisms have been proposed to be involved in the pathogenesis of diabetes. Insulin insensitivity in peripheral

tissue is the leading phenomenon, which is strongly related to obesity and physical inactivity [24]. Several hormones, cytokines, and nonesterified fatty acids originating from adipocytes modulate insulin action. Increasing the number of triglycerides stored in the adipose depots, especially visceral fat, leading to resistance to the lipolysis-inhibitory effects of insulin. This process increases the release of nonesterified fatty acids and glycerol, which increases insulin resistance in skeletal muscle and liver. Another mechanism is the gradual reduction of the beta cells of the islets of Langerhans, which disrupts insulin production. Studies show that insulin secretion is significantly reduced in people with diabetes compared to nondiabetic people, but even before the development of persistent hyperglycemia, which itself affects cellular function, secretory defects in people with impaired glucose tolerance and impaired fasting glucose are observed. Also, genetic predisposition plays an important role in the occurrence of diabetes in different populations. So far, several vigorous genes have been discovered, the information about which is described in detail in another article [25, 26].

To our knowledge, this is the first study to describe a nonlinear dose–response association between BMI and FBG using a restricted cubic spline to relate quantitative data to the occurrence of outcomes. Nevertheless, there are a few limitations to this research. First, this study is a cross-sectional study, so the results should be checked with caution. Second, although we tried to adjust the results based on the most important variables, it is recommended to repeat this study prospectively based on other confounding factors such as socioeconomic status, and physical activity. Third, the sample size was large and data were obtained from subgroups stratified by sex (male/female) and age (under 40 years, 40–60 years, over 60 years), subgroup analyses might be statically inefficient due to loss of statistical power. This study has been conducted in rural areas, and the results were approximately robust, but it may not be representative of the whole country, and it is necessary to conduct a similar cohort study in the urban areas. In summary, our findings indicated that a higher BMI is a dose-dependent, independent risk factor for diabetes. As a result, prevention initiatives should think about emphasizing ongoing BMI modifications.

Author Contributions

Fatemeh Par: conceptualization, data curation. **Fatemeh Sarvi:** conceptualization, formal analysis. **Mahmoud Khodadost:** formal analysis, writing – original draft, conceptualization. **Babak Pezeshki:** data curation. **Hassan Doosti:** writing – original draft. **Reza Tabrizi:** conceptualization, data curation, formal analysis, writing – original draft.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data of Fasa Adults Cohort Study (FACS) was used in this study are not publicly available due to confidentiality of information; however, the data is available from the corresponding author on a reasonable request basis.

Transparency Statement

The Reza Tabrizi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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