Association of Serum Osteopontin with Osteoporosis in Pre- and Postmenopausal Women and Its Relation to Diabetes Status

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Abstract: Osteoporosis is a metabolic skeletal disorder characterized by reduced bone mineral density and increased susceptibility to fractures. Osteopontin (OPN) is a multifunctional glycoprotein involved in bone remodelling through regulation of osteoblast and osteoclast activity. This study aimed to evaluate serum OPN levels in women with osteoporosis and investigate its association with diabetic status and metabolic parameters. This case-control study included 100 women aged 40 years and older, classified according to menopausal status (premenopausal and postmenopausal), type 2 diabetes mellitus status, and healthy controls. Serum OPN, fasting blood glucose, fasting insulin, HbA1c, and HOMA-IR were measured and compared among groups. The results demonstrated significantly elevated serum OPN levels in all osteoporotic groups compared with controls ($p < 0.01$), indicating increased bone remodelling activity. HbA1c and fasting blood glucose levels were also significantly higher in patient groups, whereas fasting insulin showed no significant differences. HOMA-IR was increased in some patient subgroups, particularly among older participants, but differences were not consistent across all categories. No significant correlations were observed between OPN and glycemic parameters, suggesting that OPN elevation is primarily associated with bone metabolism rather than glucose regulation. Receiver operating characteristic (ROC) analysis showed excellent diagnostic performance of OPN for identifying osteoporosis, with an area under the curve (AUC) of 0.985, sensitivity of 91%, specificity of 100%, and accuracy of 92%. These findings indicate that serum OPN may represent a promising biomarker for osteoporosis detection and reflect alterations in bone remodelling independent of metabolic status. Further studies with larger populations and longitudinal designs are required to confirm its clinical applicability.

1 INTRODUCTION

Osteoporosis is a chronic systemic skeletal disease characterised by reduced bone mass and deterioration of bone microarchitecture, leading to increased fragility and fracture risk. The World Health Organisation (WHO) defines osteoporosis as a metabolic disorder of the skeleton that affects an estimated 200 million people globally; the term literally means “porous bone” [1]. Osteoporosis is a primary global health concern and affects people worldwide, it particularly impacts postmenopausal women due to estrogen deficiency. The lifetime fracture risk is about 1 in 3 for women and 1 in 5 for men over 50, fragility fractures, especially those of the hip and vertebrae, are associated with high morbidity and mortality [2], [3]. The relationship between osteoporosis and diabetes mellitus has been extensively studied; however, the interaction between osteoporosis in pre-/postmenopausal women and glycemic markers remains insufficiently explained [4], [5]. There is an evident influence of biomarkers, such as osteopontin, on menopausal status and diabetes markers. Osteoporosis is classified into two main types: primary and secondary, primary osteoporosis develops naturally with aging and is not associated with an underlying disease, it includes Type I (postmenopausal osteoporosis), which mainly affects trabecular bone in postmenopausal women and increases the risk of spine and wrist fractures, and Type II (senile osteoporosis), which occurs after the age of 70 in both sexes and affects both trabecular and cortical bone, leading to a higher risk of hip and spine fractures [6]. Secondary osteoporosis results from

identifiable medical conditions or lifestyle factors such as chronic diseases, endocrine disorders, nutritional deficiencies, physical inactivity, and smoking [7]. The severity of osteoporosis ranges from mild bone loss to advanced stages with fragility fractures, which influences treatment and prevention strategies [8].

Diabetes Mellitus (DM) is a chronic metabolic disorder characterised by persistent hyperglycemia resulting from defects in insulin secretion, action, or both [9]. Epidemiological studies report that individuals with T2DM are at an elevated risk of fractures, though findings about bone mineral density (BMD) are inconsistent [10].

Osteopontin (OPN) is a multifunctional glycoprotein expressed in various tissues, including bone, liver, and immune cells. It participates in bone remodelling by regulating osteoblast and osteoclast activity and is also involved in inflammatory signalling pathways. Recent evidence indicates that OPN levels are altered in metabolic disorders, including insulin resistance, obesity, and T2DM. This suggests its potential role as a mediator linking metabolic dysregulation with skeletal health [11]. In bone metabolism, OPN also facilitates osteoclast attachment to the bone surface and regulates bone remodeling; abnormal levels may disrupt the balance between bone formation and resorption, contributing to osteoporosis and increased skeletal fragility [12].

