

# Longitudinal Trend of Fasting Blood Glucose and Related Factors in Patients with Type 2 Diabetes

## Abstract

**Background:** Control of diabetes plays an important role in improving complications and disabilities and quality of life. This study aimed to evaluate the 3-year changes in fasting blood glucose (FBG) values and its related factors in patients with type 2 diabetes. **Methods:** In this retrospective cohort study, 500 patients with type 2 diabetes covered by the National Diabetic Prevention and Care Plan during 2013–2016 were selected based on random cluster systematic sampling. A linear mixed model was used to study changes in FBG levels and their related factors. The data were analyzed using the R3.2.0 software. **Results:** The patients' mean age was 47.7 years. Among these patients, 58.6% were female, 19.8% had a history of smoking. High FBG was associated with high disease duration, high body mass index (BMI), low age, normal BMI at baseline, insulin therapy, smoking, and family history of diabetes. Trend of FBG in follow-up was decreasing. **Conclusions:** Given that patients who received insulin therapy had higher mean FBG, it is recommended to examine their insulin dose and modifications should be made in terms of the patients' needs during their continuous follow-up. Weight loss during follow-up and cessation of smoking indicate a favorable prognosis of disease. More attention should be paid to younger patients in care. Patients are encouraged to start treatment and care at the same time diagnose.

**Keywords:** Blood glucose, body mass index, diabetes mellitus type 2, insulin, smoking

## Introduction

Diabetes mellitus type 2 is a chronic disease that causes complications and increases mortality risks. According to the American Diabetes Association (ADA) in 2015, the prevalence of diabetes was estimated to be about 4.9% in the United States.<sup>[1]</sup> In Iran, 14–25% of those over the age of 30 years are diabetic or have glucose intolerance. Diabetes results in a 5–10-year decrease in life expectancy, and 2.4 times more patients are hospitalized because of diabetes than other chronic diseases.<sup>[2]</sup> Diabetes substantially impair the quality of life (QOL).<sup>[3,4]</sup> The results of studies in Iran have indicated that the complications are neuropathy (65.8% and 77.3%), ocular disease, (26.8% and 27.7%), and others.<sup>[5-9]</sup>

Evidence suggests that performing variety of interventions such as self-management, healthy diet, and exercise can be effective to prevent acute complications.<sup>[10]</sup> The monitoring of patient during illness is necessary to achieve appropriate level of

blood glucose because its control reduces mortality and the complications. The goal of treatment is not only to reduce complications but also to improve overall QOL.<sup>[3,4]</sup> The ADA recommends that blood glucose be assessed twice a year and patients should visit doctors or healthcare centers at least four times per year instead of two times.<sup>[11]</sup>

Both fasting blood glucose (FBG) and HbA1c have been considered indicators of diabetes management.<sup>[2,12-18]</sup> In studies, the follow-up period ranges between 3 and 7 years and the trend of changes was descending<sup>[15]</sup> or remained unchanged.<sup>[17]</sup> The effective factors of changes were examined by various statistical models, such as generalized equations estimation (GEE), linear mixed (LM) model, and logistic regression. Some of the factors were age,<sup>[16,17,19]</sup> smoking,<sup>[17,20,21]</sup> family history of diabetes,<sup>[2,22,23]</sup> diabetes duration,<sup>[2,17,21,24]</sup> weight,<sup>[19,21]</sup> frequency of visits to doctors,<sup>[13,14]</sup> and insulin therapy.<sup>[18,19,21,25]</sup>

The number of longitudinal studies to define the factors influencing diabetes

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**DOI:**  
10.4103/ijpvm.IJPVM\_195\_18

## Quick Response Code:



**How to cite this article:** Khatirnamani Z, Bakhshi E, Naghipour A, Teymouri R, Hosseinzadeh S. Longitudinal trend of fasting blood glucose and related factors in patients with type 2 diabetes. *Int J Prev Med* 2020;11:177.

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and particularly based on FBG is very limited in Iran. Considering the importance of issue and the existence of a few studies in the National Diabetes Prevention and Care plan (NDPCP) in Iran, this study aimed to examine the trend of FBG levels in patients with type 2 diabetes and define their influencing factors.

