Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Opposite-Phase Seasonal Oscillations of Fasting and Integrated Glycaemia in Pregnancy: Glycated Albumin Evidence and Implications for Gestational Diabetes Diagnosis

JiaPing Lu
Jinhua People's Hospital
Heng Xu
xheng0248@sina.com

Jinhua People's Hospital
Qiulian Xu
Jinhua People's Hospital

Research Article

Keywords: gestational diabetes, seasonality, glycated albumin, oral glucose tolerance test, chronobiology, fasting glucose

Posted Date: November 23rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11390760/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background.

Studies of seasonal variation in glucose tolerance during pregnancy have yielded inconsistent results, and post-hoc analysis of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) cohort suggested that opposing seasonal trends in fasting and post-load glucose cancel out, leaving gestational diabetes mellitus (GDM) prevalence unaffected. Glycated albumin (GA), a marker of integrated glycaemia over 2–3 weeks, has never been examined seasonally in pregnancy. We characterised seasonal oscillations of maternal glycaemic markers and quantified their association with GDM diagnosis in a Chinese population.

Methods.

Retrospective cohort of 20,897 singleton deliveries (2017–2018) at a tertiary hospital in Jinhua, China (29.08°N); 3,980 women had a complete 75-g oral glucose tolerance test (OGTT) and 2,131 had GA measurements. Single-component cosinor models adjusted for gestational age at testing, maternal age, and calendar year estimated amplitude and acrophase for fasting glucose, 1-h and 2-h glucose, GA, TSH, and free T4; albumin, uric acid, and creatinine were analysed as dilution/negative-control markers. Individual-level associations with actual monthly mean ambient temperature (NASA POWER) were estimated by linear regression. GDM was defined by IADPSG criteria. Internal replication was performed by calendar year.

Results.

Fasting glucose and GA oscillated in opposite phases: fasting glucose peaked in mid-January (amplitude 0.112 mmol/L, 95% CI 0.082–0.142, i.e. 2.4% of the mean) whereas GA peaked in July (amplitude 0.61 percentage points, 95% CI 0.50–0.72, i.e. 5.3% of the mean); 2-h glucose peaked in early autumn. Per 1°C increase in ambient temperature, fasting glucose decreased by 0.011 mmol/L and GA increased by 0.052% (both $p < 10^{-14}$). All patterns replicated independently in 2017 and 2018. GDM positivity was 31.0% for OGTTs performed in winter versus 20.6% in summer, driven entirely by the fasting criterion (22.9% vs 9.2%; OR 2.96). The absolute winter excess of fasting-positive results was 13.7 percentage points (~ 137 per 1,000 winter OGTTs); under the conservative assumption that summer rates represent the season-free baseline, up to 60% of winter fasting-positive results were season-associated. Albumin peaked in winter (indicating summer haemodilution, which the GA ratio inherently corrects), whereas uric acid and creatinine showed no annual rhythm, arguing against a generic preanalytical artefact.

Conclusions.

Fasting and integrated glycaemia oscillate in opposite phases during pregnancy. In fasting-predominant GDM populations these oscillations do not cancel out and are associated with substantial seasonal variation in GDM diagnosis. Season of testing should be considered when interpreting borderline fasting glucose values, and GA merits prospective evaluation as a complementary, season-aware marker.

Background

Seasonal variation in glucose metabolism has been recognised for decades, yet its implications for pregnancy screening remain unresolved. Schmidt et al. first reported that oral glucose tolerance in pregnant Brazilian women varied with ambient temperature, with GDM frequency rising from 4.8% in winter to 14.8% in summer [1]. A Swedish cohort of 11,538 women subsequently found peak GDM frequency and higher 2-h post-load glucose values in summer [2]. In contrast, a post-hoc analysis of 2,120 participants from the Australian HAPO centre found that fasting plasma glucose was highest in winter while post-load values were highest in summer—opposing trends that cancelled each other, leaving GDM prevalence without significant seasonal variation [3]. Reconciliation of these contradictory findings has been hampered by the absence of a marker of integrated glycaemia: all previous studies relied on single-time-point OGTT values.

