Association of T2DM、Serum Glucose、HbA1c With Lumbar Spine Bone Mineral Density in 40-59 years adults: A Cross Sectional Study Based on the 2011-2018 NHANES Database

Bo Liu
The Affiliated Hospital of Qingdao University
Jingshuang Liu
The Affiliated Hospital of Qingdao University
Junpeng Pan
The Affiliated Hospital of Qingdao University
Hui Zong
The People's Hospital of Qingyun
Chengliang Zhao
The Affiliated Hospital of Qingdao University https://orcid.org/0000-0002-2673-3398
Zhijie Wang (simonwang1969@163.com)
The Affiliated Hospital of Qingdao University https://orcid.org/0000-0002-4944-1750

Research Article

Keywords: Type 2 diabetes mellitus, lumbar spine bone mineral density, serum glucose, HbA1c, cross sectional study, NHANES database

Posted Date: October 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-997527/v1

Abstract

Backgrounds:

Our purpose is to discuss the relationship among the status and duration of T2DM, serum glucose, glycosylated hemoglobin(HbA1c), and lumbar spine bone mineral density (LSBMD).

Methods:

We selected participants whose age was 40-59 in the NHANES of 2011-2018 for a cross-sectional study. We used the multiple linear regression model to evaluate the status and duration of T2DM, serum glucose, HbA1c, and LSBMD had a linear correlation. We used the smooth curve fitting and threshold effect methods to explore the potential curvilinear relationship and inflection point, further analyzed the subgroups stratified by genders and race and completed the curve fitting.

Result:

Finally, 5,329 people met the standard. Finally, we found that the positively correlation between the status of T2DM and the LSBMD, however, the duration of T2DM was not associated with the LSBMD.We further used the smooth curve fitting method to explore. And then we found that blood glucose and level of HbA1c had a curvilinear relationship with the BMD of the lumbar spine in the model. The curve was U-shaped. After the saturation effect and threshold effect analysis, the inflection point was 7.77mmol/L and 5.4%, respectively. According to the further subgroup analysis, we found that the blood glucose and HbA1c of male non-Hispanic whites were positively correlated to the BMD of the lumbar spine. However, in female non-Hispanic black people and Mexican Americans, they had the relationship of a U-shaped curve with the BMD of the lumbar spine.

Conclusion:

The BMD of the lumbar spine of middle-aged people suffering from T2DM was significantly higher than those who do not suffer from diabetes. However, the duration of T2DM was not associated with the LSBMD.Generally speaking, blood glucose and level of HbA1c had a curvilinear relationship with the BMD of the lumbar spine. The curve was U-shaped (The inflection point was 7.77mmol/L and 5.4%, respectively). The blood glucose and HbA1c of male non-Hispanic whites were positively correlated to the BMD of the lumbar spine. However, in the female non-Hispanic black people and Mexican Americans, they had the relationship of a U-shaped curve with the BMD of the lumbar spine.

Introduction

With the increase of the average longevity of people and the aging of society, diabetes and osteoporosis have become a hot topic of research. Generally, the diabetes of teenagers under the age of 20 and children is often T1DM. However, there are some exceptions. The diabetes of most middle-aged and elderly people whose age is above 40 is T2DM [1].Based on the BMD of the lumbar spine, we can

diagnose osteoporosis. T value is the commonly used expression value of the BMD in medicine. When the T value is less than -2.5, it indicates that the patient should be alert for the phenomenon of osteoporosis and receive the treatment timely and as early as possible.

Diabetes may cause a significant increase in the risk of osteoporosis, which has been proved[2].The BMD of T1DM patients decreases. However, the BMD of T2DM patients is usually normal and even becomes slightly higher [3–5]. The bone turnover of diabetes patients decreases and properties of bone materials and bone microstructure change.

The NHANES is a cross-sectional survey based on the crowds. It aims to collect the information about health and nutrition of families and populations in the United States. In the NHANES, the stratified multi-stage sampling design was used to obtain the representative samples of American residents.Many researchers have used a large amount of data for cross-sectional research.However, up to now, the correlation between the serum glucose, HbA1c and BMD is unknown. The purpose of this study is to explore the correlation between the status and duration of T2DM, serum glucose, and HbA1c and LSBMD.It also could provide a basis for the control of chronic complications of diabetes.

Methods

We summarized the NHANES data of 4 cycles including 2011-2012; 2013-2014; 2015-2016; 2017-2018. The inclusion and exclusion criteria were as follows. The age range is 40-59; It were excluded for the data of LSBMD, serum glucose, or HbA1c was missing; and the same for other missing covariate values. Finally, 5,329 research objects meeting the standard were included. NHANES protocol was approved by the Review Committee of the National Health Statistics Ethics Research Center. The written informed consent of all the adult participants was obtained. For participants under the age of 18, the agreement of parents or guardians was required.