The present study aims to assess the association between osteopontin (OPN) levels and bone health, as well as key metabolic indicators, HOMA-IR, in women with osteoporosis, considering menopausal status (pre- or post-menopause) and diabetes.

2 METHODOLOGY

This case-control study included 100 women aged 40 years and older, with no upper age limit, stratified by age into two categories (40–50 and ≥51 years, as shown in Table 1) and divided into five groups according to menopausal status and diabetes status (with or without diabetes), and a healthy control group .Inclusion criteria included women aged 40≥60 years. Data were collected from October 2025 to April 2026 at Imam Al-Hassan Al-Mujtaba Hospital. The collected data included age, menopausal status, type 2 diabetes status, weight, height, and BMI. Inclusion and exclusion criteria were as follows: Women aged 40 to ≥60 years, with or without diabetes, were included. Women were excluded if they had conditions or medications affecting bone health (e.g., liver disease, chronic kidney disease, malignancies, arthritis, systemic lupus erythematosus, long-term corticosteroids, hormonal therapies, specific osteoporosis treatments), other significant bone diseases, recent fractures, or were pregnant or breastfeeding.

A 5 mL venous blood sample was collected from each participant. The blood was centrifuged to separate the serum, while another portion was collected in an EDTA tube for the measurement of HbA1c and complete blood count (CBC) [13].

The separated serum was stored at −18°C until osteopontin, fasting insulin, and fasting blood glucose were analysed in accordance with the study protocol. Osteopontin (OPN) was measured with a commercial ELISA kit based on the Sandwich ELISA principle. The colour intensity is proportional to OPN concentration. Kit: Elabscience®, USA. Fasting insulin was measured with an ELISA kit. Colour intensity reflects insulin concentration. Kit: Elabscience, USA. Fasting blood glucose was measured using a commercial kit based on the Trinder enzymatic colourimetric assay, in which glucose is converted to a red dye, and the colour intensity is proportional to the glucose concentration in the sample. The assay was performed using a kit from Linear Chemicals, Spain, suitable for human samples. HOMA-IR assesses insulin resistance and is calculated from fasting glucose and insulin levels. Glycated Haemoglobin (HbA1c) shows average blood glucose over 2–3 months by measuring glucose-bound haemoglobin. It is widely used to assess long-term glycemic control in diabetes [14], [15].

Table 1: Demographic Criteria in pre-post osteoporosis patients related to diabetes state compared with control.

Parameters	Groups	Control	Post with D.M	Post without D.M	Pre with D.M	Pre without D.M	p-value
Age (years)	40-50	40.0%	0.0%	0.0%	60.0%	60.0%	<0.001
	≥ 51	60.0%	100.0%	100.0%	40.0%	40.0%	
BMI kg/m²	normal weight	100.0%	24.0%	16.0%	20.0%	13.3%	<0.001
	Over weight	0.0%	32.0%	32.0%	40.0%	20.0%	
	Obese	0.0%	44.0%	52.0%	40.0%	66.7%	

2.1 Ethical Statement

The Ethics Committee approved the conduct of this study at the College of Applied Medical Sciences, Department of Pathological Analysis, University of Karbala. CLAMSKY/20.

2.2 Statistical Analysis

Statistical analysis was performed using SPSS version 26. The normality of data distribution was assessed using the Shapiro–Wilk test, which indicated that the data were normally distributed. Accordingly, after confirming the underlying assumptions, a one-way ANOVA was applied to compare means across multiple groups for continuous variables. The Chi-square test was used to evaluate associations between categorical variables. A p-value of less than 0.05 was considered statistically significant.

3 RESULTS

The result presents the distribution of participants by clinical demographic characteristics, showing statistically significant differences ($p < 0.01$) in age, body mass index (BMI), between osteoporotic female patients in pre-post menopause and the control group Table 1.

As shown in Table 2, the result exhibited significantly elevated serum osteopontin levels for premenopausal osteoporosis with and without diabetes mellitus compared to controls across both age categories. In addition, HbA1c and fasting blood glucose levels were significantly higher in patient groups, whereas no significant differences were detected in fasting insulin levels. HOMA-IR was statistically significant only in the older age group (≥51 years). No significant variation was observed within the same age groups.