Glycated albumin (GA) reflects mean glycaemia over the preceding 2–3 weeks and, because albumin turnover is rapid, is more sensitive than HbA1c to glycaemic excursions in pregnancy [4, 5]. GA has been validated against continuous glucose monitoring in pregnant women and is increasingly used for glycaemic assessment in gestational diabetes in East Asia [6]. Although seasonal variation of GA has been reported in non-pregnant populations (peaking in late spring/summer) [7, 8], no study has examined GA seasonality in pregnancy. If post-load and integrated glycaemia genuinely peak in summer, GA should reproduce this phase—a prediction independent of the preanalytical and behavioural factors that complicate interpretation of OGTT values.

The population structure of GDM may determine whether seasonal oscillations matter clinically. In East Asian populations a larger fraction of GDM diagnoses rests on the fasting criterion alone than in the HAPO population [9, 10]. Where fasting glucose dominates diagnosis, a winter peak in fasting glucose should translate directly into a winter excess of GDM diagnoses—the opposite of the HAPO “cancellation” scenario.

We analysed a hospital-based cohort of 20,897 singleton pregnancies in Jinhua, China, with linked antenatal laboratory data, to (i) characterise seasonal oscillations of fasting, post-load, and integrated (GA) glycaemia; (ii) test their associations with actual ambient temperature and photoperiod; (iii) quantify the seasonal variation in GDM diagnosis; and (iv) assess internal replicability across calendar years. Albumin and two negative-control markers (uric acid, creatinine) were examined to probe preanalytical and dilutional explanations, and seasonal patterns of thyroid indices were analysed as a secondary endocrine panel.

Methods

Study design and population

This retrospective cohort study included all deliveries recorded in the obstetric discharge registry of Jinhua People's Hospital, a tertiary referral centre in Jinhua, Zhejiang Province, China (29.08°N), between January 2017 and December 2019 (n = 21,327). Delivery records were linked to the hospital laboratory information system by national ID number or name. Laboratory data were available for tests performed during 2017–2018 (n = 8,673 deliveries). We excluded multiple gestations (n = 410) and pregestational diabetes mellitus (n = 23), leaving 20,897 singleton pregnancies. The analytic samples were: complete 75-g OGTT (fasting, 1-h, 2-h; n = 3,980); GA (n = 2,131); thyroid panel (TSH, free T4; n ≈ 2,750). A woman contributed one record (her delivery-linked pregnancy). The study was approved by the institutional ethics committee of Jinhua People's Hospital; informed consent was waived for this retrospective analysis of de-identified data. Reporting follows the STROBE guideline [11].

Laboratory measurements

Glucose was measured by the hexokinase method, GA by an enzymatic method expressed as the percentage of glycated relative to total albumin, and TSH/free T4 by chemiluminescent immunoassay, according to routine hospital protocols. Gestational age at each test was calculated from the test date and the estimated date of delivery; implausible values (outside 10–42 completed weeks) were set to missing.

Environmental data

Monthly mean 2-m air temperature for Jinhua (29.08°N, 119.65°E) for January 2017–December 2018 was obtained from the NASA POWER meteorological reanalysis [12] and linked to each test by calendar month. Theoretical day length at 29.08°N was computed astronomically for the 15th of each month.

Definitions

GDM was defined by IADPSG criteria: fasting ≥ 5.1, 1-h ≥ 10.0, or 2-h ≥ 8.5 mmol/L [13]. Winter was defined as December–February and summer as June–August. "Fasting-only" GDM denoted positivity on the fasting criterion alone.

Statistical analysis

Seasonal rhythmicity of each biomarker was assessed by single-component cosinor regression [14]: the marker (log-transformed where right-skewed) was regressed on sine and cosine harmonics of calendar month, adjusting for gestational age at testing, maternal age, and calendar year. Amplitude (half the

peak-to-trough difference) and acrophase (peak month) were derived from the harmonic coefficients; to ensure comparability across markers, amplitudes are reported in original units and as a percentage of each marker's mean (for log-transformed markers, the percentage is computed on the geometric scale). Rhythm significance was assessed by a joint F-test of the harmonic terms. Internal replication was assessed by fitting identical models separately for 2017 and 2018.

