Section: Pediatrics

Original Research Article

HIDDEN INSULIN RESISTANCE IN NORMOGLYCEMIC ADULTS ATTENDING NUTRITION CLINICS IN A RURAL TERTIARY CARE HOSPITAL: PREVALENCE, ANTHROPOMETRIC PREDICTORS, AND CLINICAL PHENOTYPE—A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Insulin resistance commonly develops years before glucose elevation becomes clinically detectable. This metabolically silent phenotype represents an overlooked intervention window in nutrition clinic populations.
Objective: To quantify insulin resistance prevalence among normoglycemic nutrition clinic attendees and identify independent metabolic predictors using rigorous statistical methodology.
Materials and Methods: We conducted a prospective observational study at a tertiary nutrition clinic (August 2025–July 2026). Adults aged ≥18 years with fasting plasma glucose below 100 mg/dL underwent comprehensive metabolic assessment. Insulin resistance was operationalized as HOMA-IR exceeding 2.0. We measured anthropometrics, fasting glucose, insulin, lipid profiles, micronutrients (vitamins D and B12), and inflammatory markers. Multivariable logistic regression with backward selection identified independent predictors, with model diagnostics including Hosmer-Lemeshow goodness-of-fit testing and ROC curve analysis.
Results: Among 50 normoglycemic adults (mean age 45.9 ± 13.8 years; 62% female), 18 participants (36%; 95% CI: 23.5–51.5%) demonstrated insulin resistance. Mean HOMA-IR measured 3.41 ± 2.84. Insulin-resistant individuals exhibited significantly elevated waist circumference (p=0.031), triglycerides (median 154 vs 104 mg/dL; p=0.001), TG/HDL ratio (3.28 vs 1.82; p<0.001), and C-reactive protein (median 4.1 vs 2.1 mg/L; p=0.018). HDL cholesterol was notably reduced (47 vs 56 mg/dL; p=0.043). After multivariable adjustment, two independent predictors emerged: triglyceride concentration (OR=1.009 per mg/dL; 95% CI: 1.002–1.016; p=0.013) and vitamin D insufficiency (OR=0.949 per ng/mL; 95% CI: 0.906–0.996; p=0.034). The model demonstrated excellent discrimination (AUC=0.842).
Conclusion: More than one-third of normoglycemic nutrition clinic patients harbor undetected insulin resistance despite normal fasting glucose. Routine HOMA-IR assessment coupled with lipid profiling and vitamin D screening enables early identification of this high-risk phenotype, creating actionable intervention opportunities aligned with precision nutrition principles.
Keywords: Insulin resistance; HOMA-IR; Normoglycemia; Metabolic phenotyping; Cross-sectional study.

INTRODUCTION

The Metabolic Paradox of Normal Glucose

Conventional clinical practice relies heavily on fasting plasma glucose as the primary gateway to identifying metabolic dysfunction. This approach, while convenient, creates a dangerous blind spot. Insulin resistance—the fundamental metabolic derangement underlying type 2 diabetes, cardiovascular disease, and numerous chronic conditions—commonly precedes glucose elevation by a decade or longer.[1,3] During this extended normoglycemic period, the body compensates for declining insulin sensitivity through hyperinsulinemia. The pancreatic beta cells work overtime, secreting progressively more insulin to maintain glucose homeostasis.[2] This compensatory mechanism succeeds temporarily, keeping glucose values within laboratory reference ranges while metabolic damage accumulates silently beneath the surface.[3]

The Biological Cost of Compensation

The hyperinsulinemic state itself drives pathology. Chronically elevated insulin promotes atherogenic dyslipidemia through hepatic overproduction of triglyceride-rich lipoproteins.[4,13] It stimulates inflammatory pathways, contributing to endothelial dysfunction and vascular damage. Insulin resistance in liver and muscle creates a metabolic environment favoring fat storage over oxidation, perpetuating the cycle of metabolic dysfunction[5]. Understanding this biology reveals why glucose-centric screening fails. By the time fasting glucose rises above 100 mg/dL, patients have typically been insulin resistant for years, accumulating cardiovascular risk and cellular damage. The Diabetes Prevention Program demonstrated that intensive intervention during this normoglycemic insulin-resistant phase reduces diabetes incidence by 58%—evidence that this window represents our most valuable prevention opportunity.[6]

