Diabetes, Metabolic Syndrome and Obesity

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Association Between Serum Folic Acid Levels and Type 2 Diabetes Mellitus in Overweight or Obese Patients: A Retrospective Study

Yaji Dai[1,*], Mingfei Guo[2,*], Jianglei Xiong[1], Lei Jiang[1]

[1]Department of Pharmacy, Anhui No.2 Provincial People's Hospital, Hefei, Anhui, People's Republic of China; [2]Department of Scientific Research, The First Affiliated Hospital of Anhui Medical University, Anhui Public Health Clinical Center, Hefei, Anhui, People's Republic of China

*These authors contributed equally to this work

Correspondence: Lei Jiang, Department of Pharmacy, Anhui No.2 Provincial People's Hospital, Hefei, Anhui, People's Republic of China, Email 13155192069@163.com

Purpose: The relationship between folic acid (FA) levels and type 2 diabetes mellitus (T2DM) with overweight or obesity remains uncertain. This study aimed to further investigate the relationship between them.

Methods: A retrospective study was conducted on 149 patients, comprising 64 patients with T2DM and normal weight and 85 patients with T2DM and overweight or obese status.

Results: Our findings revealed significantly lower levels of FA and neutrophil-to-lymphocyte ratio (NLR) in overweight/obese T2DM patients compared to their normal-BMI counterparts ($P < 0.001$). The overweight/obese cohort exhibited elevated metabolic parameters, including fasting C-peptide, serum uric acid, total cholesterol (TC), triglycerides (TG), and very low-density lipoprotein cholesterol (VLDL-C) levels ($P < 0.05$). Notably, correlation analysis demonstrated a significant positive association between FA levels and both age ($r = 0.341$, $P < 0.001$), diabetes duration ($r = 0.278$, $P = 0.001$), and NLR ($r = 0.212$, $P = 0.009$). Conversely, inverse correlations were observed between FA levels and C-peptide ($r = -0.240$, $P = 0.004$), TG ($r = -0.254$, $P < 0.001$), and VLDL-C ($r = -0.271$, $P = 0.001$).

Conclusion: This research found that FA levels were significantly associated with T2DM in individuals who were overweight or obese.

Keywords: T2DM, folic acid, overweight, obesity

Introduction

Overweight and obesity are well-established risk factors for the development of type 2 diabetes mellitus (T2DM), with complex pathophysiological interconnections between these conditions.[1] The pathological expansion of adipose tissue, particularly visceral fat deposition, disrupts glucose and lipid homeostasis through multifaceted pathways. This dysregulation exacerbates skeletal muscle insulin resistance and hepatic insulin resistance, impairing peripheral glucose uptake while promoting excessive hepatic gluconeogenesis. Concurrently, dysfunctional pancreatic β-cells fail to compensate for rising insulin demands, while hyperactive α-cells exacerbate hyperglycemia through pathological glucagon secretion. The diminished incretin effect further compromises postprandial insulin secretion and amplifies glycemic variability. These metabolic perturbations are compounded by augmented renal glucose reabsorption and neurotransmitter dysregulation, which collectively disrupt energy balance and appetite control. The resultant insulin-resistant state triggers a compensatory hyperinsulinemic response, accelerating β-cell exhaustion through glucolipotoxicity.[2] Clinical evidence demonstrates that sustained weight reduction (>15% total body weight loss) can reverse these processes by ameliorating ectopic fat deposition and restoring insulin sensitivity.[3] Furthermore, obesity-associated chronic inflammation interacts synergistically with nutrient overload to destabilize metabolic equilibrium, driving β-cell apoptosis via oxidative stress

Received: 2 March 2025
Accepted: 8 July 2025
Published: 15 July 2025

and endoplasmic reticulum dysfunction.[4,5] This integrated pathophysiology, as conceptualized in De Fronzo's Octet framework, elucidates the transition from compensated insulin resistance to overt T2DM through eight interdependent mechanisms.[6]