Individual-level temperature associations were estimated by linear regression of the marker on monthly mean temperature with the same covariates. For GDM diagnosis, season-specific positivity rates were compared by logistic regression including harmonic terms and covariates. Because no season can be assumed a priori to be free of seasonal influence, seasonal variation in diagnosis is reported primarily as the absolute winter–summer difference in positivity; the excess relative to the summer rate, (p_winter − p_summer)/p_winter, is additionally reported as an upper-bound estimate of the season-associated fraction among winter-positive women, on the explicit and conservative assumption that summer rates approximate the season-free baseline. Age-stratified analyses examined the consistency of the winter–summer fasting contrast across maternal age groups. Unmeasured-confounder sensitivity was addressed by quantitative bias analysis (see Results). Two-sided $p < 0.05$ was considered significant. Analyses used Python 3.12 (pandas, statsmodels, SciPy).

Results

Cohort

The OGTT cohort (n = 3,980) had a mean age of 30.3 ± 4.7 years and mean gestational age at testing of 31.1 ± 4.5 weeks (Table 1). Overall, 13.6% of women met the fasting criterion and 24.4% met at least one IADPSG criterion; among positive women, 37% were positive on the fasting criterion alone, confirming a fasting-predominant diagnostic structure.

Table 1
Characteristics of the OGTT cohort overall and by season of testing.

Characteristic	All (n = 3,980)	Winter (n = 883)	Summer (n = 1,078)
Maternal age, years	30.3 ± 4.7	30.8 ± 4.5	29.8 ± 4.6
Gestational age at test, weeks	31.1 ± 4.5	30.1 ± 5.0	31.6 ± 4.1
Fasting glucose, mmol/L	4.70 ± 1.65	4.99 ± 2.55	4.60 ± 1.32
1-h glucose, mmol/L	7.96 ± 1.79	7.95 ± 1.76	7.95 ± 1.73
2-h glucose, mmol/L	6.68 ± 1.32	6.61 ± 1.22	6.72 ± 1.24
Fasting ≥ 5.1 mmol/L, %	13.6	22.9	9.2
Any IADPSG criterion, %	24.4	31.0	20.6

Opposite-phase oscillations of glycaemic markers

Fasting glucose showed a significant annual rhythm with acrophase in mid-January (amplitude 0.112 mmol/L, 95% CI 0.082–0.142, 2.4% of the mean; $p = 3.2\times10^{-12}$; Table 2, Fig. 1B). GA peaked in early July with a larger relative amplitude (0.61 percentage points, 95% CI 0.50–0.72, 5.3% of the mean; $p = 3.0\times10^{-26}$). The two acrophases were separated by approximately half a year (Fig. 1D). Two-hour post-load glucose peaked in early autumn (amplitude 0.131 mmol/L, 2.5% of the mean; $p = 5.3\times10^{-5}$); the 1-h value showed the same phase direction without reaching significance (p = 0.18). Every glycaemic pattern replicated in direction and phase when 2017 and 2018 were fitted independently (Fig. 2 and Additional file 1: Table S1; fasting peak months 3.0 and 0.2; GA peak months 6.4 and 7.7).

Table 2
Cosinor analysis of maternal biomarkers, adjusted for gestational age, maternal age, and calendar year. Amplitudes are given in original units and, in parentheses, as a percentage of the marker mean (geometric mean for log-transformed markers).

Marker	N	Amplitude, original units (95% CI)	Amplitude, % of mean	Peak month	P (joint F)
Fasting glucose, mmol/L	7,390	0.112 (0.082–0.142)	2.4%	1.6	3.2×10^{-12}
1-h glucose, mmol/L	3,713	0.079 (− 0.004–0.162)	1.0%	8.6	0.18
2-h glucose, mmol/L	4,180	0.131 (0.073–0.190)	2.5%	8.8	5.3×10^{-5}
Glycated albumin, %	2,131	0.608 (0.499–0.717)	5.3%	6.8	3.0×10^{-26}
TSH, mIU/L (log-analysed)	2,746	—	6.5% (geometric)	6.0	0.015
Free T4, pmol/L	2,748	0.350 (0.254–0.445)	3.2%	11.0	6.2×10^{-12}
Albumin, g/L (dilution marker)	7,062	1.16 (—)	3.1%	1.5	1.5×10^{-88}
Uric acid, µmol/L (negative control)	3,112	3.44 (—)	1.4%	9.0	0.07
Creatinine, µmol/L (negative control)	3,113	0.32 (—)	0.8%	5.8	0.13