Variables

The exposure variables included the status of T2DM, the duration, serum glucose, and HbA1c. The status of T2DM is defined as “The doctor told that he/she suffered from diabetes.” The duration is calculated as the age of participating the NHANES minus the age when first told you had diabetes. The serum glucose and HbA1c were both obtained from the part of“Laboratory Data”in NHANES, including BIOPRO_G; BIOPRO_H; BIOPRO_I; BIOPRO_J and GHB_G; GHB_H; GHB_I; GHB_J. Serum glucose (non-fasting) was measured by means of a Roche/Hitachi cobas C Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN) or a Roche/Hitachi Modular P Chemistry Analyzer. HbA1c was measured on a Tosoh Automated Analyzer HLC-723G8 (Tosoh Medics, Inc., San Francisco, CA) or a Tosoh G7 Automated HPLC Analyzer.

The BMD of the lumbar spine was an outcome variable. The spine scans were acquired on Hologic Discovery model A densitometers (Hologic, Inc., Bedford, Massachusetts), using software version Apex 3.2. The radiation exposure from DXA for the spine scan is extremely low at less than 20 uSv. All scans in

the “DXXSPN_G; DXXSPN_H; DXXSPN_I; DXXSPN_J” file were analyzed with Hologic APEX version 4.0 software.

The following data was confounding variables. Age, gender, race, family income, poverty rate, educational level, smoking at least 100 cigarettes in life, active entertainment activities, body mass index (BMI), and other information were obtained by self-reporting. At the same time, in the standardized biochemical test, data such as serum sodium, serum potassium, serum phosphorus, alkaline phosphatase, serum uric acid, blood urea nitrogen, serum creatinine, total protein, total cholesterol, and serum calcium was obtained.

Statistical method

R version 3.4.3 software package (http:// www.R-project.org) and EmpowerStats (http:// www.empowerstats.com) were used. If the P-value is less than 0.05, the difference is statistically significant. The multivariable logistic regression model was used to evaluate the relationship between the status and duration of T2DM, serum glucose, and HbA1c and BMD of the lumbar spine. We built 3 models. In Model 1, covariates were not adjusted; in the Model 2, age, gender and race were adjusted; and in the Model 3, all the covariates were adjusted. At the same time, according to gender, T2DM status,duration, serum glucose, and HbA1c, the subgroup analysis was made. The smooth curve fitting was used to explore the non-linear relationship. We further used the two-segment linear regression model to calculate the inflection points. Finally, we further made the subgroup analysis according to the relationship between serum glucose and HbA1c and BMD of the lumbar spine in different genders and races. We completed the curve fitting.

Results

The Demographic of Cohort with and without Type 2 Diabetes

As shown in Table 1, finally, 5,329 people met the standard, including 4,639 non-diabetes patients and 690 diabetes patients. Compared with non-diabetes patients, T2DM patients were older(P<0.001). Their BMI and LSBMD were higher (P<0.001). Adults suffering from T2DM had few entertainment activities and low family income, poverty rate, and education level. Among them, differences between the two groups were significant in alkaline phosphatase, total cholesterol, blood urea nitrogen, serum sodium, serum potassium, serum calcium, blood glucose, and HbA1c in the standard serum biochemical test (P<0.001).

Table 1
Weighted Characteristics of Study Sample with and without Type 2 Diabetes

	Type 2 Diabetes(690)	Non-Diabetes(4639)	P-value	P-value*
Age	50.76 ± 5.37	49.07 ± 5.71	<0.001	<0.001
Gender			0.084	-
Male	360 (52.17%)	2257 (48.65%)		
Famale	330 (47.83%)	2382 (51.35%)		
Race			<0.001	-
Mexican American	130 (18.84%)	637 (13.73%)		
Other Hispanic	74 (10.72%)	494 (10.65%)		
Non-Hispanic White	174 (25.22%)	1638 (35.31%)		
Non-Hispanic Black	186 (26.96%)	1014 (21.86%)		
Other Race	126 (18.26%)	856 (18.45%)		
BMI	33.37 ± 7.60	29.16 ± 6.49	<0.001	<0.001
Duration	8.88 ± 8.27	/		
Education			<0.001	-
Less than 9th grade	79 (11.45%)	356 (7.67%)		
9-11th grade	110 (15.94%)	571 (12.31%)		
High school graduate	152 (22.03%)	1025 (22.10%)		
Some college or AA degree	219 (31.74%)	1358 (29.27%)		
College graduate or above	130 (18.84%)	1329 (28.65%)		
Ratio of family income to poverty	2.36 ± 1.59	2.78 ± 1.69	<0.001	<0.001
Vigorous Activities			<0.001	-
Yes	103 (14.93%)	1087 (23.43%)		
No	587 (85.07%)	3552 (76.57%)		
Smoked			0.268	-

Results in the table: mean + SD / N (%)

P value *: if it is a continuous variable, it shall be obtained by Kruskal Wallis rank sum test. If the theoretical number of counting variables is less than 10, it shall be obtained by Fisher exact probability test.