Folic acid (FA), a water-soluble essential micronutrient, is ubiquitously distributed in various dietary sources, including green leafy vegetables, fruits, whole grains, and animal-derived products. As a critical cofactor in one-carbon metabolism, FA serves as a fundamental methyl group donor, playing pivotal roles in nucleic acid biosynthesis (DNA and RNA) and amino acid metabolism. Clinical evidence has established that FA deficiency is associated with multiple pathological conditions, including oncogenesis, cardiovascular disorders, neural tube defects, and neurodegenerative diseases such as Alzheimer's. Emerging evidence suggests that FA supplementation has beneficial effects in overweight and obese male patients with T2DM. A clinical investigation demonstrated that FA intervention significantly modulates various metabolic parameters, including glycemic control markers (fasting blood glucose [FBG] and HbA1c) and lipid profile components (total cholesterol [TC], triglycerides [TG], and low-density lipoprotein cholesterol [LDL-C]).[7] Furthermore, a comprehensive meta-analysis revealed that FA supplementation effectively reduces plasma homocysteine (Hcy) concentrations, potentially attenuating cardiovascular disease risk in T2DM patients.[8]

Recent investigations have further elucidated the relationship between FA status and insulin resistance in T2DM populations. A clinical study focusing on Chinese T2DM patients identified a significant inverse correlation between FA concentrations and homeostatic model assessment of insulin resistance (HOMA-IR) indices.[9] These findings suggest that FA levels may serve as an independent determinant of insulin sensitivity in T2DM patients, potentially offering novel insights for diabetes management and therapeutic strategies.

However, the relationship between FA and T2DM with overweight or obesity was still uncertain. Therefore, this study retrospectively collected clinical cases to investigate the relationship between FA and other biochemical indicators in overweight or obese patients with T2DM.

Methods

Data and Sample Sources

A total of 149 patients with T2DM were hospitalized in the Department of Endocrinology at Anhui No. 2 Provincial People's Hospital from January 1, 2023, to December 26, 2024, and their data were collected. 64 and 85 patients were divided into normal weight group (normal group) and patients overweight or obesity group (abnormal group) based on body mass index (BMI<24 or BMI $\geq$ 24),[10–12] respectively. At the same time, the age of the patients was controlled between 18 and 70 years old. This study was approved by the Medical Ethics Committee of the Anhui No.2 Provincial People's Hospital (Approval Number: (R) 2025–015). The filtering process is shown in Figure 1.

Patients with diabetes were eligible for inclusion if they met the diagnostic criteria established by the 2020 edition of the guideline for the prevention and treatment of T2DM in China.[13] These criteria encompassed the presence of typical diabetes symptoms accompanied by a random blood glucose $\geq$ 11.1 mmol/L, or typical symptoms along with a fasting blood glucose (FBG) $\geq$ 7.0 mmol/L, or typical symptoms in conjunction with a 2-hour blood glucose $\geq$ 11.1 mmol/L following an oral glucose tolerance test (OGTT). Additionally, patients exhibiting classic glucuria symptoms along with a glycosylated hemoglobin (HbA1c)$\geq$ 6.5% or higher were also considered eligible. In cases where classic diabetes symptoms were absent, the tests as mentioned earlier, were repeated to confirm the diagnosis.

To ensure the accuracy of our study, we scrutinized the participants' previous medical records and excluded individuals who did not meet the inclusion criteria. The exclusion criteria were systematically applied as follows: (1) patients with diabetes mellitus classifications other than T2DM, including type 1 diabetes mellitus (T1DM), specific types of diabetes (eg, monogenic diabetes, drug-induced diabetes), and gestational diabetes mellitus (GDM); (2) individuals presenting with acute diabetic complications, specifically diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS), or severe hypoglycemic episodes requiring medical intervention; (3) patients exhibiting significant organ dysfunction, defined as New York Heart Association (NYHA) class III/IV heart failure, Child-Pugh class B/C liver cirrhosis, or chronic kidney disease stage 4/5, as well as those with active malignancies; (4) individuals diagnosed with severe neurological disorders (eg, advanced Parkinson's disease, multiple sclerosis) or psychiatric conditions (eg,