Temperature and photoperiod associations

At the individual level, each 1°C increase in monthly mean temperature was associated with a 0.011 mmol/L decrease in fasting glucose (95% CI − 0.013 to − 0.008; $p = 3.4\times10^{-15}$) and a 0.052% increase in GA (95% CI 0.043–0.062; $p = 3.2\times10^{-26}$). Monthly median fasting glucose correlated inversely with monthly temperature (r = − 0.66) and GA positively (r = 0.67); GA also correlated with day length (r = 0.86).

Dilution and negative-control markers

Albumin showed a marked annual rhythm peaking in mid-winter (amplitude 1.16 g/L, 3.1% of the mean; $p = 1.5\times10^{-88}$), consistent with summer haemodilution. Because GA is expressed as the ratio of glycated to total albumin, dilutional effects on albumin concentration cancel out and cannot account for the GA summer peak. Two negative-control markers chosen a priori—uric acid (amplitude 1.4% of the mean; p = 0.07) and creatinine (amplitude 0.8% of the mean; p = 0.13)—showed no significant annual rhythm, arguing against a generic preanalytical or storage artefact affecting all serum analytes (Additional file 1: Figure S1).

Seasonal variation in GDM diagnosis

GDM positivity was 31.0% among women tested in winter versus 20.6% in summer (adjusted harmonic joint $p = 8.8\times10^{-4}$; Table 3). The difference was driven entirely by the fasting criterion (22.9% vs 9.2%; OR 2.96, 95% CI 2.33–3.76), whereas 1-h and 2-h positivity rates did not differ materially by season. The absolute winter excess of fasting-positive results was 13.7 percentage points, corresponding to approximately 137 additional fasting-positive results per 1,000 winter OGTTs. Under the conservative assumption that summer rates approximate the season-free baseline, the season-associated fraction among winter fasting-positive women was at most 60%; if winter is instead taken as the baseline, the same data imply a symmetric summer deficit, and the true season-associated fraction lies between these bounds. The winter–summer fasting contrast was directionally consistent across all maternal age strata (winter minus summer difference: +0.23, + 0.31, + 0.34, and + 0.14 mmol/L for ages < 25, 25–29, 30–34, and ≥ 35 years; Additional file 1: Table S2), excluding age-composition effects. In the least-biased subset tested within the standard 24–28 + 6-week window (n = 635), the winter–summer contrast persisted after adjustment (fasting positivity 21.0% vs 6.9%; p = 0.006).

Table 3
Seasonal variation in GDM diagnosis (75-g OGTT cohort, n = 3,980).

Outcome	Winter (%)	Summer (%)	Absolute difference, pp	OR (95% CI)	Adjusted p*
Fasting ≥ 5.1 mmol/L	22.9	9.2	+ 13.7	2.96 (2.33–3.76)	9.9×10^{-11}
Fasting-only positivity	15.4	6.5	+ 8.9	2.64 (1.99–3.49)	—
Any IADPSG criterion	31.0	20.6	+ 10.4	1.74 (1.44–2.10)	8.8×10^{-4}
24–28 + 6-wk window: fasting ≥ 5.1 (n = 635)	23.7	9.9	+ 13.8	—	0.006

* Harmonic joint test from logistic regression adjusted for gestational age, maternal age, and year. The absolute winter excess corresponds to ~ 137 additional fasting-positive results per 1,000 winter OGTTs; the season-associated fraction among winter fasting-positive women is at most 60% under the assumption that summer rates approximate the season-free baseline (see Methods).

Quantitative bias analysis for unmeasured confounding by adiposity

Pre-pregnancy BMI and parity were unavailable for the laboratory-linked subset. For seasonal variation in BMI to explain the observed fasting amplitude of 0.112 mmol/L, even assuming a strong BMI–fasting glucose gradient of 0.02–0.05 mmol/L per 1 kg/m² (consistent with the positive BMI–glucose association reported in HAPO [15]), maternal BMI would need to oscillate by roughly 2–6 kg/m² between winter and summer. Reported seasonal body-weight variation in adults is an order of magnitude smaller (approximately 0.5–1 kg, or < 0.4 kg/m²) [16, 17], which would account for less than one tenth of the observed fasting amplitude. Residual confounding by seasonal adiposity change is therefore unlikely to explain the findings, although direct confirmation with measured BMI remains necessary.