	Type 2 Diabetes(690)	Non-Diabetes(4639)	P-value	P-value*
Yes	308 (44.64%)	1967 (42.40%)		
No	382 (55.36%)	2672 (57.60%)		
Standard Biochemical Examination				
HbA1c	7.94 ± 2.12	5.58 ± 0.67	<0.001	<0.001
Serum glucose	9.35 ± 4.92	5.38 ± 1.37	<0.001	<0.001
Alkaline Phosphatase	77.02 ± 26.39	69.98 ± 23.98	<0.001	<0.001
Blood Urea Nitrogen	5.26 ± 2.56	4.69 ± 1.64	<0.001	<0.001
Serum Cholesterol	4.90 ± 1.28	5.24 ± 1.04	<0.001	<0.001
Serum Creatinine	84.79 ± 84.90	76.09 ± 27.72	<0.001	0.329
Phosphorus	1.20 ± 0.19	1.19 ± 0.18	0.032	0.124
Uric Acid	324.77 ± 89.53	318.51 ± 83.43	0.069	0.155
Sodium	138.40 ± 2.83	139.41 ± 2.28	<0.001	<0.001
Potassium	4.04 ± 0.37	3.95 ± 0.33	<0.001	<0.001
Total Proten	71.79 ± 5.03	71.46 ± 4.48	0.075	0.126
Total Calcium	2.34 ± 0.09	2.33 ± 0.09	<0.001	<0.001
Lumbar Spine BMD	1.05 ± 0.17	1.02 ± 0.16	<0.001	<0.001
Results in the table: mean + SD / N (%)				
P value *: if it is a continuous variable, it shall be obtained by Kruskal Wallis rank sum test. If the theoretical number of counting variables is less than 10, it shall be obtained by Fisher exact probability test.				

Relationship between the status and duration of T2DM and lumbar spine BMD

As shown in Table 2, we finally built three models. Among them, Model 1: β = 0.039, 95% CI: 0.025-0.054, P<0.00001; Model 2 : β = 0.043, 95% CI: 0.029-0.057, P<0.00001; and Model 3 (full-adjusted model): β = 0.023, 95% CI: 0.004-0.041, P=0.01829. We can know that they were all positively correlated.

Table 2

Associations Between the status of T2DM and Lumbar Spinal Bone Mineral Density (g/cm^2)

Exposure	Non-adjusted Model	Adjust Model I	Adjust Model II
Non-Diabetes	Reference	Reference	Reference
Type 2 Diabetes	0.039 (0.025, 0.054) <0.00001	0.043 (0.029, 0.057) <0.00001	0.023 (0.004, 0.041) 0.01829
Male with Non-Diabetes	Reference	Reference	Reference
Male with Type 2 Diabetes	0.050 (0.030, 0.070) <0.00001	0.045 (0.025, 0.065) <0.00001	0.015 (-0.013, 0.042) 0.29783
Famale with Non-Diabetes	Reference	Reference	Reference
Famale with Type 2 Diabetes	0.027 (0.007, 0.047) 0.00770	0.038 (0.019, 0.058) 0.00009	0.032 (0.007, 0.057) 0.01349
Data in the table: β (95%CI) P-value; Outcome variable: lumbar spine BMD; Exposure variable: Type 2 Diabetes Non-adjusted model adjust for: None; Adjust I model adjust for: Age; Gender; Race ;Adjust II model adjust for: Age; Gender; Race; Education; Ratio; BMI; Duration;Vigorous Activities; Smoking; HbA1c; Serum glucose;Alkaline Phosphatase; Blood Urea Nitrogen; Serum Cholesterol; Serum Creatinine; Phosphorus;Uric Acid; Sodium; Potassium; Total Proten; Total Calcium			

According to the subgroup stratified by gender, we had the following further findings. For men suffering from diabetes, Model 1: β = 0.050, 95% CI: 0.030-0.070, P<0.00001; Model 2: β = 0.045 95% CI: 0.025-0.065, P<0.00001; and Model 3: β = 0.015 95% CI:-0.013-0.042, P=0.29783. For women suffering from diabetes, Model 1: β = 0.027, 95% CI: 0.007-0.047, P=0.0077; Model 2: β = 0.038, 95% CI: 0.019-0.058, P=0.00009; and Model 3: β = 0.032, 95% CI: 0.007-0.057, P=0.01349. In summary, the positive correlation between the two was relatively stable.

However, as shown in Table 3, there was no significant association between disease duration of T2DM and LSBMD in both genders in all three models (in the Model 3, for males: β = 0.001, 95% CI:-0.0015–0.0035, P=0.433215; for females: β= -0.0018, 95% CI: -0.0037–0.0001,P=0.061801).

Table 3

Associations Between T2DM Duration (Year) and Lumbar Bone Mineral Density (g/cm^2)

Model	Non-adjusted Model	Adjust Model I	Adjust Model II
Total	-0.0003 (-0.0018, 0.0013) 0.742754	-0.0004 (-0.0019, 0.0011) 0.613685	-0.0007 (-0.0022, 0.0008) 0.363552
Male	0.0010 (-0.0015, 0.0035) 0.432817	0.0003 (-0.0021, 0.0028) 0.784566	0.0010 (-0.0015, 0.0035) 0.433215
Famale	-0.0013 (-0.0032, 0.0006) 0.197111	-0.0011 (-0.0029, 0.0007) 0.226405	-0.0018 (-0.0037, 0.0001) 0.061801

Data in the table: β (95%CI) Pvalue; Outcome variable: lumbar spine BMD; Exposure variable: Duration
Non-adjusted model adjust for: None; Adjust I model adjust for: Age; Gender; Race ;Adjust II model adjust for: Age; Gender; Race; Education; Ratio; BMI; Vigorous Activities; Smoking; HbA1c; Serum glucose; Alkaline Phosphatase; Blood Urea Nitrogen; Serum Cholesterol; Serum Creatinine; Phosphorus; Uric Acid; Sodium; Potassium; Total Proten; Total Calcium

