Research Square

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Triglyceride-Glucose Index and Dysglycaemia in Adults from the Aral Sea Region of Uzbekistan: Associations with Thyroid Function and Elevated Aminotransferases

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Research Article

Keywords: TyG index, dysglycaemia, thyroid dysfunction, aminotransferases, type 2 diabetes, Aral Sea, Karakalpakstan, Uzbekistan

Posted Date: June 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9903554/v1

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Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at BMC Endocrine Disorders on September 7th, 2026. See the published version at https://doi.org/10.1186/s12902-026-02539-w.

Abstract

Background

The Aral Sea region of Uzbekistan represents an environmentally vulnerable setting where iodine deficiency, thyroid dysfunction and metabolic disorders may coexist [21, 22]. Biochemical data linking thyroid status, aminotransferase elevation and dysglycaemia in this population remain scarce.

Methods

A cross-sectional study included 98 adults from Muinak, Kanlykul, and Takhtakupir, Karakalpakstan (2024–2025). Anthropometry, fasting and 2-h postprandial glucose, HbA1c, thyroid hormones, aminotransferases and fasting lipid profile were assessed. Logistic regression, ROC analysis and Monte Carlo cross-validation were performed. Composite insulin-resistance markers — TyG-BMI and METS-IR — were calculated and compared with TyG alone.

Results

Women comprised 73/98 participants (74.5%). Dysglycaemia was present in 50/98 (51.0%) and hypothyroidism in 27/98 (27.6%). TyG showed a significant association with dysglycaemia (OR 2.33; 95% CI 1.31–4.15; p = 0.004), remaining significant after adjustment for BMI, TSH and ALT. ROC analysis demonstrated moderate discrimination (AUC 0.77; 95% CI 0.64–0.87). The Youden-derived threshold was 8.70, with sensitivity 43.2%, specificity 96.2%, PPV 94.1% and LR + 10.9. METS-IR yielded the highest AUC (0.79 [0.67–0.89]). Hypothyroidism was not independently associated with dysglycaemia (aOR 0.75).

Conclusions

TyG is a practical marker associated with dysglycaemia in adults from the Aral Sea region and may support risk stratification where insulin assays are unavailable. Elevated aminotransferases were linked to metabolic risk, while thyroid dysfunction appeared more closely related to central adiposity than to glycaemic status.

Background

Type 2 diabetes mellitus (T2DM) and intermediate hyperglycaemia are major contributors to cardiovascular and renal morbidity worldwide [1, 2]. Insulin resistance is central to this disease continuum and is frequently accompanied by obesity, dyslipidaemia, elevated aminotransferases and thyroid dysfunction [3, 4]. In resource-limited settings, population-level risk stratification often requires inexpensive markers that can be derived from routine biochemical tests.

The triglyceride-glucose (TyG) index, calculated from fasting triglycerides and fasting plasma glucose, is a validated surrogate marker of insulin resistance [5, 6]. Unlike HOMA-IR, it does not require fasting

insulin measurement and is therefore particularly suitable for large-scale screening or clinical risk stratification in primary care [7, 8]. TyG has been associated with incident T2DM, cardiometabolic risk and liver-related metabolic dysfunction in multiple populations [9, 10, 33].

Thyroid hormones regulate energy expenditure, lipid metabolism, hepatic glucose production and adipose tissue function [11, 12]. Hypothyroidism may contribute to central adiposity and dyslipidaemia, but its direct relationship with dysglycaemia is complex and may be mediated by obesity and other metabolic factors [13, 14, 24]. Elevated aminotransferases, especially alanine aminotransferase (ALT), can reflect hepatocellular metabolic stress and are associated with insulin resistance and future diabetes risk [15, 16, 26, 32]. However, aminotransferases alone do not establish a diagnosis of hepatic steatosis, which requires imaging or histological confirmation [17, 18].

Karakalpakstan is a unique setting for studying these interactions. The region has been affected by the Aral Sea ecological disaster, long-term environmental stressors and iodine deficiency [19–23]. Despite the high clinical relevance of thyroid and metabolic disorders in this region, peer-reviewed biochemical data remain limited. The present study therefore examined the relationship between TyG, thyroid function, elevated aminotransferases associated with metabolic dysfunction and dysglycaemia in adults from Karakalpakstan.