## Methods

The present study was based on a retrospective cohort design. The population included all patients with type 2 diabetes and sample included patients who had referred to health centers of Golestan University of Medical Sciences and covered by the NDPCP during 2013–2016. Five health centers in Golestan Province were randomly selected. One hundred patients' records were then chosen using a systematic random sampling from each center. In total, 500 patients' records were screened. The inclusion criteria were the diagnosis of type 2 diabetes, age older than 18 years.

The NDPCP has been performing across the healthcare system since 1999 in Iran and since 2004 in Golestan province. Patients with type 2 diabetes were under the supervision of a physician residing in health centers. Each patient was treated independently of others. The intervention included general and essential information about diabetes, advice on nutrition and exercise, self-care, diagnosis of complications, foot care, pharmaceutical treatments, and, if necessary, insulin, and encouraging patients to use self-monitoring. Once every 3 months, the tests were performed and their results along with other clinical examinations were recorded in the patient's form.<sup>[26]</sup>

## Data collection

The gathered data included demographic and contextual characteristics. Based on data gathering and longitudinal model in the study, variables are fixed or time varying. Fixed variable such as gender, patient's age at the time of entering the plan (baseline age), family history of diabetes (yes/no), history of hypertension status at the time of entering the plan (yes/no), cholesterol status at the time of entering the plan (yes/no), smoking at the time of entering the plan (yes/no), duration of disease at the time of entering the plan (baseline duration), and body mass index (BMI) at the time of entering the plan (baseline BMI). To introduce baseline BMI variable into the model, it was first divided into three groups: normal weight (normal,  $18.5 < \text{BMI} < 24.9$ ), overweight (overweight,  $25 < \text{BMI} < 29.9$ ), and obese (obese,  $\text{BMI} > 29.9$ ). Time-varying variables were insulin therapy (yes/no), BMI, FBG, and time of measuring of blood factors (time).

Referral to centers occurred after being allowed by the university and health centers.

## Statistical analysis

Quantitative and categorical variables were described by mean  $\pm$  SD and  $n$  (%) retrospectively. LM model was used for trend of FBG and to examine effect of independent variables on the levels of the patients' FBG. Categorical variables were entered in the model as dummy variables. FBG per each time of measuring (1–14 times) followed normal distribution based on central limit theorem (at least 214 cases). FBG correlation structure checked by Pearson correlation coefficient between each measures, the closer measures had larger correlation ( $r = 0.83 - 0.5$ ) and farther measures had the smaller correlation ( $r = 0.49 - 0.2$ ), also other correlation structures were checked for data in the model, autoregressive correlation structure (AR (1)) has the smallest AIC. Plot of residuals was used for model checking (normality, equal variances, and outliers).

This model were fitted in the R3.2.0 software using the "nlme" package (lme function) and AR (1). The significance level was considered to be 0.05.

## Results

Among 500 diabetic patients in this study, 293 (58.6%) were female. During the follow-up, 95 patients (14.6%) received insulin. At the time of entering the plan, the mean age was 47.7 years (SD = 8.9, range: 25–78 years). Other demographic characteristics were showed in Table 1. In average, the number of repeated measurements in each patient was 6.4 (SD = 3.8) and the mean follow-up duration of patients was 16.20 months (SD = 11.28).

Gender, high blood pressure history, and baseline cholesterol did not significantly influence FBG over time ( $P$  value  $> 0.05$ ) and they were excluded from model. The effects of the other variables were significant. Results of the LM model were presented in Table 2.

SD of random intercept value equaled 25.71, which was significant (95% CI: 22.71–29.11). In other words, the LM model is appropriate. The findings of model demonstrated that high FBG was associated with high disease duration, high BMI, low age, normal BMI at baseline, insulin therapy, smoking, and family history of diabetes.