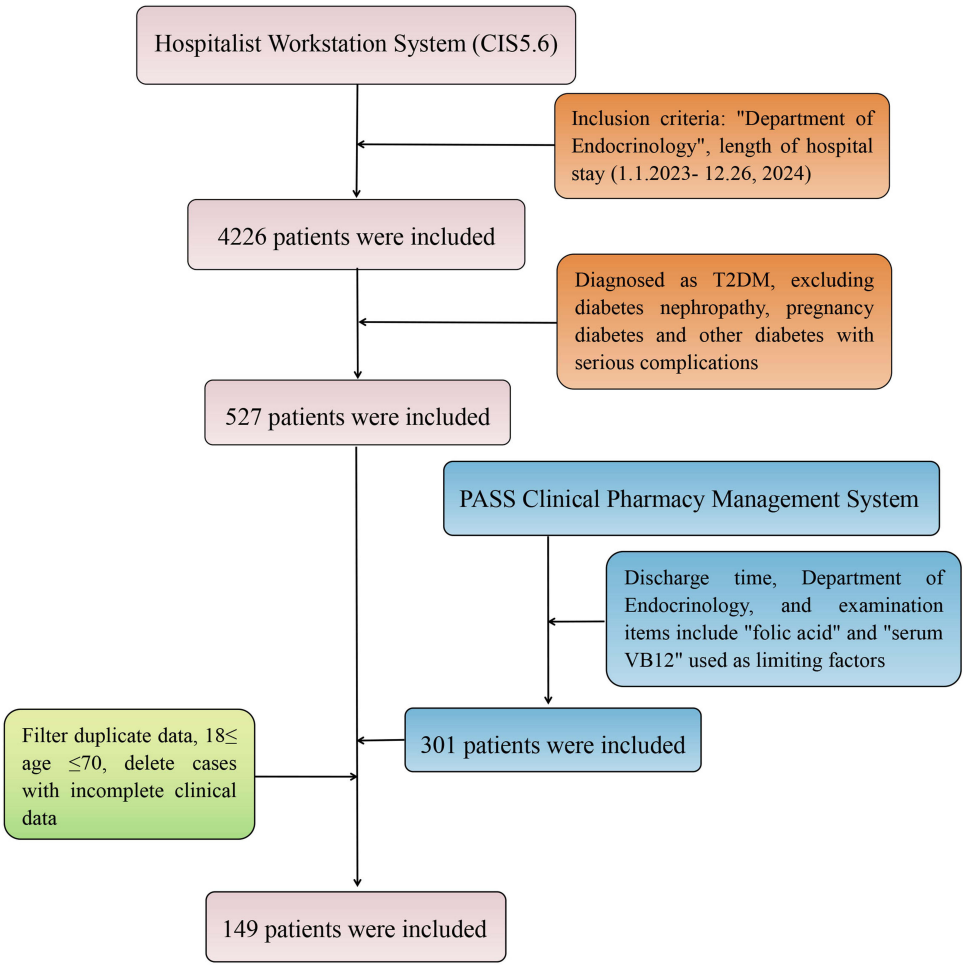

Figure 1 Clinical case selection flowchart.

schizophrenia, bipolar disorder); (5) patients receiving any form of FA supplementation, vitamin B complex, or related derivatives within the preceding three months.[14,15]

Data Collection

We systematically collected patient data through the PASS system and inpatient physician workstation system, including demographic characteristics (gender, age), clinical history (diabetes status), anthropometric measures (BMI), and hemodynamic parameters (systolic and diastolic blood pressure). Comprehensive biochemical profiling was performed, including metabolic markers (HbA1c, fasting C-peptide), hepatic function tests (ALT, AST), lipid profile (TG, VLDL-C), electrolyte balance (K, Na, Ca), hematologic indices (white blood cell count), vitamin status (serum FA, vitamin B12, 25 (OH)D3, 25-hydroxyvitamin D), thyroid function (uTSH, fT3, fT4), and autoimmune markers (anti-ICA, anti-IAA, GADA). Serum uric acid levels were also measured to assess metabolic status.