Relationship between serum glucose and lumbar spine BMD

As shown in Table 4, we built 3 models. Among them, Model 1: β = 0.004, 95% CI: 0.002-0.005,P=0.00029; Model 2: β = 0.005, 95%CI: 0.003-0.006,P=<0.00001; and Model 3: β = 0.004, 95%CI: 0.000-0.007,P=0.02742.We found that there seems to be a slightly linear relationship. We further explored the relationship between the quartile of serum glucose and BMD of the lumbar spine. Finally,We found that they did not have a linear correlation(Model 1:P for trend= 0.734, Model 2:P for trend= 0.092, and Model 3:P for trend= 0.909). We further used the smooth curve fitting method to directly find that they had the relationship of a U-shaped curve (Figure 1). According to the saturation effect and threshold effect analysis, the inflection point was 7.77 mmol/L and the log-likelihood ratio P=0.031 0.05 (Table 5). It indicated that the curvilinear relationship was established. The subgroups of different genders and races were analyzed. According to the smooth curve fitting, the serum glucose of male ,non-Hispanic whites, Spanish, and other races had a line relationship with the BMD of the lumbar spine. The serum glucose of female non-Hispanic black people and Mexican Americans had the relationship of a U-shaped curve with the BMD of the lumbar spine. (Figure 3, Figure 4)

Table 4

Associations Between Serum Glucose (mmol/L) and Lumbar Spinal Bone Mineral Density (g/cm^2)

Exposure	Non-adjusted	Adjust I	Adjust II
Serum Glucose	0.004 (0.002, 0.005) 0.00029	0.005 (0.003, 0.006) <0.00001	0.004 (0.000, 0.007) 0.02742
Serum Glucose			
Q1	Reference	Reference	Reference
Q2	0.003 (-0.009, 0.015) 0.61733	0.007 (-0.004, 0.019) 0.21283	0.011 (-0.001, 0.023) 0.06510
Q3	-0.005 (-0.017, 0.006) 0.36505	0.000 (-0.012, 0.012) 0.99526	-0.000 (-0.012, 0.012) 0.98841
Q4	0.006 (-0.007, 0.018) 0.37293	0.014 (0.002, 0.026) 0.02401	0.003 (-0.011, 0.017) 0.66512
P for trend	0.734	0.092	0.909

Data in the table: β (95%CI) P-value; Outcome variable: lumbar spine BMD; Exposure variable:Serum Glucose (mmol/L)

Non-adjusted model adjust for: None; Adjust I model adjust for: Age; Gender; Race ;Adjust II model adjust for: Age; Gender; Race; Education; Ratio; BMI; Duration;Vigorous Activities; Smoking; HbA1c;Serum glucose;Alkaline Phosphatase;Blood Urea Nitrogen;Serum Cholesterol;Serum Creatinine ;Phosphorus;Uric Acid;Sodium;Potassium;Total Proten;Total Calcium

Table 5

Nonlinearity addressing of Serum glucose(mmol/L)and Lumbar spinal Bone Mineral Density (g/cm^2)

Outcome:	**β 95%CI P value**
Model 1: Fitting model by standard linear regression	0.004 (0.000, 0.007) 0.0274
Model2: Fitting model by two-piecewise linear regression Inflection point	
Inflection point	7.77
< 7.77	-0.001 (-0.007, 0.004) 0.6271
> 7.77	0.007 (0.002, 0.011) 0.0021
P for log likelyhood rati o	0.031
Data in the table: β (95%CI) P-value; Outcome variable: lumbar spine BMD; Exposure variable:Serum Glucose (mmol/L)	
Non-adjusted model adjust for: None; Adjust I model adjust for: Age; Gender; Race ;Adjust II model adjust for: Age; Gender; Race; Education; Ratio; BMI; Duration;Vigorous Activities; Smoking; HbA1c;Serum glucose;Alkaline Phosphatase;Blood Urea Nitrogen;Serum Cholesterol;Serum Creatinine ;Phosphorus;Uric Acid;Sodium;Potassium;Total Proten;Total Calcium	

Relationship between HbA1c and lumbar spine BMD

As shown in Table 6, we built 3 models. Among them, Model 1: β = 0.007, 95% CI: 0.004-0.011,P=0.00018; Model 2: β = 0.009, 95% CI: 0.005-0.013,P<0.00001; and Model 3: β = 0.001, 95% CI:-0.007-0.008,P=0.87344. We explored the relationship between the quartile of HbA1c and BMD of the lumbar spine. We found that they did not have a linear correlation((Model 1:P for trend= 0.332, Model 2:P for trend= 0.843, and Model 3:P for trend= 0.016). We further used the smooth curve fitting method to directly find that they had the relationship of a U-shaped curve (Figure 2). According to the saturation effect and threshold effect analysis, the inflection point was 5.4% and the log-likelihood ratio P□0.001 (Table 7). It indicated that the Curve relation was established. We further made the subgroup analysis with gender and race. According to the smooth curve fitting, HbA1c of male,non-Hispanic whites and other Spanish had a line relationship with the BMD of the lumbar spine. The HbA1c of female non-Hispanic black people and Mexican Americans had the relationship of a U-shaped curve with the BMD of the lumbar spine. (Figure 3, Figure 4)