Thyroid panel

TSH peaked in May (amplitude 6.5% on the geometric scale; p = 0.015) and free T4 in November (amplitude 0.35 pmol/L, 3.2% of the mean; $p = 6.2\times10^{-12}$), with near-identical acrophases in both calendar years (Table 2).

Discussion

Principal findings

In this large Chinese pregnancy cohort, fasting glucose and glycated albumin oscillated in opposite seasonal phases—fasting glucose peaking in mid-winter and integrated glycaemia (GA), together with 2-h post-load glucose, peaking in summer/autumn. To our knowledge this is the first demonstration of GA seasonality in pregnancy and the first study to document opposite-phase fasting and integrated glycaemic rhythms within the same pregnant population. Three lines of internal evidence support a physiological rather than artefactual basis: the patterns replicated independently in two calendar years; the GA summer peak is structurally immune to the haemodilution and preanalytical glycolysis that could influence glucose measurements; and uric acid and creatinine showed no annual rhythm, indicating that the laboratory pipeline did not impose a generic seasonal drift.

Reconciling the literature

Our results offer a structural explanation for the inconsistencies among previous studies. The HAPO authors concluded that GDM prevalence shows no seasonality because winter elevations of fasting glucose are offset by summer elevations of post-load glucose [3]. That cancellation holds only where the post-load criteria contribute a substantial share of diagnoses. In our population, 37% of GDM cases were diagnosed on the fasting criterion alone (and 50% of winter cases), consistent with the fasting-predominant phenotype of GDM described in Chinese and other East Asian populations [9, 10]. Under this structure, the fasting limb dominates and the winter fasting peak translates directly into a 1.7-fold winter excess of GDM diagnoses. Conversely, in populations with post-load-predominant diagnosis, the Swedish/Brazilian pattern of summer excess would be expected [1, 2]. Seasonal GDM variation is thus not a single phenomenon but a population-structure-dependent composite of two opposite-phase rhythms.

Clinical implications

The absolute winter excess—approximately 137 additional fasting-positive results per 1,000 winter OGTTs—is our primary estimate and does not depend on assuming any season to be season-free. Because a GDM diagnosis triggers dietary counselling, glucose monitoring, increased surveillance, and potential intervention, seasonal variation in diagnosis carries real costs and iatrogenic potential, whichever season anchors the baseline. Borderline fasting values (5.1–5.5 mmol/L) obtained in winter warrant confirmation before diagnosis, as contemplated in some national guidance [18]. Our effect sizes (fasting amplitude 0.11 mmol/L) imply that any seasonal adjustment would be modest relative to the diagnostic threshold but consequential at the margin. GA, which integrates 2–3 weeks of glycaemia and is unaffected by the fasting state, may be a useful adjunct when a winter fasting result is discrepant with clinical impression, although its own (summer-peaking) seasonality must likewise be considered.

Mechanisms: internal evidence and external hypotheses

Three findings from our own data constrain the mechanistic interpretation. First, the winter peak of albumin (3.1% amplitude) confirms summer haemodilution, which would bias summer glucose values downward; the fasting rhythm may therefore be partly dilutional, whereas the GA rhythm cannot be, because GA is a within-sample ratio. Second, the absence of any rhythm in uric acid and creatinine—

analytes drawn, transported, and analysed through the same pipeline—argues against seasonal preanalytical artefact as a general explanation. Third, the winter–summer fasting contrast was consistent across maternal age strata, excluding compositional effects. Beyond these internal anchors, several non-exclusive external mechanisms remain plausible: cold-induced sympathetic activation and increased hepatic glucose output in winter [19]; photoperiodic melatonin signalling, which modulates insulin secretion through MTNR1B-dependent pathways [20, 21]; winter nadir of vitamin D [22]; and summer arterialisation of venous samples and behavioural changes raising post-challenge glucose [1, 3]. The distinct acrophases of TSH (May) and free T4 (November) further suggest a broader circannual endocrine organisation in pregnancy [23, 24]. These external hypotheses are speculative and are presented to guide future work rather than as interpretations of our data.