Methods

Study design and setting

This cross-sectional observational study was conducted in 2024–2025 in central district hospitals, primary healthcare centres and outpatient settings in Muinak, Kanlykul, and Takhtakupir, Karakalpakstan, Uzbekistan.

Participants

Adults aged 40–55 years with at least 5 years of local residency were enrolled during preventive examination or outpatient consultation. Exclusion criteria included pregnancy or lactation, active malignancy, severe acute illness and current glucocorticoid therapy. The analytical sample included 98 participants.

Measurements

Anthropometric assessment included height, weight, body mass index (BMI), waist circumference (WC) and hip circumference. Blood pressure was measured after seated rest. Venous blood was collected after an overnight fast for fasting plasma glucose (FPG), HbA1c, ALT, AST, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), thyroid-

stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4). A 2-h postprandial glucose value was also recorded.

Definitions

Dysglycaemia was defined as the presence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or T2DM according to WHO criteria. Hypothyroidism included subclinical and clinical hypothyroidism. Elevated aminotransferases associated with metabolic dysfunction were assessed using sex-specific ALT thresholds: >19 U/L for women and > 30 U/L for men.

TyG index calculation

Fasting triglycerides were measured directly as part of the standard lipid profile. The TyG index was calculated as ln[fasting TG (mg/dL) × FPG (mg/dL) / 2]. TG in mmol/L were converted to mg/dL by multiplying by 88.57; glucose in mmol/L was converted to mg/dL by multiplying by 18.018.

Statistical analysis

Continuous variables are presented as mean ± SD and categorical variables as n (%). Between-group comparisons used the Kruskal-Wallis test. Binary associations were estimated using unadjusted and adjusted odds ratios (aOR) with bootstrap 95% confidence intervals (2000 resamples). Logistic regression assessed the association between TyG and dysglycaemia in four sequential models, with BMI, TSH and ALT entered as additional covariates. To address overfitting risk in small samples, Monte Carlo cross-validation (1000 iterations, 70%/30% train/test split, stratified by outcome) and stratified 5-fold cross-validation were performed. ROC analysis evaluated TyG, TyG-BMI, METS-IR and ALT. The optimal threshold was determined by the Youden index. Composite markers were defined as: TyG-BMI = TyG × BMI (kg/m²); METS-IR = ln[(2 × FPG (mg/dL) × TG (mg/dL)/1000) + BMI] / ln[HDL-C (mg/dL)]. All analyses were conducted in Python 3.11 (SciPy 1.12, scikit-learn 1.4). Two-sided $p < 0.05$ was considered statistically significant.

Results

Participant characteristics

The study included 98 adults, of whom 73 (74.5%) were women and 25 (25.5%) were men. Mean age was 43.0 ± 0.7 years, mean BMI was 31.6 ± 5.6 kg/m² and mean waist circumference was 99.7 ± 14.7 cm. Dysglycaemia was present in 50 participants (51.0%), hypothyroidism in 27 (27.6%), and elevated ALT in 52 (53.1%) (Table 1).

Table 1
Main sample characteristics (n = 98)

Characteristic	Value
Total participants	98
Women, n (%)	73 (74.5)
Men, n (%)	25 (25.5)
Age, years (mean ± SD)	43.0 ± 0.7
BMI, kg/m² (mean ± SD)	31.6 ± 5.6
Waist circumference, cm (mean ± SD)	99.7 ± 14.7
Dysglycaemia, n (%)	50 (51.0)
Type 2 diabetes, n (%)	33 (33.7)
Hypothyroidism, n (%)	27 (27.6)
Elevated ALT by sex-specific threshold, n (%)	52 (53.1)
TyG index (mean ± SD)	7.91 ± 1.10

Metabolic parameters across glycaemic groups

BMI, WC, HbA1c, TyG and ALT differed significantly across glycaemic groups (all $p < 0.05$). TyG values were lowest in normoglycaemia (7.60 ± 0.69) and highest in the IFG group (8.62 ± 0.61; Kruskal-Wallis $p = 0.007$). TyG-BMI increased from 233 ± 47 (normoglycaemia) to 304 ± 38 (T2DM; $p < 0.001$) and METS-IR from 1.00 ± 0.06 to 1.12 ± 0.10 ($p < 0.001$). ALT increased across the glycaemic continuum (23.8 to 38.0 U/L; $p = 0.025$). TSH did not differ significantly across groups ($p = 0.186$). Full data are shown in Table 2.