Table 6

Associations Between Glycohemoglobin (%) and Lumbar Spinal Bone Mineral Density (g/cm^2)

Exposure	Non-adjusted	Adjust I	Adjust II
HbA1c	0.007 (0.004, 0.011) 0.00018	0.009 (0.005, 0.013) <0.00001	0.001 (-0.007, 0.008) 0.87344
HbA1c			
Q1	Reference	Reference	Reference
Q2	-0.029 (-0.040, -0.018) <0.00001	-0.023 (-0.034, -0.011) 0.00008	-0.020 (-0.031, -0.008) 0.00081
Q3	-0.031 (-0.044, -0.019) <0.00001	-0.024 (-0.037, -0.012) 0.00013	-0.020 (-0.033, -0.007) 0.00328
Q4	-0.006 (-0.019, 0.007) 0.34641	-0.001 (-0.014, 0.012) 0.90267	-0.018 (-0.034, -0.002) 0.02599
P for trend	0.332	0.843	0.016

Data in the table: β (95%CI) P-value; Outcome variable: lumbar spine BMD; Exposure variable:Glycohemoglobin (%);Non-adjusted model adjust for: None; Adjust I model adjust for: Age; Gender; Race ;Adjust II model adjust for: Age; Gender; Race; Education; Ratio; BMI; Duration;Vigorous Activities; Smoking; HbA1c;Serum glucose;Alkaline Phosphatase;Blood Urea Nitrogen;Serum Cholesterol;Serum Creatinine ;Phosphorus;Uric Acid;Sodium;Potassium;Total Proten;Total Calcium

Table 7

Nonlinearity addressing of Glycohemoglobin (%) and Lumbar Spinal Bone Mineral Density (g/cm^2)

Outcome:	β 95%CI P value
Model 1: Fitting model by standard linear regression	0.001 (-0.007, 0.008) 0.8734
Model2: Fitting model by two-piecewise linear regression Inflection point	
Inflection point	5.4
< 5.4	-0.039 (-0.064, -0.014) 0.0021
> 5.4	0.006 (-0.002, 0.015) 0.1374
P for log likelyhood ratio	<0.001

Data in the table: β (95%CI) P-value; Outcome variable: lumbar spine BMD; Exposure variable:Glycohemoglobin (%); Non-adjusted model adjust for: None; Adjust I model adjust for: Age; Gender; Race ;Adjust II model adjust for: Age; Gender; Race; Education; Ratio; BMI; Duration;Vigorous Activities; Smoking; HbA1c;Serum glucose;Alkaline Phosphatase;Blood Urea Nitrogen;Serum Cholesterol;Serum Creatinine ;Phosphorus;Uric Acid;Sodium;Potassium;Total Proten;Total Calcium

Discussion

The morbidity of diabetes has the trend of increasing around the world. 422 million people suffer from diabetes worldwide. 90% of them suffer from T2DM, which is characterized by insulin resistance. T1DM decreases. It is mainly characterized by insulin deficiency. Children and teenagers are the main crowds of diabetes. Diabetes patients often have chronic complications of the cardiovascular system, eyes, kidneys, nervous system, and other systems. In particular, bone strength is also impaired[6–9]. However, up to now, researchers do not know the correlation between the fluctuation of serum glucose and the content of HbA1c and BMD.

In this study, the relationship between T2DM, serum glucose, and HbA1c and BMD of the lumbar spine was explored. In the study, we found that compared with non-T2DM patients T2DM patients had a higher BMD of the lumbar spine, which was positively correlated. Many studies proved that T1DM patients had a lower BMD compared to normal people at the same age and T2DM patients had a normal or higher BMD [10–20]. Our study also provided evidence for the conclusion, perhaps because T2DM patients had insulin resistance. Insulin is a kind of synthetic hormone. Too much hormone in their body promoted the increase of bone metabolism and synthesis, so the BMD is higher. Some researchers believed that BMD was positively correlated to BMI. We can believe that the increase of BMD is a physiological phenomenon to adapt to the current physical load [6, 21, 22]. However, the risk of fracture of T1DM or T2DM patients is higher than that of normal people [4, 6, 23–26]. Most T2DM patients are fat. However, the high BMD caused by obesity may not necessarily provide better protection for fracture. There may be a BMI threshold value, beyond which the bones cannot adapt any more. Therefore, the special parts of the body (such as wrist joints, humerus, etc.) may have a fracture.

According to this study, blood glucose and HbA1c have a non-linear relationship with BMD of the lumbar spine. According to the smooth curve effect, we found that they had a relationship of a U-shaped curve. Further, according to the saturation effect analysis, we found that the test effect value of the log-likelihood ratio of the two curves was 0.031 and less than 0.001, respectively. The inflection point of the two curves was 7.77mmol/L and 5.4%, respectively. In a Chinese study, Xu et al. [27] separated monocytes from the marrow of C57BL/6 mice. When the combination of hyperglycemia and hyperinsulinemia was simulated, the osteoclast differentiation and expression of marker genes were down-regulated. Finally, the BMD became higher. However, Jia et al. [3] found in their study that BMD and BMC of the T2DM group were lower than those of the normal group. Our study suggested that blood sugar content and BMD of the lumbar spine had a curvilinear relationship. Besides, when the blood sugar content was 7.77mmol/L, the BMD of the lumbar spine was the lowest. In our study, we further analyzed subgroups of different genders and races. According to the smooth curve fitting, the blood sugar content of male non-Hispanic whites, Spanish, and other races had a line relationship with the BMD of the lumbar spine. The blood sugar content of female non-Hispanic black people and Mexican Americans had the relationship of a U-shaped curve with the BMD of the lumbar spine.