Data Analysis

We conducted data analysis using SPSS17 software. Normal or approximate normal distribution were expressed as Mean ± standard deviation (Mean ± SD). Two independent sample *t*-tests were used to compare groups with normally distributed data. Median and interquartile interval (P25, P75) were used to represent skewed distribution data. Parameters that do not follow a normal distribution are tested using Mann Whitney *U*-test. Additionally, to further investigate the relationship between serum FA and other indices, Spearman correlation analysis was utilized. A p-value of less than 0.05 was considered statistically significant.

Results

Basic Information Feature and Clinical Data

The study cohort comprised 149 patients with T2DM, stratified into two groups based on BMI: normal weight (n = 64) and overweight/obese (n = 85). Comparative analysis of serum biochemical markers between the two groups revealed significant differences in multiple parameters (Table 1). The overweight/obese group demonstrated significantly lower FA levels (10.29 ± 3.71 vs 13.02 ± 4.78, P < 0.001) and NLR (2.08 ± 1.00 vs 2.62 ± 1.51, P =0.011), higher fasting C-peptide levels (0.53 (0.39, 0.78) vs (0.33 (0.18, 0.48), P < 0.001). Blood pressure measurements were significantly elevated in the overweight/obese group (SBP: 133.95 ± 16.21 vs 123.25 ± 16.41; DBP: 87.88 ± 11.64 vs 78.94 ± 11.95, P < 0.001). Lipid profile analysis showed higher TG (2.18 (1.51, 4.25) vs 1.13 (0.91, 1.87), P < 0.001) and VLDL-C (0.98 (0.69, 1.89) vs 0.53 (0.41, 0.85), P < 0.001) levels in the overweight/obese group. Liver function markers were also elevated in this group (AST: 26.00 (18.00, 38.50) vs (18.00 (13.00, 23.00); ALT: 25.00 (16.50, 40.00) vs 20.00 (14.00, 27.00), P < 0.001 and P = 0.005, respectively). Additionally, the overweight/obese group was younger (47.80 ± 12.59 vs 55.22 ± 12.66, P < 0.001) and exhibited higher SUA levels (323.74 ± 87.69 vs 278.98 ± 78.96, P = 0.002), while showing slightly lower serum sodium levels (139.00 (138.00, 141.00) vs 140.00 (139.00, 142.00), P = 0.022).

To further investigate the associations between FA levels and clinical parameters, Spearman correlation analysis was performed. As presented in Table 2, FA levels demonstrated significant positive correlations with age (r = 0.341, P < 0.001),