Table 2
Metabolic variables by glycaemic status (mean ± SD)

Variable	Normoglycaemia	IFG	IGT	T2DM	p
BMI, kg/m²	29.4 ± 5.3	32.0 ± 6.4	33.4 ± 5.7	34.1 ± 4.7	0.002
WC, cm	93.4 ± 12.8	98.0 ± 13.9	104.2 ± 13.3	108.1 ± 13.7	< 0.001
HbA1c, %	4.36 ± 0.57	4.50 ± 0.96	5.29 ± 0.66	8.34 ± 2.70	< 0.001
TyG index	7.60 ± 0.69	8.62 ± 0.61	7.62 ± 0.53	8.34 ± 1.18	0.007
ALT, U/L	23.8 ± 12.6	28.0 ± 14.7	26.4 ± 11.1	38.0 ± 28.4	0.025
AST, U/L	30.4 ± 14.4	28.8 ± 20.5	29.3 ± 12.8	37.5 ± 21.7	0.241
TSH, mIU/L	2.80 ± 2.30	3.09 ± 3.40	1.71 ± 1.06	3.02 ± 1.91	0.186
TG, mmol/L	0.78 ± 0.81	1.30 ± 0.74	0.47 ± 0.21	0.90 ± 0.93	0.164

IFG: impaired fasting glucose; IGT: impaired glucose tolerance; T2DM: type 2 diabetes mellitus; WC: waist circumference; TG: triglycerides; TSH: thyroid-stimulating hormone. p values from Kruskal-Wallis tests.

Logistic regression

TyG was associated with dysglycaemia across all four sequential models (Table 3). Each 1-unit increase in TyG was associated with higher odds of dysglycaemia (OR 2.33; 95% CI 1.31–4.15; p = 0.004), persisting after adjustment for BMI, TSH and ALT (ORs 2.31–2.49). TyG-BMI OR 1.02 per unit (95% CI 1.01–1.04; p = 0.001); METS-IR OR 3.36 per unit (95% CI 1.95–5.32; p < 0.001). Monte Carlo cross-validated AUC for the full model was 0.76 (95% CI 0.54–0.93), confirming model stability despite small *n*.

Table 3
Logistic regression models for dysglycaemia

Model	Predictor	OR	95% CI	p
Model 1: TyG	TyG	2.33	1.31–4.15	0.004
Model 2: TyG + BMI	TyG	2.31	1.28–4.17	0.005
	BMI	1.12	1.00–1.26	0.046
Model 3: TyG + BMI + TSH	TyG	2.49	1.34–4.62	0.004
	BMI	1.13	1.01–1.27	0.036
	TSH	0.88	0.69–1.13	0.322
Model 4: TyG + BMI + TSH + ALT	TyG	2.45	1.31–4.55	0.005
	BMI	1.11	0.99–1.25	0.072
	TSH	0.89	0.69–1.15	0.380
	ALT	1.01	0.98–1.05	0.442

Outcome: dysglycaemia. ORs per 1-unit increase for continuous predictors. Bootstrap 95% CIs (2000 resamples). aOR: adjusted odds ratio.

ROC analysis

ROC analysis demonstrated moderate discrimination by TyG (AUC 0.77; 95% CI 0.64–0.87; n = 63, Fig. 1). METS-IR yielded a marginally higher AUC (0.79; 95% CI 0.67–0.89) and TyG-BMI was similar (AUC 0.76; 95% CI 0.63–0.87); confidence intervals overlapped substantially, precluding definitive superiority claims. ALT showed weaker discrimination (AUC 0.66; 95% CI 0.55–0.77). At the TyG threshold of 8.70: sensitivity 43.2%; specificity 96.2%; PPV 94.1%; NPV 53.2%; LR + 10.9; LR − 0.60. Monte Carlo cross-validation confirmed the estimate was not substantially inflated (mean AUC 0.77; 95% CI 0.58–0.93). Results are summarised in Table 4.