HbAlc reflects the control of average blood glucose in the last 2-3 months and is not affected by glycometabolism and eating[17, 28]. The higher HbA1c is, the poorer the control of blood glucose is. At present, many scholars have different opinions on the correlation between HbA1c and BMD. Guo et al. [29] found that when HbA1c was greater than 8.0% the BMD of the neck of the femur significantly decreased. However, Majima et al.[15] believed that the BMD of the distal radius of men and women and that of the neck of the femur of women gradually decreased with the increase of HbA1c. Some researchers even found that the BMD and HbA1c had no clear relationship[30, 31]. However, in our study, we found that HbA1c and BMD of the lumbar spine had a curvilinear relationship. Besides, when HbA1c was 5.4%, BMD of the lumbar spine was the lowest. Gender and race were used for further subgroup analysis and smooth curve fitting. We found that the content of HbA1c of male non-Hispanic whites and other Spanish had a line relationship with the BMD of the lumbar spine. The content of HbA1c of female non-Hispanic black people, other Spanish, and Mexican Americans had the relationship of a U-shaped curve with the BMD of the lumbar spine.

Limitation

However, our study also has the following limitations. First, the crowds suffering from diabetes were defined by the self-reporting of diabetes, which caused a big bias. Second, this study is a cross-sectional study. The above conclusion only shows that they are correlated, but they do not have a causal relationship. Finally, in our study, only some covariates were included, As far as I know, BMD is used as the outcome variable. We only selected lumbar BMD, including hip joint BMD and rib BMD. However, in other year cycles, hip joint BMD has some and some do not. The data of bone turnover markers are very old. There are cycles, but not later. The fracture data only passed the questionnaire and was not detailed. We can only hope that the next researcher will continue to study and make more detailed results. Such as whether there is a correlation between the use of antidiabetic drugs and lumbar spine BMD in diabetic patients. If possible, all the confounding factors should be included.

Conclusion

The BMD of the lumbar spine of middle-aged people suffering from T2DM was significantly higher than that of people not suffering from diabetes. Generally speaking, blood glucose and level of HbA1c had a curvilinear relationship with BMD. The curve was U-shaped (The inflection point was 7.77mmol/L and 5.4%). The blood glucose and HbA1c of male non-Hispanic whites were positively correlated to the BMD of the lumbar spine. However, in female non-Hispanic black people and Mexican Americans, they had a relationship of a U-shaped curve with the BMD of the lumbar spine.

Abbreviations

T2DM：Type 2 diabetes mellitus；LSBDN：Lumbar spinal bone mineral density；NHANES; National Health and Nutrition EXamination Survey; HbA1c: Glycosylated hemoglobin; OR: Odds ratio; CI: Confidence interval.

Declarations

Acknowledgements

None.

Authors' contributions

BL performed the data analysis. BL and JSL wrote the manuscript. JSL,JPP,HZ and CLZ contributed to the manuscript revise. BL, JSL and CLZ contributed to literature search and data extraction. BL, CLZ and ZJW conceived and designed the study. All authors have read and approved the final version of the manuscript.

Funding

This study was financially supported by the Department of Science Technology of Shandong Province for Key Technology Research and Development Program of Shandong（CN）（NO. 2018GSF118080）and Qingdao Municipal Science and Technology Bureau for demotic science ar technology program（NO. 19-6-1-16-nsh）

Availability of data and materials

The authors thank the staff and participants of the NHANES study for their valuable contributions

Ethics approval and consent to participate

The National Center for health statistics ethical review board approved all NHANES protocols, and written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