Table 1 Baseline Data of Overweight or Obesity with Type 2 Diabetes

Variables	Total (n=149)	Normal Group (n=64)	Abnormal Group (n=85)	P-value	Z/t
Gender, n (%)				0.358	0.922
Male	97 (65.1)	39 (60.9)	58 (68.2)		
Female	52 (34.9)	25 (39.1)	27 (31.8)		
Age, year	51.44±13.15	55.22±12.66	47.80±12.59	<0.001	3.550
T, °C	36.31±0.18	36.30±0.19	36.31±0.18	0.521	−0.643
SBP, mmHg	129.5±17.13	123.25±16.41	133.95±16.21	<0.001	−3.968
DBP, mmHg	84.02±12.55	78.94±11.95	87.88±11.64	<0.001	−4.591
Diabetes duration, years	6.75±6.00	7.48±6.0	6.01±5.76	0.132	1.515
WBC, (10^9)	6.43±1.7	6.28±1.56	6.48±1.81	0.477	−0.713
TG, mmol/L	1.72 (1.08, 2.91)	1.13 (0.91, 1.87)	2.18 (1.51, 4.25)	<0.001	−6.245
VLDL-C, mmol/L	0.81 (0.50, 1.32)	0.53 (0.41, 0.85)	0.98 (0.69,1.89)	<0.001	−5.937
AST, U/L	20.00 (15.00, 32.00)	18.00 (13.00, 23.00)	26.00 (18.00,38.50)	<0.001	−4.584
ALT, U/L	21.00 (15.00,32.00)	20.00 (14.00, 27.00)	25.00 (16.50, 40.00)	0.005	−2.825
HbA1c, %	8.00 (6.90, 10.30)	8.05 (6.73,10.55)	8.5 (7.00,10.15)	0.659	−0.441
SUA, μmol/L	306.72±88.74	278.98±78.96	323.74±87.69	0.002	−3.217
C-peptide, nmol/L	0.44 (0.29, 0.70)	0.33 (0.18, 0.48)	0.53 (0.39, 0.78)	<0.001	−5.308
uTSH, pmol/L	2.06 (1.27, 3.34)	1.96 (1.11, 2.99)	2.12 (1.31, 3.36)	0.375	−0.888
fT3, pmol/L	4.74±0.88	4.60±0.93	4.85±0.83	0.069	−1.831
fT4, pmol/L	16.71±3.21	16.15±3.54	17.19±2.87	0.051	−1.970
anti-ICA	4.92 (4.14, 6.56)	4.98 (4.23, 6.57)	4.91 (3.95, 6.81)	0.45	−0.755
GADA	5.89 (4.50, 7.97)	6.34 (4.65, 9.66)	5.54 (4.38, 7.37)	0.059	−1.891
anti-IAA	5.26 (2.93, 6.20)	5.49 (3.55, 7.3)	5.15 (2.73, 5.88)	0.013	−2.487
25(OH)D3	15.88±6.53	16.65±7.07	15.44±7.07	0.266	1.117
25(OH)D	16.00±6.53	16.89±7.09	15.47±6.07	0.191	1.314
Vitamin B12, (pmol/L)	353.00 (281.50,562.00)	357.50 (282.00, 579.25)	349.00 (280.50, 538.50)	0.936	−0.091
FA, (nmol/L)	11.99±5.73	13.02±4.78	10.29±3.71	<0.001	3.922
K, mmol/L	3.91±0.35	3.91±0.33	3.92±0.36	0.801	−0.253
Na, mmol/L	140.00 (138.00,141.00)	140.00 (139.00, 142.00)	139.00 (138.00, 141.00)	0.022	−2.284
Ca, mmol/L	2.24±0.12	2.22±0.10	2.25±0.13	0.117	−1.578
NLR	2.31±1.27	2.62±1.51	2.08±1.0	0.011	2.584

Table 2 Correlation Analysis Between Serum FA and Other Indexes

Variables	r	P-value
Age	0.341	<0.001
Diabetes duration	0.278	0.001
NLR	0.212	0.009
TG	−0.254	0.001
VLDL-C	−0.271	0.001
AST	−0.217	0.008
C-peptide	−0.24	0.004
BMI	−0.297	0.001

diabetes duration (r = 0.278, P = 0.001), and NLR (r=0.212, P = 0.009). Conversely, significant inverse correlations were observed between FA levels and BMI (r = −0.297, P = 0.001), TG (r = −0.254, P = 0.001), VLDL-C (r = −0.271, P = 0.001), AST (r = −0.217, P = 0.008), and fasting C-peptide levels (r = −0.240, P = 0.004).