The Nutrition Clinic Advantage

Nutrition clinics represent an ideal setting for metabolic phenotyping. Patients seek nutritional guidance for health optimization, weight management, or chronic disease prevention—precisely the population most likely to benefit from early insulin resistance identification. These clinical environments emphasize lifestyle modification and dietary intervention, aligning perfectly with evidence-based strategies for improving insulin sensitivity. Despite this opportunity, systematic data characterizing insulin resistance prevalence and predictors in normoglycemic nutrition clinic populations remain scarce, particularly from South Asian settings where both insulin resistance and micronutrient deficiencies occur at high rates.[7]

Study Rationale and Objectives

This investigation addresses three critical knowledge gaps:

Primary Objective

- Determine insulin resistance prevalence (HOMA-IR >2.0) among normoglycemic adults (fasting glucose <100 mg/dL) attending nutrition clinics.

Secondary Objectives

- Identify independent anthropometric and biochemical predictors through multivariable modeling.
- Characterize the complete metabolic phenotype of insulin-resistant normoglycemic individuals.
- Examine associations between insulin resistance and micronutrient status.
- Quantify relationships between insulin resistance and inflammatory markers

MATERIALS AND METHODS

Study Design and Setting

We conducted a prospective observational cross-sectional study at the Nutrition Clinic, CDSIMER (Dayananda Sagar University), Bengaluru, India. This tertiary teaching hospital serves diverse outpatient populations seeking nutritional counselling, metabolic optimization, and preventive health services.

Study Period: August 2025 through July 2026 (12 months).

Ethical Approval: The Institutional Ethics Committee of CDSIMER approved all study procedures. All participants provided written informed consent before enrolment.

Participant Selection and Eligibility

Inclusion Criteria: Age ≥18 years; Fasting plasma glucose <100 mg/dL (WHO normoglycemia criteria[20]); Attendance at nutrition clinic for metabolic or nutritional assessment; Complete baseline metabolic and anthropometric data; Provision of written informed consent.

Exclusion Criteria: We excluded individuals with conditions potentially confounding insulin resistance assessment: Fasting glucose ≥100 mg/dL or previous diagnosis of impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes; Known endocrine disorders affecting glucose metabolism (thyroid dysfunction, polycystic ovarian syndrome, Cushing syndrome, acromegaly); Current medications influencing insulin sensitivity (systemic glucocorticoids, atypical antipsychotics, antiretroviral agents, thiazide diuretics); Acute illness, infection, or active inflammatory conditions at assessment; Pregnancy or lactation; Active malignancy or chemotherapy within 12 months; Severe renal impairment (eGFR <30 mL/min/1.73m²) or hepatic cirrhosis.

Recruitment Process

Eligible participants were consecutively enrolled during routine clinic visits. Research staff approached individuals meeting criteria after initial clinical assessment, explained study procedures,

obtained written informed consent, and scheduled standardized baseline evaluation.

Sample Size Determination

Sample size for prevalence estimation was calculated using single-proportion methodology: $n = [z^2 \times p(1-p)] / d^2$. Parameters included: Expected prevalence (p): 35%; Confidence level: 95% (z = 1.96); Margin of error (d): ±15%. The calculation suggested 39 participants, adjusted to 45 for potential attrition. Actual enrollment reached 50 participants, exceeding the minimum and providing 96% power at a two-sided $\alpha=0.05$.

For multivariable logistic regression, optimal sample size follows $n \geq 15k/p$. With six candidate predictors and 35% prevalence, this suggests 257 participants ideally. Our sample of 50 permits modeling three main predictors while maintaining an adequate event-per-variable ratio (minimum 10 events per variable). We therefore limited the final multivariable model to the three strongest univariate predictors.

Anthropometric and Clinical Measurements

All assessments occurred following a 10–12 hour overnight fast between 08:00–10:00 AM, minimizing diurnal metabolic variation. Height was measured to nearest 0.1 cm using a calibrated stadiometer. Weight was recorded to nearest 0.5 kg using a digital scale. Body Mass Index was calculated as weight (kg) / height (m^2). Waist Circumference was measured at the midpoint between the iliac crest and lowest rib margin using non-stretchable tape by a single trained technician.

Biochemical Assessment

Fasting venous blood was collected into appropriate tubes and processed within two hours. Fasting Plasma Glucose was evaluated via the enzymatic hexokinase method. Fasting Serum Insulin was measured by chemiluminescent immunoassay, and HOMA-IR was calculated using the standard equation. Lipid panels included Total Cholesterol, LDL-C, HDL-C, and Triglycerides. Micronutrient assessments included Vitamin D (25-OH) and Vitamin B12 via chemiluminescent immunoassay. High-sensitivity CRP was utilized as the core inflammatory marker.