The results of Table 3 showed that also significant increase ($p<0.01$) in the level of osteopontin in postmenopausal osteoporosis patients as compared to controls. HbA1c and fasting blood glucose were significantly increased. Fasting insulin did not differ, whereas HOMA-IR was higher in patients, indicating increased insulin resistance.

The results show the effect of body mass index (BMI) on biochemical parameters, with higher osteopontin levels across all patient groups than in the control group. It also demonstrates increased HbA1c and fasting blood glucose levels, particularly in overweight and obese groups. Fasting insulin showed minimal changes, while HOMA-IR showed statistically significant differences only in some BMI categories. No significant differences were observed within groups according to BMI in Table 4.

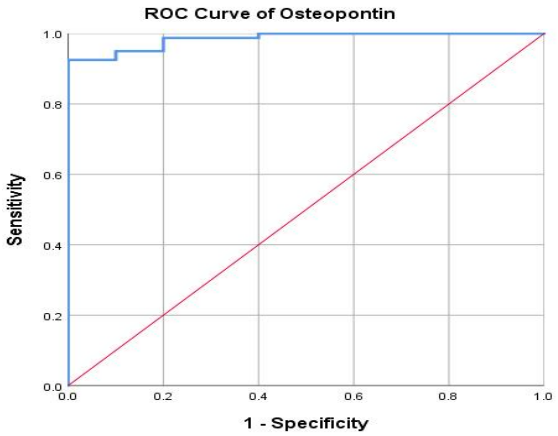

Figure 1: Receiver Operating Characteristic (ROC) Curve for Osteopontin biomarker.

The results show no significant correlation between osteopontin and HbA1c, fasting blood glucose, fasting insulin, or HOMA-IR. This means osteopontin is not directly related to glycemic status in Table 5.

Results in Table 6 and Figure 1 show that osteopontin has excellent diagnostic ability. The AUC was 0.985, with 91% sensitivity, 100% specificity, and 92% accuracy. This indicates that osteopontin is a strong biomarker for detecting osteoporosis.

4 DISCUSSION

The present study demonstrated a significant elevation in serum osteopontin (OPN) levels in all osteoporotic groups compared with the control group, indicating increased bone turnover and enhanced bone remodelling activity. These findings are consistent with the established biological role of OPN as a marker of both bone resorption and formation, particularly in conditions associated with reduced bone mineral density and an increased risk of osteoporosis [16].

Furthermore, OPN levels were markedly elevated in both premenopausal and postmenopausal women with osteoporosis, suggesting that age-related hormonal changes may contribute to the activation of bone remodelling. However, no significant differences were observed when groups were stratified by age or body mass index (BMI),

indicating that neither factor directly influences OPN levels within the same disease category[17], [12].

Garding glycemic control parameters, no significant correlations were identified between OPN and HbA1c, fasting blood glucose, insulin, or HOMA-IR. This suggests that OPN elevation is primarily associated with bone turnover activity rather than glucose metabolism or insulin resistance [18], [19].

With respect to bone mineral density, OPN levels were significantly higher in patients with reduced bone density compared with controls, confirming its association with osteoporosis. However, no clear differences were observed across degrees of bone loss, indicating that OPN is more useful for detecting disease than assessing its [20].

From a diagnostic perspective, ROC curve analysis demonstrated excellent performance of OPN in distinguishing osteoporotic patients from healthy controls, with an AUC of 0.985, high sensitivity, high specificity, and strong overall diagnostic accuracy (Ardizzone et al., 2025). These findings support its potential value as a reliable biomarker for early detection of [21], [22].

Overall, the results of this study indicate that OPN mainly reflects bone-remodelling activity in both pre- and postmenopausal osteoporosis, with no clear association with metabolic parameters such as glycemic control, supporting its role as a promising biomarker for the assessment and diagnosis of osteoporosis.

Table 2: Comparison of steopontin, glycemic parameters in premenopausal osteoporosis related to diabetes mellitus as compared to controls based on age factor.