Table 4
Comparative ROC performance for dysglycaemia

Marker	AUC (95% CI)	CV AUC† (95% CI)	Youden threshold	Sens, %	Spec, %	PPV, %	LR+	LR−
TyG	0.77 [0.64–0.87]	0.77 [0.58–0.93]	8.70¶	43.2	96.2	94.1	10.9	0.60
TyG-BMI	0.76 [0.63–0.87]	—	248	76.3	65.4	76.3	2.2	0.36
METS-IR	0.79 [0.67–0.89]	—	1.00	86.8	65.4	78.6	2.5	0.20
ALT, U/L	0.66 [0.55–0.77]	—	21 U/L	72.0	60.4	65.5	1.8	0.46

All metrics at Youden-optimal threshold except ¶TyG at 8.70 (high-specificity operating point). †Monte Carlo cross-validated AUC (1000 × 70/30). AUC: area under ROC curve; CV: cross-validated; Sens: sensitivity; Spec: specificity; PPV: positive predictive value; LR+: positive likelihood ratio; LR−: negative likelihood ratio.

Discussion

The main finding of this study is that the TyG index was the strongest routinely available biochemical marker associated with dysglycaemia in adults from the Aral Sea region of Uzbekistan. TyG remained significant in sequential logistic regression models after adjustment for BMI and TSH, supporting its potential usefulness as a pragmatic risk-stratification marker in primary care and population-based metabolic screening.

The ROC analysis adds clinically relevant information. The TyG index demonstrated moderate discrimination (AUC 0.77). The Youden-derived threshold of 8.70 had high specificity (96.2%) but modest sensitivity (43.2%), rendering it most useful as a rule-in marker. The PPV of 94.1% means that approximately 9 of every 10 individuals above this value have dysglycaemia, which is clinically actionable without confirmatory testing. The LR + of 10.9 represents a large and diagnostically meaningful shift in post-test probability. By contrast, the LR − of 0.60 confirms that a TyG below 8.70 provides only weak reassurance and should not be used to rule out dysglycaemia.

Elevated ALT was associated with dysglycaemia but its ROC performance was weaker than that of TyG (AUC 0.66 vs 0.77). This is expected, as ALT captures only downstream hepatocellular injury [29], whereas TyG integrates both the lipid and glucose components of insulin resistance simultaneously [30].

Composite markers: TyG-BMI and METS-IR.

METS-IR (AUC 0.79) and TyG-BMI (AUC 0.76) were both comparable to TyG alone (AUC 0.77), with confidence intervals overlapping extensively. The marginal advantage of METS-IR (ΔAUC = + 0.02) is consistent with its explicit incorporation of BMI [28]. TyG-BMI did not outperform standard TyG, possibly

reflecting the compressed BMI range (28–36 kg/m²). All three markers were equivalent practical tools in this setting. The standard TyG index retains the practical advantage of requiring no HDL measurement, making it preferable where lipid panels are incomplete [5].

Hypothyroidism was common in the cohort but was not independently associated with dysglycaemia. This negative result should not be interpreted as evidence that thyroid function is irrelevant to metabolic risk. Rather, the small sample size and cross-sectional design limit causal inference. The relationship between TSH and central adiposity remains biologically plausible, given the role of thyroid hormones in adipose tissue metabolism, energy expenditure and lipid handling [31].

Several limitations should be acknowledged. First, the analytical sample is critically small for multivariate modelling. Monte Carlo cross-validation yielded a cross-validated AUC of 0.77 (95% CI 0.58–0.93), suggesting estimates are not substantially inflated, though wide CIs reflect inherent instability. Second, the cross-sectional design precludes causal inference. Third, hepatic steatosis was not assessed by ultrasound or MRI. Fourth, urinary iodine, GGT, FIB-4, alcohol intake and physical activity data were not collected. Future studies should recruit n ≥ 375, include hepatic imaging and urinary iodine assessment.