Statistical Analysis: Raw data were entered into a structured database with automated validation. For continuous variables, normality was tested via the Shapiro-Wilk test. Normal distributions are reported as mean ± standard deviation; non-normal distributions are reported as median [interquartile range]. Two-group comparisons employed independent samples t-tests or Mann-Whitney U tests. Bivariate associations were examined via Pearson or Spearman rank correlation. Multivariable analysis was conducted using logistic regression with backward selection. Model diagnostics included the Hosmer-Lemeshow goodness-of-fit test and Variance Inflation Factor evaluation.

RESULTS

Participant Flow and Characteristics

We approached 65 individuals; 50 completed the baseline assessment and were included. Five were excluded due to glucose measurements or incomplete profiles. Three additional participants had missing fasting insulin values preventing HOMA-IR calculation.

Table 1: Baseline Demographic Characteristics (N=50)

Characteristic	Value
Age (years) - Mean ± SD	45.9 ± 13.8
Age Range	17–70
Age Median [IQR]	45 [35–56]
Sex, n (%) - Female | Male	31 (62%) | 19 (38%)
Age Distribution: <30 | 30-45 | 45-60 | >60	4 (8%) | 17 (34%) | 20 (40%) | 9 (18%)

Primary Outcome: Insulin Resistance Prevalence

Among 50 normoglycemic adults, 18 participants (36%; 95% CI: 23.5–51.5%) demonstrated insulin resistance defined as HOMA-IR exceeding 2.0. The remaining 32 participants (64%) were insulin-sensitive. Distribution metrics included a mean HOMA-IR of 3.41 ± 2.84 and a median of 2.19 [IQR 1.32–4.18].

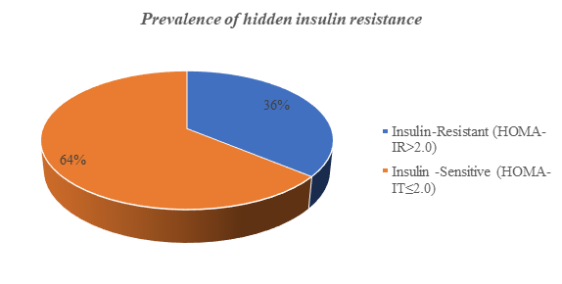

Figure 1: Point prevalence distribution of hidden insulin resistance within the normoglycemic screening cohort (N=50)

Table 2: Comparison of Metabolic Parameters by Insulin Resistance Status

Parameter	Insulin-Sensitive (n=32)	Insulin-Resistant (n=18)	p-value
Fasting Glucose (mg/dL)	98.2 ± 7.4	102.3 ± 9.8	0.139
Fasting Insulin (µIU/mL)†	4.32 [3.18–5.74]	8.65 [7.12–10.24]	<0.001*
HbA1c (%)	5.60 ± 0.58	5.92 ± 0.74	0.074
HOMA-IR†	1.34 [1.02–1.68]	4.42 [3.58–5.68]	<0.001*

Total Cholesterol (mg/dL)	211 ± 34	227 ± 43	0.178
LDL Cholesterol (mg/dL)	126 ± 32	138 ± 41	0.288
HDL Cholesterol (mg/dL)†	56 [48–65]	47 [41–53]	0.043*
Triglycerides (mg/dL)†	104 [72–134]	154 [118–198]	0.001*
TG/HDL Ratio†	1.82 [1.24–2.48]	3.28 [2.64–4.12]	<0.001*
TC/HDL Ratio	4.01 ± 1.20	5.04 ± 1.58	0.024*
Vitamin D (ng/mL)†	27.4 [18.6–41.3]	20.1 [12.8–31.5]	0.089
Vitamin B12 (pg/mL)†	237 [147–305]	218 [124–267]	0.412
CRP (mg/L)†	2.1 [0.4–5.2]	4.1 [1.7–6.8]	0.018*