Biomarkers	Age Categories	Pre with D.M	Pre without D.M	Control	p-value
		Mean ± S.D.	Mean ± S.D..	Mean ± S.D.	
Osteopontin ng/mL	40-50	58.93 ±25.80	49.14 ±27.57	14.33 ±9.18	0.024
	≥ 51	71.34 ±19.01	59.53 ±25.52	13.10 ±8.41	<0.001
	p-value	0.333	0.475	0.831	
HBA1c %	40-50	7.08 ±1.11	4.92 ±.52	5.48 ±.38	<0.001
	≥ 51	6.88 ±.31	5.30 ±.54	5.48 ±.55	<0.001
	p-value	0.679	0.202	0.992	
Fasting blood glucose mg/dL	40-50	156.01 ±32.42	190.77 ±50.35	99.59 ±14.36	0.004
	≥ 51	169.23 ±52.70	192.25 ±63.49	97.90 ±20.44	0.012
	p-value	0.555	0.961	0.890	
Fasting blood insulin µIU/mL	40-50	2.35 ±1.31	1.74 ±1.09	1.14 ±.54	0.206
	≥ 51	1.46 ±.95	2.01 ±1.22	.97 ±.32	0.177
	p-value	0.117	0.667	0.549	
HOMA-IR	40-50	.89 ±.47	.79 ±.49	.29 ±.17	0.096
	≥ 51	.55 ±.32	.81 ±.41	.24 ±.11	0.019

Table 3: Comparison of osteopontin, glycemic profile between postmenopausal osteoporosis patients with and without diabetes mellitus and control groups based on age factor.

Biomarkers	Age Categories	Post with D.M	Post without D.M	Control	p-value
		Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	
Osteopontin ng/mL	≥ 51	55.07 ±20.87	61.65 ±30.22	13.10 ±8.41	<0.001
HBA1c %	≥ 51	7.46 a ±.85	5.54 b ±.41	5.48 b ±.55	<0.001
Fasting blood glucose mg/dL	≥ 51	149.36 ±34.58	163.75 ±47.48	97.90 ±20.44	0.003
Fasting blood insulin µIU/mL	≥ 51	1.88 ±1.10	2.01 ±1.22	.97± .32	0.135
HOMA-IR	≥ 51	.70 ±.48	.77 ±.49	.24 ±.11	0.045

Table 4: Comparison of Osteopontin, glycemic profile between pre-postmenopausal osteoporosis patients with and without diabetes mellitus and control groups based on BMI factor.

Biomarkers	BMI Categories	Post with DM	Post without DM	Pre with DM	Pre without DM	Control	p-value
		Mean ±S.D.	Mean ±S.D.	Mean ±S.D.	Mean ±S.D.	Mean ±S.D.	
Osteopontin ng/mL	Normal weight	64.74 ±28.29	66.11 ±24.07	73.36 ±26.96	40.83 ±.30	13.59±8.23	0.002
	Over weight	50.42 ±23.06	58.98 ±31.37	59.34 ±24.06	69.52 ±44.57		<0.001
	Obese	53.19 ±14.01	61.92 ±33.11	63.71 ±24.26	50.93 ±22.59		<0.001
	p-value	0.430	0.933	0.730	0.468		
HBA1c%	Normal weight	7.72 A ±.83	5.47 B ±.68	6.34 A ±.72	4.86 B ±.35	5.48 B ±.47	0.003
	Over weight	7.09 A ±.66	5.64 B ±.30	6.90 A ±.88	4.59 B ±.17		<0.001
	Obese	7.58 A ±.95	5.51 B ±.39	7.43 A ±.79	5.26 B ±.56		<0.001
	p-value	0.321	0.721	0.197	0.150		
Fasting blood glucose mg/dL	Normal weight	134.28 ±35.15	168.51 ±67.16	198.07 ±43.89	166.50 ±56.15	98.58 C±17.37	0.006
	Over weight	162.10 A ±36.47	161.99 A ±38.10	156.09 A ±34.72	235.69 B ±26.58		<0.001
	Obese	148.32 ±32.45	163.38 ±50.26	148.13 ±39.45	183.04 ±55.83		<0.001
	p-value	0.341	0.976	0.209	0.275		
Fasting blood insulin µIU/mL	Normal weight	2.27 ±1.05	3.27 ±1.40	1.77 ±1.00	1.30 ±.60	1.04 ±.40	0.027
	Over weight	1.74 ±1.21	2.08 ±1.29	2.51 ±1.59	2.00 ±.91		0.135
	Obese	1.77 ±1.11	1.57 ±.88	1.59 ±.86	1.92 ±1.27		0.311
	p-value	0.635	0.043	0.436	0.772		
HOMA-IR	Normal weight	.77 ±.45	1.12 ±.46	.84 ±.52	.49 ±.07	.26 ±.13	0.004
	Over weight	.69 ±.54	.84 ±.56	.91 ±.50	1.06 ±.46		0.022
	Obese	.67 ±.48	.61 ±.41	.56 ±.31	.78 ±.46		0.057
	p-value	0.913	0.166	0.367	0.386		

Table 5: The correlation between osteopontin with glycemic profile parameters in all patients.