Discussion

Overweight and obesity represent significant risk factors for T2DM, contributing substantially to disease morbidity and mortality. The global burden of T2DM continues to escalate, with projections indicating an increase from 536 million cases in 2021 to approximately 783 million by 2045.[16] Furthermore, in 2030, this epidemic poses substantial health and economic challenges, particularly in China, where direct medical costs for T2DM and its complications are estimated to reach 47.2 billion USD. Notably, epidemiological data reveal that over 50% of T2DM patients in China present with overweight or obesity.[17,18] The pathophysiological mechanisms linking adiposity to T2DM are multifactorial, encompassing enhanced genetic and epigenetic susceptibility, microenvironmental alterations leading to insulin signaling disruption, β-cell dysfunction, chronic inflammation, and dysregulation of the microbiome-gut-brain axis.[4,19] These complex interactions underscore the critical role of weight management in T2DM prevention and control strategies.

Our findings demonstrated significantly higher FA levels in normal BMI patients compared to overweight/obese individuals, with a significant inverse correlation between FA and BMI in T2DM patients. These results align with previous epidemiological evidence from a large-scale cross-sectional study involving 3079 Chinese children and adolescents (aged 6–17 years), which established an inverse relationship between serum FA/vitamin B12 levels and obesity risk.[20] However, our investigation found no significant difference in vitamin B12 levels between groups, suggesting potential age-related variations in micronutrient metabolism. The observed FA-BMI relationship may be partially explained by gut microbiota alterations in obesity, as demonstrated by Riggen-Bueno et al in their characterization of the intestinal microbiome in obese adults from Western Mexico.[21] Their findings revealed reduced microbial diversity and richness, along with increased proinflammatory bacterial populations. Notably, functional analysis using PICRUSt2 indicated impaired vitamin B9 (folate) metabolism alongside enhanced saccharolytic pathways, potentially contributing to the lower FA status observed in obese individuals. These microbiome alterations may represent the mechanistic between obesity and FA metabolism, warranting further investigation in T2DM populations.

Accumulating evidence highlights the diagnostic challenges in T2DM management, primarily due to the unpredictable onset and variable duration of the prediabetic phase. This diagnostic uncertainty often results in delayed detection, with many patients remaining undiagnosed until they present with complications associated with comorbid obesity and T2DM. Supporting this clinical observation, Vitiello et al conducted a comprehensive nutritional assessment in 139 patients undergoing bariatric surgery, revealing significant micronutrient deficiencies.[22] Their results demonstrated that 66.7% of patients exhibited insufficient or deficient vitamin D levels, while 43.7% showed FA deficiency prior to surgical intervention. These findings underscore the critical need for early nutritional assessment and intervention in high-risk populations.

Emerging evidence suggests that FA supplementation may have therapeutic potential in T2DM management. A recent clinical trial demonstrated that 8-week folic acid supplementation (5 mg/d) significantly improved glycemic control in

overweight and obese T2DM patients receiving metformin therapy (≥1500 mg/d), as evidenced by reductions in HbA1c, fasting blood glucose, serum insulin levels, insulin resistance, and plasma homocysteine concentrations.[7] These findings underscore the importance of routine FA monitoring and potential supplementation in overweight/obese T2DM patients. Furthermore, these results align with the growing concept of "precision nutrition", an emerging paradigm that emphasizes individualized nutritional interventions based on specific metabolic profiles and nutritional status, which may represent a promising direction for future T2DM management strategies.[23,24] In parallel, predictive tools leveraging machine learning for early identification of diabetes complications, such as diabetic retinopathy, have demonstrated clinical promise in type 1 diabetes populations,[25] further supporting the integration of individualized risk assessment strategies in diabetes care. This approach mirrors the need for precision-based frameworks in T2DM, where biomarkers like FA could be combined with advanced predictive modeling to optimize metabolic outcomes and mitigate complications. Together, these advances highlight the potential for integrating nutritional biomarkers and data-driven technologies to refine personalized diabetes management strategies.