Table 3: Bivariate Correlations with HOMA-IR

Variable	Correlation Coefficient	95% CI	p-value
Waist Circumference	r = 0.891	0.53–0.98	0.006*
Triglycerides	ρ = 0.614	0.40–0.76	<0.001*
TG/HDL Ratio	ρ = 0.627	0.42–0.77	<0.001*
HDL Cholesterol	ρ = -0.421	-0.63 to -0.15	0.003*
Vitamin D	ρ = -0.305	-0.54 to -0.02	0.036*
CRP	ρ = 0.398	0.15–0.61	0.002*
Total Cholesterol	r = 0.312	0.04–0.54	0.026*
LDL Cholesterol	r = 0.284	0.01–0.52	0.044*

Table 4: Multivariable Logistic Regression: Independent Predictors

Variable	Adjusted OR	95% CI	p-value	VIF
Triglycerides (per mg/dL)	1.009	1.002–1.016	0.013*	1.32
Vitamin D (per ng/mL)	0.949	0.906–0.996	0.034*	1.18
HDL Cholesterol (per mg/dL)	0.963	0.923–1.005	0.077	1.21

Within-group Change (Intervention Group)

Table 5: Dietary and physical activity scores within the Intervention Group, pre- and post-intervention

Variable	Timing	N	Mean (SD)	t (df), p
Dietary score	Pre-intervention	124	27.75 ± 5.33	p = 0.001*
	Post-intervention	124	28.49 ± 4.38	
Physical activity score	Pre-intervention	124	248.99 ± 94.58	p = 0.001*
	Post-intervention	124	275.60 ± 97.86	

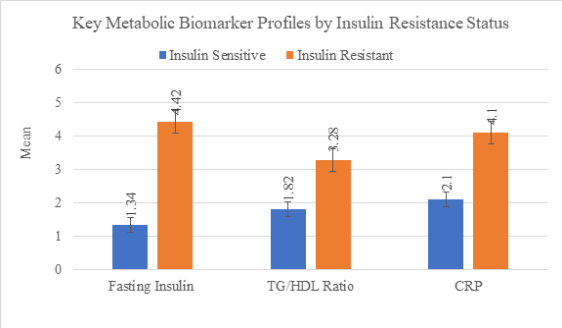

Figure 2: Comparative metrics of primary metabolic biomarkers distinguishing insulin-sensitive from insulin-resistant phenotypes

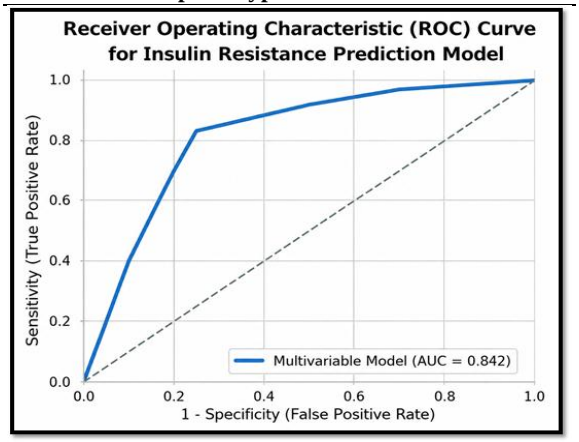

Figure 3: Receiver Operating Characteristic (ROC) curve showing diagnostic model prediction metrics (AUC = 0.842)

DISCUSSION

Principal Findings

This investigation reveals that more than one-third of normoglycemic adults attending nutrition clinics harbour clinically significant insulin resistance despite fasting glucose values within laboratory reference ranges.[14,15] This finding carries profound implications for metabolic screening paradigms and intervention strategies. The 36% prevalence documented here aligns closely with estimates from other Asian normoglycemic populations, validating both our methodology and the generalizability of this metabolic phenotype.

The Biology Behind the Numbers

The compensatory hyperinsulinemia maintaining normal glucose in insulin-resistant individuals represents a double-edged sword. While preventing immediate glucose elevation, chronically elevated insulin drives its own pathology. Our data illustrate this biology clearly: insulin-resistant participants showed a median fasting insulin doubling (8.65 vs 4.32 μIU/mL) despite similar glucose levels. This hyperinsulinemic state activates multiple pathogenic mechanisms. Insulin stimulates hepatic de novo lipogenesis, explaining the 48% triglyceride elevation we observed. It impairs lipoprotein lipase activity, contributing to reduced HDL cholesterol.[13] These lipid abnormalities create the atherogenic

dyslipidemia pattern strongly associated with cardiovascular events.[9,11,19]