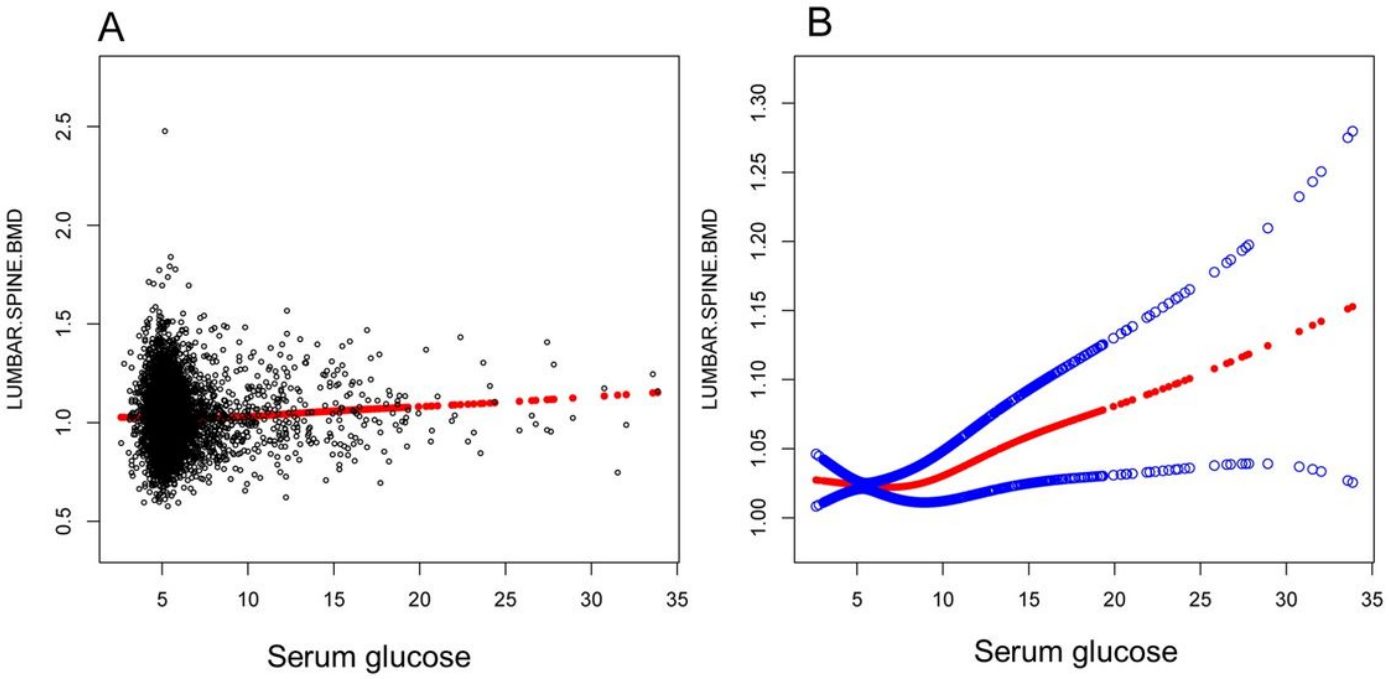

Figure 1

The association between Serum glucose and total bone mineral density. (A) Each black point represents a sample. (B) Solid rad line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit.

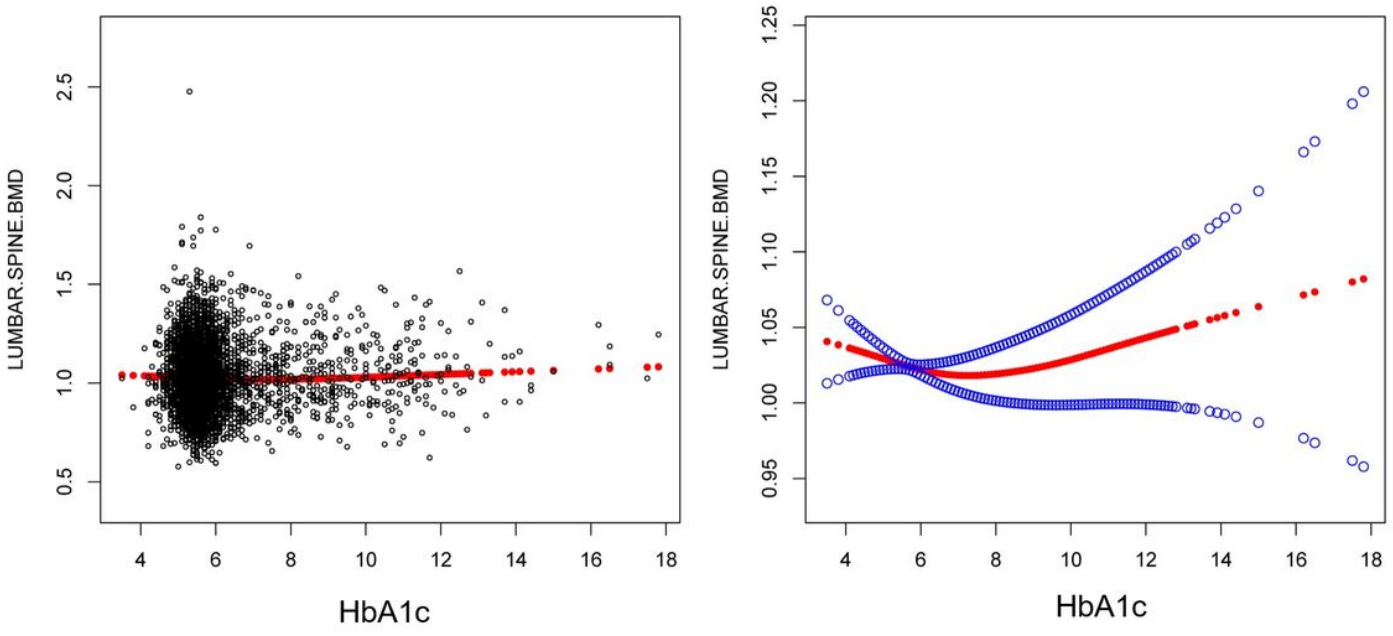

Figure 2

The association between glycosylated hemoglobin and total bone mineral density. (A) Each black point represents a sample. (B) Solid rad line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit.