The strengths of our study include the novel finding of a potential negative correlation between FA levels and BMI in overweight and obese individuals with type T2DM. Moreover, we further investigated the positive correlation between NLR, which is an emerging inflammatory biomarker associated with obesity and T2DM, and FA levels.[26] However, limitations include the retrospective design, which precludes causal inference, the single-center setting with a relatively small sample size, and potential selection bias due to the inclusion of hospitalized patients who may have more severe conditions. Future studies should focus on prospective, multicenter designs with larger samples and explore the effects of serum FA on other metabolite in T2DM with obesity.

Conclusions

In conclusion, our findings demonstrated a significant association between lower serum FA levels and overweight or obese in patients with T2DM. Further studies are warranted to validate these observations and elucidate the potential mechanistic role of FA deficiency in the pathogenesis of obesity associated with T2DM.

Data Sharing Statement

Data and materials supporting the results of this study can be obtained from the corresponding authors.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the revised Declaration of Helsinki and received approval from the Medical Ethics Committee of the Anhui No.2 Provincial People's Hospital (Approval Number: (R) 2025-015). The research posed no adverse effects on participant rights or health, with stringent measures implemented to protect privacy and personal identity information. Owing to the retrospective nature of the study involving analysis of historical clinical data, the Ethics Committee waived the requirement for individual patient informed consent. Medical records of patients who explicitly refused consent were excluded from the analysis.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was financially supported by the National Natural Science Foundation of China (82404953), the Key Scientific Research Project of Anhui Provincial Department of Education (2023AH050655, 2023AH053383) and the Research Fund of Anhui Institute of Translational Medicine (2023zhyx-C93).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Tong Y, Xu S, Huang L, Chen C. Obesity and insulin resistance: pathophysiology and treatment. *Drug Discov Today*. 2022;27(3):822–830. doi:10.1016/j.drudis.2021.11.001
2. Ahmed B, Sultana R, Greene MW. Adipose tissue and insulin resistance in obese. *Biomed Pharmacother*. 2021;137:111315. doi:10.1016/j.biopha.2021.111315
3. Artasensi A, Mazzolari A, Pedretti A, Vistoli G, Fumagalli L. Obesity and type 2 diabetes: adiposopathy as a Triggering Factor and Therapeutic Options. *Molecules*. 2023;28(7):3094. doi:10.3390/molecules28073094
4. Ruze R, Liu T, Zou X, et al. Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. *Front Endocrinol*. 2023;14:1161521. doi:10.3389/fendo.2023.1161521
5. Ying W, Fu W, Lee YS, Olefsky JM. The role of macrophages in obesity-associated islet inflammation and β-cell abnormalities. *Nat Rev Endocrinol*. 2020;16(2):81–90. doi:10.1038/s41574-019-0286-3
6. DeFronzo RA, Ferrannini E, Groop L, et al. Type 2 diabetes mellitus. *Nat Rev Dis Primers*. 2015;1:15019. doi:10.1038/nrdp.2015.19
7. Gargari BP, Aghamohammadi V, Aliasgharzadeh A. Effect of folic acid supplementation on biochemical indices in overweight and obese men with type 2 diabetes. *Diabet Res Clin Pract*. 2011;94(1):33–38. doi:10.1016/j.diabres.2011.07.003
8. Mokgalaboni K, Mashaba GR, Phoswa WN, Lebelo SL. Folic acid supplementation on inflammation and homocysteine in type 2 diabetes mellitus: systematic review and meta-analysis of randomized controlled trials. *Nutr Diabetes*. 2024;14(1):22. doi:10.1038/s41387-024-00282-6