**Table 1: Characteristics of patients**

variables	$n$ (%)	variables	Mean $\pm$ SD
Sex (male)	207 (41.4)	age (years)	47.7 $\pm$ 8.9
Baseline	99 (19.8)	BMI (kg/m <sup>2</sup> )	29 $\pm$ 4.4
Smoking (yes)		Diabetes	2.5 $\pm$ 2.4
Diabetes family	322 (64.5)	duration (years)	
History (yes)		FBS	307.9 $\pm$ 58.7
Baseline hypertension	352 (70.4)		
(yes)			
Insulin therapy	95 (14.6)		
Baseline	301 (60.2)		
cholesterol (yes)			

Baseline is entering time of patient into the project (NDPCP)

The time variable indicates measurement times and has negative coefficient, indicating decreasing trend for FBG. On average, FBG decreased 1.37 mg/dl per month ( $P < 0.05$ ) [Figure 1a]. FBG in people who received insulin were 22.66 mg/dl higher than in those who did not [Figure 1b]. On average, for each year is added to the disease duration, FBG increase 2.91 mg/dl. Regarding the effect of smoking, FBG in smokers was 9.29 mg/dl higher than nonsmokers if all conditions were fixed [Figure 1c]. FBG among those having a family history of diabetes were about 8.73 lower [Figure 1d]. The effect of baseline BMI on the model indicated that those who were overweight or obese at the beginning of the study, compared with normal patients, had lower FBG about 26.78 and 26.24, respectively [Figure 1e]. The effects of BMI (during follow-up period) and its interaction with time were significant. The effect of increase BMI on FBG in the early of care is more than last care. Per unit of BMI, the level of FBG equaled  $[(1.98) - (0.07) \times (\text{time})]$ . FBG was decreased about 0.44 mg/dl when 1 year was added to patients' ages.

## Discussion

The present longitudinal study aimed to examine the trend of FBG in patients with type 2 diabetes and define influencing factors via the LM model. The findings of the present study demonstrated that high FBG was associated with high disease duration, high BMI, low age, normal BMI at baseline, insulin therapy, smoking, and family history of diabetes.

More importantly, trend of FBG in follow-up was decreasing. From the beginning to the end of the study, the mean FBG ranged from 307 to 164 mg/dl, representing the improved conditions for patients. The studies indicated that the recovery process was better among patients who regularly visited a doctor.<sup>[13,14,15]</sup> In some studies, the trend of HbA1c in patients was stable.<sup>[16,17]</sup> In a study, a descending trend was found for HbA1c response for the first 3 years, although it exhibited ascending trend between

3 and 5 years.<sup>[18]</sup> There are various reasons underlying why it is important to control FBG or HbA1c. Hu (2012) assessed the effect of follow-up on clinical indicators, as well as QOL. They revealed significant improvements in the overall QOL score, FBG, and HbA1c in the intervention group. Also, changes in the overall QOL score were negatively correlated with changes in FBG.<sup>[3]</sup> Patel (2014) compared QOL between controlled and uncontrolled patients, QOL was significantly more impaired in uncontrolled patients.<sup>[4]</sup> Another studies indicated that poor controls resulting in high FBG are strongly related to diabetic complications, such as retinopathy, neuropathy, and cardiovascular disease.<sup>[27-30]</sup> Continuous contact between doctors and patients results in sharing greater information to allow doctors to be acquainted with patients' conditions, symptoms, and moods, making illness management easier and better.

Based on the results of the present study, the changes in FBG were descending in both groups: those who received insulin and did not undergo insulin therapy. However, mean FBG among patients who received insulin were higher. A 3-year study demonstrated that HbA1c decrease at a faster rate after insulin injection in the first quarter, while it decreases at a slower rate later.<sup>[25]</sup> In another study, insulin was regarded as a risk factor and those who received insulin had higher HbA1c.<sup>[18]</sup> A study with 3 years follow-up period indicated that HbA1c were more likely to be higher among those who received insulin.<sup>[19]</sup> Based on the results, better care and matching doses with patients' conditions during care is necessary.