Biomarkers		HBA1c %	FBS mg/dL	FBI µIU/mL	HOMA-IR
Osteopontin *ng/mL*	*R-value*	0.008	0.012	0.128	0.146
	P-value	0.945	0.914	0.259	0.196

Table 6: Receiver Operating Characteristic (ROC) curve for osteopontin biomarker.

Metric	S.E.	p-value	Asymptotic 95% Confidence Interval		Cut-off point	AUC	Accuracy	Specificity	Sensitivity
			Lower Bound	Upper Bound					
Osteopontin ng/mL	.011	<0.001	.964	1.000	30.865	0.985	92%	100%	91%

5 CONCLUSIONS

This study demonstrated significantly increased serum osteopontin (OPN) levels in women with osteoporosis compared with healthy controls, indicating enhanced bone remodelling activity. Elevated OPN levels were observed regardless of menopausal status and diabetic condition, suggesting that OPN is closely associated with osteoporotic changes rather than metabolic alterations.

No significant correlations were identified between OPN and glycemic parameters, including HbA1c, fasting blood glucose, fasting insulin, and HOMA-IR. These findings indicate that OPN may

reflect bone metabolic activity independently of glucose regulation and insulin resistance.

ROC curve analysis demonstrated excellent diagnostic performance of OPN, supporting its potential value as a biomarker for osteoporosis detection. However, further investigations involving larger multicenter cohorts, longitudinal follow-up, and comparison with established bone turnover markers are necessary before its clinical application.

REFERENCES

[1] H. Y. Wu et al., "Tai Chi on Bone Mineral Density of Postmenopausal Osteoporosis: A Protocol for Systematic Review and Meta-Analysis," Medicine (United States), vol. 99, no. 36, p. E21928, 2020, [Online]. Available: https://doi.org/10.1097/MD.0000000000021928.

[2] Y. Shen et al., "The Global Burden of Osteoporosis, Low Bone Mass, and Its Related Fracture in 204 Countries and Territories, 1990-2019," Frontiers in Endocrinology, vol. 13, pp. 1-11, 2022, [Online]. Available: https://doi.org/10.3389/fendo.2022.882241.

[3] S. Özmen et al., "Prevalence and Risk Factors of Osteoporosis: A Cross-Sectional Study in a Tertiary Center," Medicina, vol. 60, no. 12, pp. 1-13, 2024, [Online]. Available: https://doi.org/10.3390/medicina60122109.

[4] A. Roomi et al., "Evaluation of Bone Mineral Density, Serum Osteocalcin, and Osteopontin Levels in Postmenopausal Women with Type 2 Diabetes Mellitus, with/without Osteoporosis," BioMed Research International, vol. 2022, 2022, [Online]. Available: https://doi.org/10.1155/2022/1437061.

[5] D. Fodor et al., "The Value of Osteopontin in the Assessment of Bone Mineral Density Status in Postmenopausal Women," Journal of Investigative Medicine, vol. 61, no. 1, pp. 15-21, 2013, [Online]. Available: https://doi.org/10.2310/JIM.0b013e3182761264.

[6] S. S. Amarnath, V. Kumar, and S. L. Das, "Classification of Osteoporosis," Indian Journal of Orthopaedics, vol. 57, no. S1, pp. 49-54, 2023, [Online]. Available: https://doi.org/10.1007/s43465-023-01058-3.

[7] M. M. Sobh et al., "Secondary Osteoporosis and Metabolic Bone Diseases," Journal of Clinical Medicine, vol. 11, no. 9, pp. 1-36, 2022, [Online]. Available: https://doi.org/10.3390/jcm11092382.

[8] V. Chitra and S. Evelyn, "Diagnosis, Screening and Treatment of Osteoporosis - A Review," Biomedical and Pharmacology Journal, vol. 14, no. 2, pp. 567-575, 2021, [Online]. Available: https://doi.org/10.13005/bpj/2159.