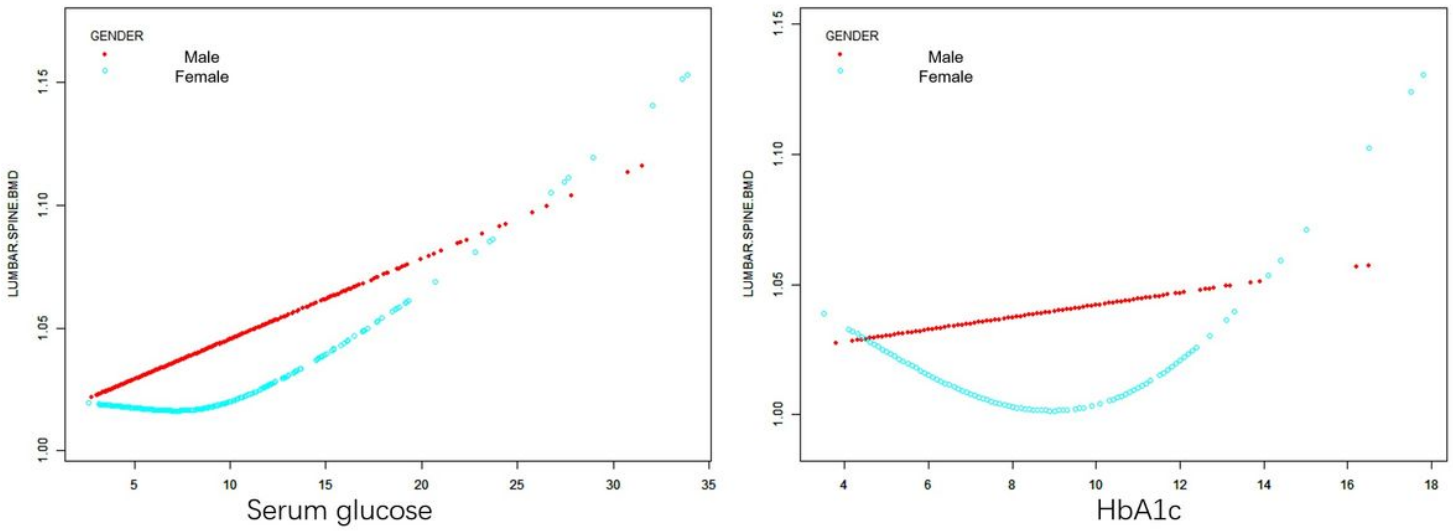

Figure 3

The associations between serum glucose, glycosylated hemoglobin and LSBDM stratified by gender.

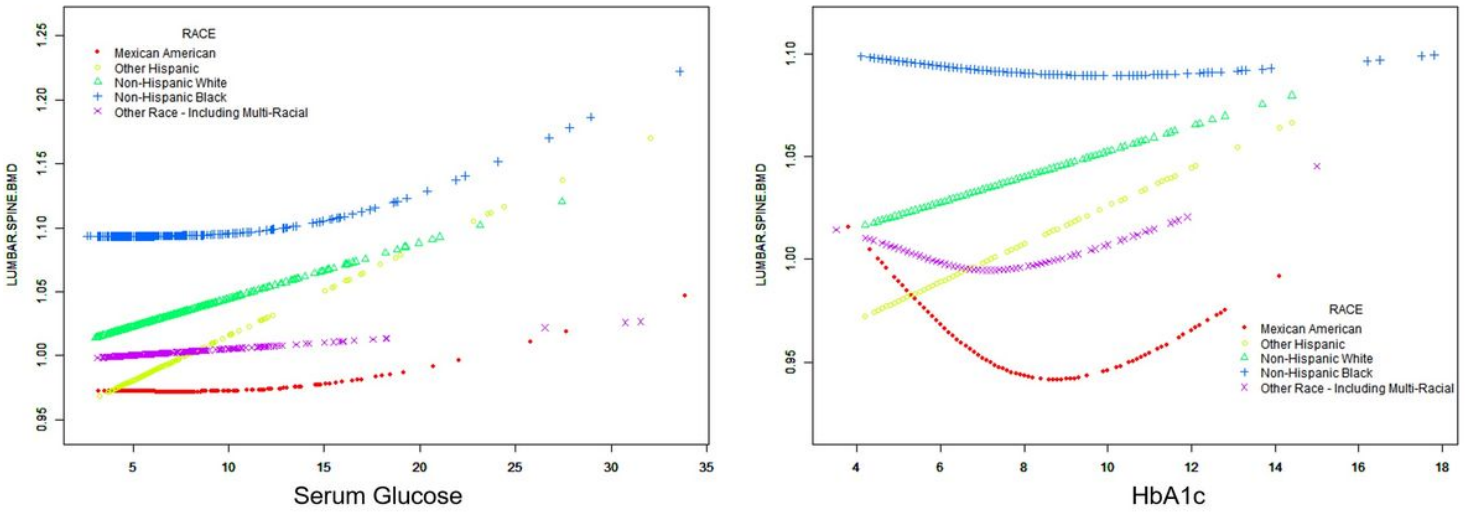

Figure 4

The associations between serum glucose, glycosylated hemoglobin and LSBDM stratified by race.