Disease duration is an effective factor in blood glucose. Those people who had longer illness duration at the time of entry into the project also had high blood glucose levels during follow-up and controlling blood glucose was difficult. The result is consistent with other studies.<sup>[17,21,24]</sup>

In this study, the inverse effect of age on FBG at the time of entry into project was significant. Younger people

**Table 2: The result of LM model to identify variable effects on FBS**

Variables (ref. level)	B	S.E	95%CI-Lower	95%CI-upper	P
Intercept	288.57	19.96	249.47	327.66	0.001
Random intercept	-	25.73	22.73	29.13	-
Time	-1.38	0.51	-2.38	-0.37	0.008
Insulin therapy (no)	23.01	3.92	15.33	30.68	0.001
Duration of diabetes	2.91	0.79	1.37	4.46	0.001
Baseline smoking (no)	9.28	4.20	1.04	17.51	0.028
Diabetic family history (no)	-8.70	3.39	-15.35	-2.04	0.011
BMI, during follow-up period	1.97	0.73	0.54	3.40	0.007
Baseline BMI					
over weight (normal BMI)	-26.64	5.99	-38.40	-14.87	0.001
obese (normal BMI)	-26.04	8.65	-43.02	-9.05	0.003
Age	-0.45	0.20	-0.84	-0.05	0.026
Interaction time*BMI	-0.08	0.02	-0.11	-0.04	0.001

Baseline is entering time of patient into the project (NDPCP)

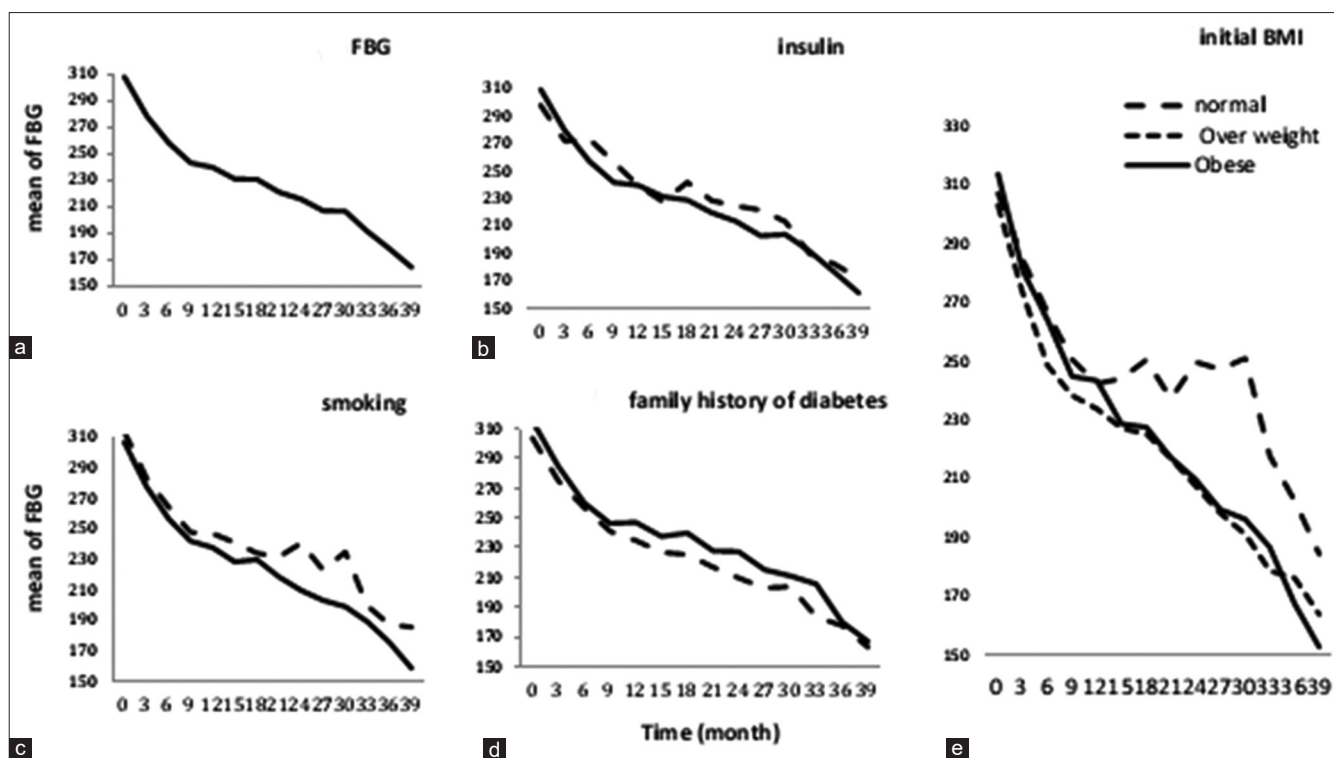


Figure 1: The mean of FBG in diabetic patients in sequential measurements: a) totally. b) by insulin, c) by smoking, d) by family history of diabetes. Solid line (-) indicates group No and dotted line (- -) shows group Yes. e) The mean of FBG in diabetic patients in sequential measurements by initial BMI