[9] A. Sanyaolu et al., "Diabetes Mellitus: An Overview of the Types, Prevalence, Comorbidity, Complication, Genetics, Economic Implication, and Treatment," World Journal of Meta-Analysis, vol. 11, no. 5, pp. 134-143, 2023, [Online]. Available: https://doi.org/10.13105/wjma.v11.i5.134.

[10] D. Care and S. S. Suppl, "2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2025," Diabetes Care, vol. 48, pp. S27-S49, 2025, [Online]. Available: https://doi.org/10.2337/dc25-S002.

[11] B. Karasalih, H. Duman, M. Bechelany, and S. Karav, "Osteopontin: Its Properties, Recent Studies, and Potential Applications," International Journal of Molecular Sciences, vol. 26, no. 12, pp. 1-27, 2025, [Online]. Available: https://doi.org/10.3390/ijms26125868.

[12] Y. Lin and Y. Li, "Posttranslational Modification in Bone Homeostasis and Osteoporosis," vol. 6, no. 4, pp. 1-22, 2025, [Online]. Available: https://doi.org/10.1002/mco2.70159.

[13] E. H. Cho, K. H. Cho, H. A. Lee, and S. W. Kim, "High Serum Osteopontin Levels Are Associated with Low Bone Mineral Density in Postmenopausal Women," Journal of Korean Medical Science, vol. 28, pp. 1496-1499, 2013, [Online]. Available: https://doi.org/10.3346/jkms.2013.28.10.1496.

[14] A. H. Alarbash, S. N. Almutairi, H. R. Alazmi, A. Almutairi, and A. Almutairi, "The Contributions of Glycated Hemoglobin (HbA1c), Triglycerides, and Hypertension to Diabetic Retinopathy: Insights From a Meta-Analysis," Cureus, vol. 17, no. 2, pp. 1-11, 2025, [Online]. Available: https://doi.org/10.7759/cureus.79066.

[15] I.-C. Chang et al., "Increased Serum Osteopontin Is a Risk Factor for Osteoporosis in Menopausal Women," Osteoporosis International, vol. 21, no. 8, pp. 1401-1409, 2010, [Online]. Available: https://doi.org/10.1007/s00198-009-1107-7.

[16] A. B. Roomi, A. M. Salih, S. D. Noori, W. Nori, and S. Tariq, "Evaluation of Bone Mineral Density, Serum Osteocalcin, and Osteopontin Levels in Postmenopausal Women with Type 2 Diabetes Mellitus, with/without Osteoporosis," BioMed Research International, vol. 2022, 2022, [Online]. Available: https://doi.org/10.1155/2022/1437061.

[17] G. Brunetti, "Recent Updates on Diabetes and Bone," International Journal of Molecular Sciences, vol. 26, p. 8140, 2025, [Online]. Available: https://doi.org/10.3390/ijms26178140.

[18] Z. Hou, H. Wang, B. He, Q. Wang, and Y. Gao, "The Association Between Glycemic Indicators and Bone Mineral Density and Osteoporosis: A Cross-Sectional Study," Scientific Reports, vol. 15, pp. 1-9, 2025, [Online]. Available: https://doi.org/10.1038/s41598-025-12925-4.

[19] X. Ma and X. Zhang, "Research Progress of Diabetic Osteoporosis: A Comprehensive Review," Frontiers in Endocrinology, 2025, [Online]. Available: https://doi.org/10.3389/fendo.2025.1595228.

[20] T. Liu, Y. Wang, B. Qian, and P. Li, "Potential Metabolic Pathways Involved in Osteoporosis and Evaluation of Fracture Risk in Individuals with Diabetes," vol. 2024, 2024, [Online]. Available: https://doi.org/10.1155/2024/6640796.

[21] J. Pan et al., "Geriatric Nutritional Risk Index as a Predictor for Fragility Fracture Risk in Elderly with Type 2 Diabetes Mellitus: A 9-Year Ambispective Longitudinal Cohort Study," Clinical Nutrition, vol. 43, no. 5, pp. 1125-1135, 2024, [Online]. Available: https://doi.org/10.1016/j.clnu.2024.03.032.

[22] Y. Chen, Y. Zhang, S. Qin, F. Yu, and Y. Ni, "The Correlation Between TyG-BMI and the Risk of Osteoporosis in Middle-Aged and Elderly Patients with Type 2 Diabetes Mellitus," Frontiers in Nutrition, 2025, [Online]. Available: https://doi.org/10.3389/fnut.2025.1525105.