9. Yang X, Hu R, Wang Z, Hou Y, Song G. Associations between serum folate level and HOMA-IR in Chinese patients with type 2 diabetes mellitus. *Diabetes Metab Syndr Obes*. 2023;16:1481–1491. doi:10.2147/DMSO.S409291
10. Chandrasekaran P, Weiskirchen R. The role of obesity in type 2 diabetes mellitus–an overview. *Int J Mol Sci*. 2024;25(3):1882. doi:10.3390/ijms25031882
11. Ryan DH. Drugs for Treating Obesity. *Handb Exp Pharmacol*. 2022;274:387–414. doi:10.1007/164_2021_560
12. Zhang PH, Zeng Q, Lu YY, et al. Expert consensus on the procedure of body weight management among patients with overweight or obesity (2021). *Chin J Health Manag*. 2021;7(4):317–322. doi:10.3760/cma.j.cn115624-20210630-00368
13. Zhu DL. Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2020 edition). *Chin J Diabetes Mellitus*. 2021;13(04):315–409. doi:10.3760/cma.j.cn115791-20210221-00095
14. Yu P, Ji Y, Wang H, Liu K. Association between RBC folate and diabetic nephropathy in Type2 diabetes mellitus patients: a cross-sectional study. *Sci Rep*. 2024;14(1):24692. doi:10.1038/s41598-024-76456-0
15. Barrea L, Vetrani C, Caprio M, et al. Nutritional management of type 2 diabetes in subjects with obesity: an international guideline for clinical practice. *Crit Rev Food Sci Nutr*. 2023;63(16):2873–2885. doi:10.1080/10408398.2021.1980766
16. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabet Res Clin Pract*. 2022;183:109119. doi:10.1016/j.diabres.2021.109119
17. Bragg F, Halsey J, Guo Y, et al. Blood pressure and cardiovascular diseases in Chinese adults with type 2 diabetes: a prospective cohort study. *Lancet Reg Health West Pac*. 2021;7:100085. doi:10.1016/j.lanwpc.2020.100085
18. Perdomo CM, Cohen RV, Sumithran P, Clément K, Frühbeck G. Contemporary medical, device, and surgical therapies for obesity in adults. *Lancet*. 2023;401(10382):1116–1130. doi:10.1016/S0140-6736(22)02403-5
19. Duan X, Zhang L, Liao Y, et al. Semaglutide alleviates gut microbiota dysbiosis induced by a high-fat diet. *Eur J Pharmacol*. 2024;969:176440. doi:10.1016/j.ejphar.2024.176440
20. Zhu QR, Dieuwertje EK, Bekele HT, et al. Association of serum folate and Vitamin B12 concentrations with obesity in Chinese children and adolescents. *Biomed Environ Sci*. 2024;37(3):242–253. doi:10.3967/bes2024.028
21. Riggen-Bueno V, Del Toro-Arreola S, Baltazar-Díaz TA, et al. Intestinal dysbiosis in subjects with obesity from Western Mexico and its association with a proinflammatory profile and disturbances of folate (B9) and carbohydrate metabolism. *Metabolites*. 2024;14(2):121. doi:10.3390/metabo14020121
22. Berardi G, Vitiello A, Abu-Abeid A, et al. Micronutrients deficiencies in candidates of bariatric surgery: results from a single institution over a 1-year period. *Obes Surg*. 2023;33(1):212–218. doi:10.1007/s11695-022-06355-8
23. Voruganti VS. Precision nutrition: recent advances in obesity. *Physiology*. 2023;38(1):42–50. doi:10.1152/physiol.00014.2022
24. Bradley M, Melchor J, Carr R, Karjoo S. Obesity and malnutrition in children and adults: a clinical review. *Obes Pillars*. 2023;8:100087. doi:10.1016/j.obpill.2023.100087
25. Montaser E, Shah VN. Prediction of incident diabetic retinopathy in adults with type 1 diabetes using machine learning approach: an exploratory study. *J Diabetes Sci Technol*. 2024. doi:10.1177/19322968241292369
26. Chen HL, Wu C, Cao L, Wang R, Zhang TY, He Z. The association between the neutrophil-to-lymphocyte ratio and type 2 diabetes mellitus: a cross-sectional study. *BMC Endocr Disord*. 2024;24(1):107. doi:10.1186/s12902-024-01637-x