had less control over their blood glucose. The results are congruent with the results of other studies.<sup>[16,17,19]</sup> Some studies that used the logistic regression model indicated that the likelihood of higher HbA1c is low in older people.<sup>[19,21]</sup> In another study, older patients were more likely to follow and adhere to doctor's prescriptions, which improves their conditions.<sup>[14]</sup> As the results of some studies indicated that long-term complications caused by diabetes such as kidney disease and death are more prevalent in younger patients,<sup>[31]</sup> paying more attention to younger patients at risk of this disease is emphasized.

Family history of diabetes was an effective factor on changes in FBG in the present study. People with a family history of diabetes had lower FBG than others during follow-up. In many studies, the effect of family history on diabetes has been discussed.<sup>[22,23]</sup> In some studies, family history had no significant effect<sup>[17]</sup> probably because these people were familiar with the methods used for preventing and controlling disease and its complications, and accordingly, they paid more attention to their health.

Smoking was regarded as another effective factor influencing FBG and smokers showed higher FBG during follow-up. The result was consistent with the study,<sup>[20]</sup> while it was inconsistent with the results of some studies.<sup>[17,21]</sup> In general, smoking can be associated with insulin resistance and finally diabetes.<sup>[32]</sup> Therefore, blood glucose decreasing in these patients becomes more difficult than in nonsmokers.

Without any disagreement among healthcare professionals, weight loss plays a pivotal role in patients. Contrary to other reports that discuss the effect of baseline BMI on the disease process, the present study considered the effect of BMI changes during follow-up. Increasing in BMI during follow-up led to increase in FBG. Of course, time plays a significant role in this trend. The results were congruent with the results of some other studies. In a study in 2008, it was indicated that by adjusting for age and gender, HbA1c were higher among patients who had stable (unchanged) weight or were overweight during the study, compared with those who experienced weight loss.<sup>[19]</sup> In another study, people with lower BMI had higher HbA1c.<sup>[17]</sup> Furthermore, based on the results of another study, HbA1c were more likely to be higher among patients who had higher baseline BMI.<sup>[21]</sup> Hence, considering the results, if people can modify their body to healthier conditions, they will have increased chances to reduce the illness process.

In the present study, gender could not significantly affect FBG, which is consistent with the results of other studies.<sup>[16,17,19,21,33]</sup> Furthermore, a history of high blood pressure could not significantly influence the changes in FBG. However, no correlation was observed in some other studies.<sup>[16,19]</sup>

The present study has several limitations that warrant consideration. First, all patients received recommendations for diet and sport as well as pharmaceutical treatments and, if necessary, insulin but nutritionist and sports practitioner

was not documented with precision and complete details for each patient. Second, amount of lipid (such as cholesterol) during care of patient were not recorded while it is an important factor. Third, education level of patients was not documented, but given that the gathered data was in small towns, the education level was low.

There were also several strengths to the present study. First, this study is longitudinal and trend of FBG was described. Second, data belongs to the NDPCP plan in Iran that has been paid less attention and less research has been published for this project.

It is suggested that disease process should be examined for a longer period of time (more than 3 years) because some studies indicated that disease process becomes completely different after 3 years. In the present study, disease process was considered by FBG while the evaluation of HbA1C is also recommended.

## Conclusions

Given that patients who received insulin therapy had higher mean FBG, it is recommended to examine their insulin dose and modifications should be made in terms of the patients' needs during their continuous follow-up. Weight loss during follow-up and cessation of smoking indicate a favorable prognosis of disease. More attention should be paid to younger patients in care. Patients are encouraged to start treatment and care at the same time diagnose.

## Acknowledgments

The authors of this study acknowledge all personnel of health centers in Kordkuy city who were involved in collecting data.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

**Received:** 03 Jul 18 **Accepted:** 14 Mar 19

**Published:** 26 Nov 20

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