Strengths and limitations

Strengths include the large sample, the first seasonal analysis of GA in pregnancy, cosinor methodology with year-stratified internal replication, linkage to actual meteorological data, dilution and negative-control analyses, and sensitivity analysis in the standard screening window. Several limitations deserve emphasis. First, laboratory data covered only two calendar years; although every reported rhythm replicated independently in both years, longer series are needed to confirm stability. Second, laboratory testing was clinically indicated rather than universal, introducing potential selection bias; persistence of findings in the 24–28 + 6-week screening window mitigates but does not eliminate this concern. Third, pre-pregnancy BMI and parity were unavailable for the laboratory-linked subset; our quantitative bias analysis suggests seasonal adiposity change is too small to explain the fasting rhythm, but residual confounding cannot be excluded. Fourth, preanalytical glycolysis in summer could spuriously lower glucose values; this would bias the fasting summer trough upward (i.e., against our fasting finding) and cannot explain the GA or 2-h summer peaks, but we could not quantify it directly. Fifth, the season-associated fraction among winter-positive women depends on the choice of baseline season and should be interpreted as an upper bound. Sixth, single-centre design in a subtropical monsoon climate limits generalisability; these rhythms are likely latitude-dependent.

Conclusions

Fasting and integrated glycaemia oscillate in opposite phases during pregnancy. In fasting-predominant GDM populations these rhythms do not cancel and are associated with substantial, quantifiable seasonal variation in GDM diagnosis. Season of testing should inform the interpretation of borderline fasting glucose, and glycated albumin merits prospective evaluation as a season-aware complementary marker. Multi-centre prospective studies with universal sampling, measured adiposity, and mechanistic biomarkers are warranted to determine whether season-adjusted diagnostic strategies improve the accuracy of GDM diagnosis.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Jinhua People's Hospital. The committee waived the requirement for informed consent because of the retrospective study design and the exclusive use of anonymized routine clinical data. All procedures were conducted in accordance with the Declaration of Helsinki and the Measures for Ethical Review of Biomedical Research Involving Humans (China).

Consent for publication

Not applicable. This manuscript does not contain any individual person's data in any form.

Availability of data and materials

The de-identified analytic dataset and the complete scripted analysis pipeline are available from the corresponding author on reasonable request and with appropriate institutional approval; the raw clinical records are not publicly available due to institutional privacy policies.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contributions

Jiaping Lu was responsible for data collection, database sorting, preliminary statistical analysis and manuscript drafting. Qiulian Xu participated in clinical data screening, case inclusion and exclusion judgment, and revision of the results section. Heng Xu conceived and designed the research framework, guided the whole statistical analysis process, revised the full manuscript repeatedly, and acted as the corresponding author of this paper. All authors read and approved the final submitted manuscript.

Acknowledgments

The authors gratefully acknowledge the contributions of all obstetricians, midwives, and nursing staff whose clinical work made this study possible.

References

1. Schmidt MI, Matos MC, Branchtein L, Reichelt AJ, Mengue SS, Iochida LC, et al. Variation in glucose tolerance with ambient temperature. Lancet. 1994;344:1054–5.
2. Katsarou A, Claesson R, Ignell C, Shaat N, Berntorp K. Seasonal pattern in the diagnosis of gestational diabetes mellitus in southern Sweden. J Diabetes Res. 2016;2016:8902742.