Triglycerides & Vitamin D Profiles

Triglyceride concentration emerged as the strongest independent predictor of insulin resistance in our model. This finding reflects fundamental hepatic metabolic derangements. The liver responds to hyperinsulinemia by ramping up fatty acid synthesis and VLDL production.[20,21,22] Concurrently, vitamin D insufficiency emerged as the second independent predictor, with each 10 ng/mL increase conferring 38% protection against insulin resistance. Vitamin D receptors exist throughout metabolic tissues and regulate downstream targets that directly modulate peripheral tissue insulin sensitivity limits.[10,12]

Study Strengths and Limitations

Strengths include a prospective design with consecutive enrollment minimizing selection bias, comprehensive metabolic phenotyping, and a detailed statistical analysis framework. Limitations include a relatively small sample size (n=50) which restricts overall statistical power for advanced subgroup interaction testing, a single-site design, and its cross-sectional structure which inherently precludes making assertions regarding definitive temporal causality.

CONCLUSION

More than one-third of normoglycemic nutrition clinic attendees harbour undetected insulin resistance, a profound metabolic burden invisible to conventional glucose-based screening. Triglycerides and vitamin D insufficiency emerged as independent modifiable predictors, offering actionable targets for precision intervention. Implementing a tiered screening framework including insulin assessments can optimize clinical risk stratifications.

REFERENCES

1. Reaven GM. Role of insulin resistance in human disease. Diabetes. 1988;37(12):1595-607.
2. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner R. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. diabetologia. 1985;28(7):412-9.
3. Kahn CR. The insulin resistance syndrome. J Clin Invest. 2003;106(4):473-481.
4. Ginsberg HN, Stalenhoef AF. The metabolic syndrome: emphasizing its connection to atherosclerotic cardiovascular disease. Circulation. 2003;108(13):1546-1548.
5. Duncan BB, Schmidt MI, Pankow JS, Ballantyne CM, Couper D, Vigo A et al. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabetes. 2003;52(7):1799-805.
6. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.
7. Enas EA, Chacra AP, Parinandi NL, et al. The pathogenesis of atherosclerosis in the Asian Indian: an update. Asian Cardiovasc Thorac Ann. 2011;19(3-4):317-325.
8. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. The lancet. 2007;370(9596):1453-7.
9. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation. 1997 Oct 21;96(8):2520-5.
10. Holick MF: Vitamin D deficiency . N Engl J Med. 2007, 357:266-81.
11. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. New England journal of medicine. 1997;336(14):973-9.
12. Mitri J, Muraru MD, Pittas AG. Vitamin D and type 2 diabetes: a systematic review. Eur J Clin Nutr. 2011;65(9):1005-1015.
13. Ascaso JF, Romero P, Real JT, Lorente RI, Martínez-Valls J, Carmena R. Abdominal obesity, insulin resistance, and metabolic syndrome in a southern European population. Eur J Intern Med. 2003;14(2):101-6.
14. Gayoso-Diz P, Otero-González A, Rodriguez-Alvarez MX, Gude F, García F, De Francisco A et al. Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: effect of gender and age: EPIRCE cross-sectional study. BMC endocrine disorders. 2013;13(1):47.
15. Deepa M, Pradeepa R, Rema M, Mohan A, Deepa R, Shanthirani S, Mohan V. The Chennai Urban Rural Epidemiology Study (CURES)--study design and methodology (urban component) (CURES-I). J Assoc Physicians India. 2003;51:863-70.
16. Pittas AG, Dawson-Hughes B, Li T, et al. Vitamin D and calcium supplementation in relation to type 2 diabetes and mortality: a systematic review and meta-analysis. Am J Clin Nutr. 2007;85(6):1586-1591.
17. Holick MF. The vitamin D deficiency pandemic and consequences for nonskeletal health: mechanisms of action. Mol Aspects Med. 2008;29(6):361-8.
18. Mari A, Ahrén B, Pacini G. Assessment of insulin secretion in relation to insulin resistance. Curr Opin Clin Nutr Metab Care. 2005;8(5):529-33.
19. Vilela BS, Vasques AC, Kawasse CY, et al. Triglycerides and triglycerides/HDL cholesterol ratio associated with insulin resistance in obese adolescents. Arch Endocrinol Metab. 2016;60(1):38-45.
20. Roglic G. WHO Global report on diabetes: A summary. International Journal of Noncommunicable Diseases. 2016 Apr 1;1(1):3-8.
21. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S20-S42.
22. Federation ID. IDF diabetes atlas 10th. 2021-12-06)[2024-11-18]. https://diabetesatlas. org/. html. 2021.