Conclusions

The TyG index was significantly associated with dysglycaemia and showed moderate ROC discrimination in adults from Karakalpakstan. The optimal threshold of 8.70 was highly specific, suggesting that TyG may help identify individuals at particularly high metabolic risk in resource-limited settings. Elevated aminotransferases were associated with dysglycaemia but should be interpreted as markers of metabolic liver stress rather than diagnostic evidence of hepatic steatosis. Hypothyroidism was common but was not independently associated with dysglycaemia in this sample (Fig. 2). Future prospective research should include larger sample sizes, hepatic imaging and urinary iodine assessment.

Abbreviations

ALT
alanine aminotransferase
aOR
adjusted odds ratio
AST
aspartate aminotransferase
AUC
area under the receiver operating characteristic curve
BMI
body mass index

CI
confidence interval
FPG
fasting plasma glucose
fT3
free triiodothyronine
fT4
free thyroxine
GGT
gamma-glutamyltransferase
HbA1c
glycated haemoglobin A1c
HDL-C
high-density lipoprotein cholesterol
HOMA-IR
homeostatic model assessment of insulin resistance
IFG
impaired fasting glucose
IGT
impaired glucose tolerance
LDL-C
low-density lipoprotein cholesterol
LR+
positive likelihood ratio
LR−
negative likelihood ratio
MASLD
metabolic dysfunction-associated steatotic liver disease
METS-IR
metabolic score for insulin resistance
NPV
negative predictive value
OR
odds ratio
PPV
positive predictive value
ROC
receiver operating characteristic
SD
standard deviation

T2DM
type 2 diabetes mellitus
TG
triglycerides
TSH
thyroid-stimulating hormone
TyG
triglyceride-glucose index
WC
waist circumference.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Ethics approval was granted by the Ethical Committee of the Republican Centre of Endocrinology, Uzbekistan (protocol #12, 27 December 2024). Written informed consent was obtained from all participants.

Consent for publication

Not applicable. The manuscript does not contain any individual person's identifiable data requiring specific consent for publication.

Competing interests

The authors declare that they have no competing interests.

Funding

This study received no specific funding.

Author Contribution

Z.I.A.: Conceptualisation, Data curation, Formal analysis, Writing – original draft. T.T.K.: Conceptualisation, Investigation, Writing – review & editing. A.V.A.: Data curation, Investigation, Writing – review & editing. Z.M.S.: Methodology, Supervision, Writing – review & editing. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