3. Moses RG, Wong VC, Lambert K, Morris GJ, San Gil F. Seasonal changes in the prevalence of gestational diabetes mellitus. Diabetes Care. 2016;39:1218–21.
4. Hiramatsu Y, Shimizu I, Omori Y, Nakabayashi M, JGA Study Group. Determination of reference intervals of glycated albumin and hemoglobin A1c in healthy pregnant Japanese women and analysis of their time courses and influencing factors during pregnancy. Endocr J. 2012;59:145–51.
5. Koga M, Kasayama S. Clinical impact of glycated albumin as another glycemic control marker. Endocr J. 2010;57:751–62.
6. Hashimoto K, Koga M. Indicators of glycemic control in patients with gestational diabetes mellitus and pregnant women with diabetes mellitus. World J Diabetes. 2015;6:1045–56.
7. Tanaka K, Meguro S, Tanaka M, Irie J, Saisho Y, Itoh H. Difference of seasonal variation between glycated albumin and glycated haemoglobin. Ann Clin Biochem. 2018;55(5):583–7.
8. Araki T, et al. Seasonal and decadal changes in glycated albumin levels of Japanese blood donors. Ann Clin Biochem. 2025. 10.1177/00045632251395550. . Online ahead of print.
9. Zhu WW, Yang HX, Wei YM, Yan J, Wang ZL, Li XL, et al. Evaluation of the value of fasting plasma glucose in the first prenatal visit to diagnose gestational diabetes mellitus in China. Diabetes Care. 2013;36:586–90.
10. Juan J, Yang H. Prevalence, prevention, and lifestyle intervention of gestational diabetes mellitus in China. Int J Environ Res Public Health. 2020;17:9517.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Lancet. 2007;370:1453–7.
12. NASA Prediction of Worldwide Energy Resources. (POWER) Project. https://power.larc.nasa.gov. Accessed [date].
13. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33:676–82.
14. Cornélissen G. Cosinor-based rhythmometry. Theor Biol Med Model. 2014;11:16.
15. HAPO Study Cooperative Research Group. Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study: associations with maternal body mass index. BJOG. 2010;117:575–84.
16. Yanovski JA, Yanovski SZ, Sovik KN, Nguyen TT, O'Neil PM, Sebring NG. A prospective study of holiday weight gain. N Engl J Med. 2000;342:861–7.
17. Ma Y, Olendzki BC, Li W, Hafner AR, Chiriboga D, Hebert JR, et al. Seasonal variation in food intake, physical activity, and body weight in a predominantly overweight population. Eur J Clin Nutr. 2006;60:519–28.
18. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S20–42.

19. Vallerand AL, Zamecnik J, Jacobs I. Plasma glucose turnover during cold stress in humans. J Appl Physiol. 1995;78:1296–302.
20. Lyssenko V, Nagorny CL, Erdos MR, Wierup N, Jonsson A, Spégel P, et al. Common variant in MTNR1B associated with increased risk of type 2 diabetes and impaired early insulin secretion. Nat Genet. 2009;41:82–8.
21. McMullan CJ, Schernhammer ES, Rimm EB, Hu FB, Forman JP. Melatonin secretion and the incidence of type 2 diabetes. JAMA. 2013;309:1388–96.
22. Godang K, Frøslie KF, Henriksen T, Qvigstad E, Bollerslev J. Seasonal variation in maternal and umbilical cord 25(OH) vitamin D and their associations with neonatal adiposity. Eur J Endocrinol. 2014;170:609–17.
23. Kim TH, Kim KW, Ahn HY, Choi HS, Won H, Choi Y, et al. Effect of seasonal changes on the transition between subclinical hypothyroid and euthyroid status. J Clin Endocrinol Metab. 2013;98:3420–9.
24. Gamble KL, Berry R, Frank SJ, Young ME. Circadian clock control of endocrine factors. Nat Rev Endocrinol. 2014;10:466–75.
25. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, HAPO Study Cooperative Research Group, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358:1991–2002.
26. Stenvers DJ, Scheer FAJL, Schrauwen P, la Fleur SE, Kalsbeek A. Circadian clocks and insulin resistance. Nat Rev Endocrinol. 2019;15:75–89.
27. Obstetrics, Subgroup, Chinese Society of Obstetrics and Gynecology; Collaborative Group for Pregnancy Complicated by Diabetes, Chinese Society of Perinatal Medicine. Guidelines for diagnosis and treatment of pregnancy complicated by diabetes mellitus (2014). Zhonghua fu chan ke za zhi. 2014;49(8):561–9. (In Chinese).
28. Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Kirkman MS, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem. 2011;57:e1–47.
29. Coustan DR. Gestational diabetes mellitus. Clin Chem. 2013;59:1310–21.
30. Refinetti R, Cornélissen G, Halberg F. Procedures for numerical analysis of circadian rhythms. Biol Rhythm Res. 2007;38:275–325.