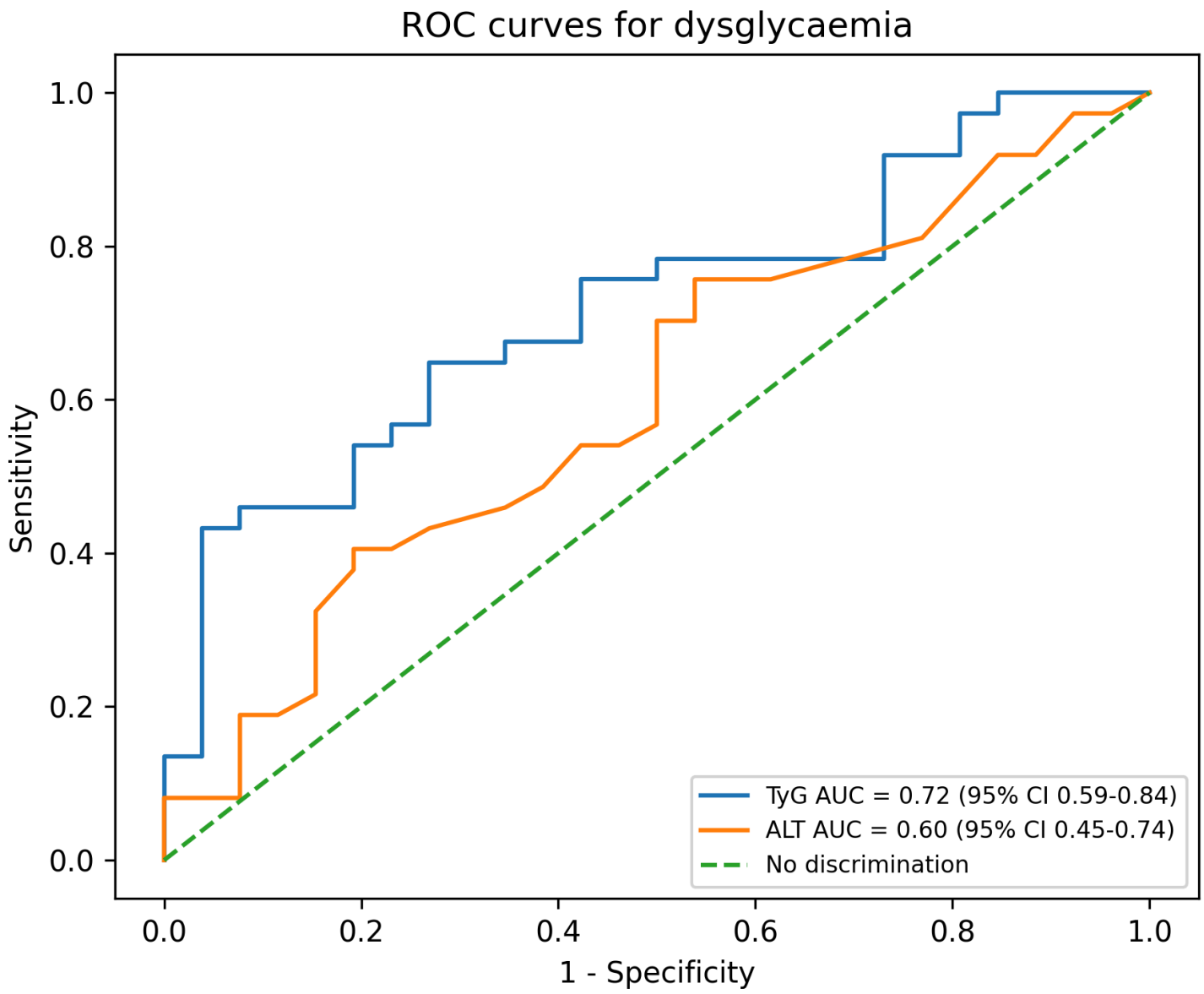


Figure 1

ROC curves for TyG index and ALT for identification of dysglycaemia.

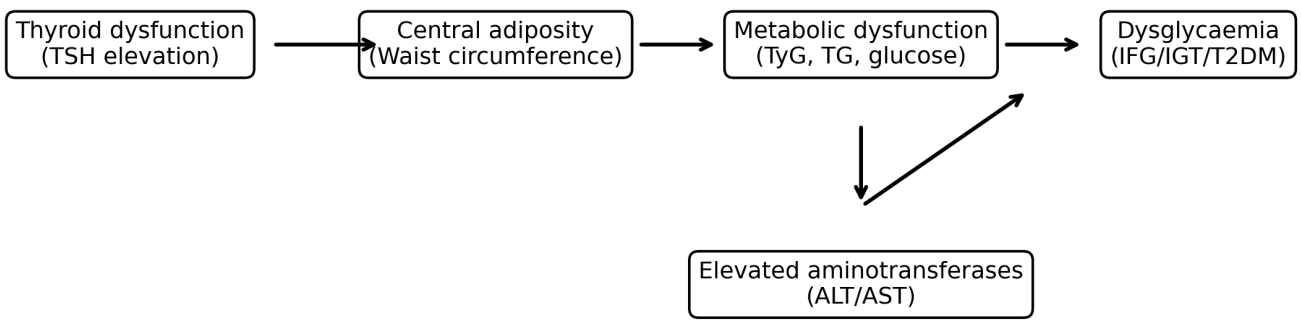


Figure 2

Conceptual model linking thyroid dysfunction, central adiposity, metabolic dysfunction and dysglycaemia.