Figures

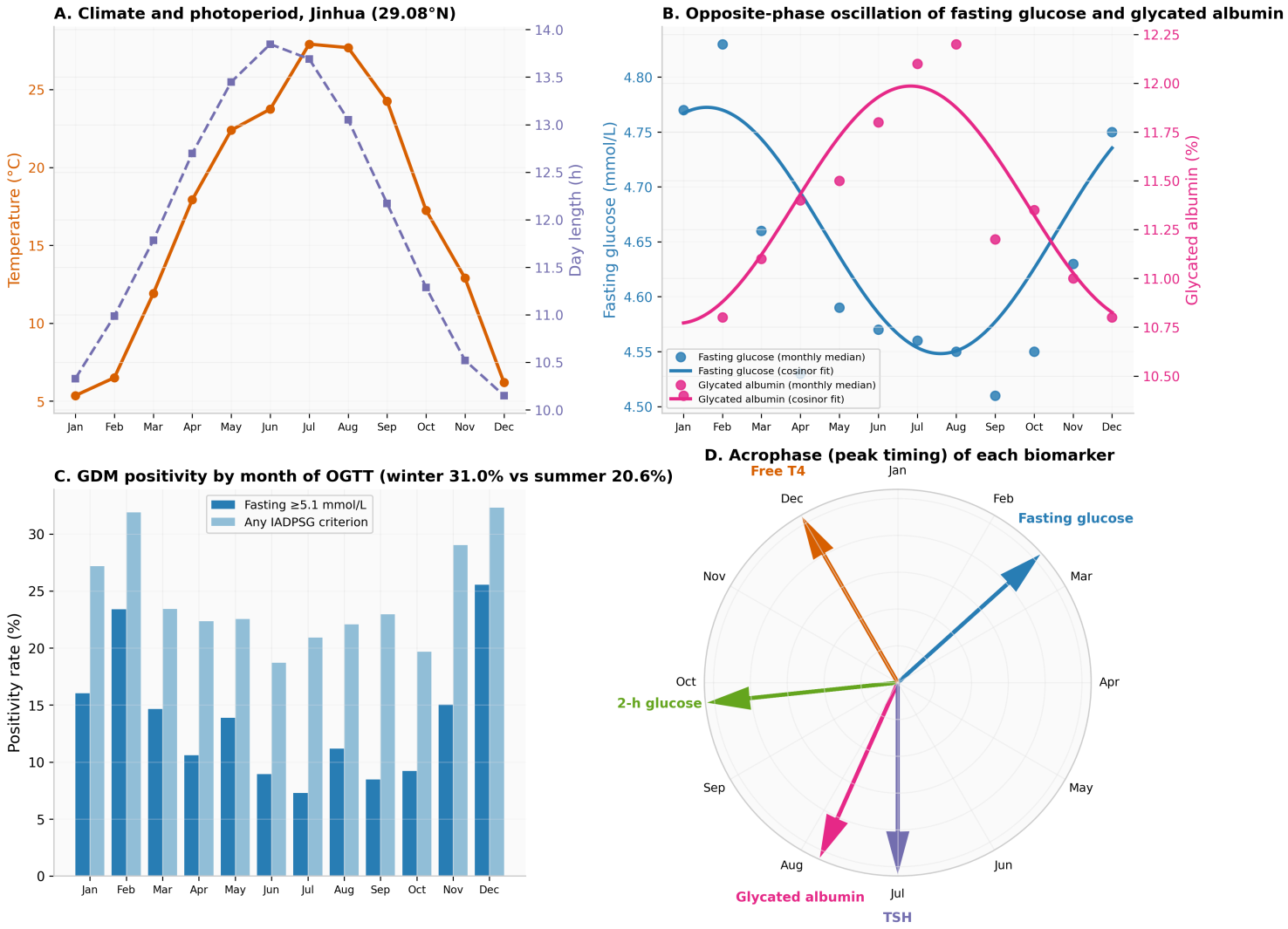


Figure 1

Seasonal oscillation of glycaemic markers. (A) Monthly mean ambient temperature (NASA POWER, 2017–2018) and theoretical day length at 29.08°N. (B) Monthly medians and cosinor fits of fasting glucose and glycated albumin, showing opposite-phase oscillation. (C) Monthly GDM positivity rates (fasting criterion and any IADPSG criterion). (D) Acrophase diagram of all biomarkers.

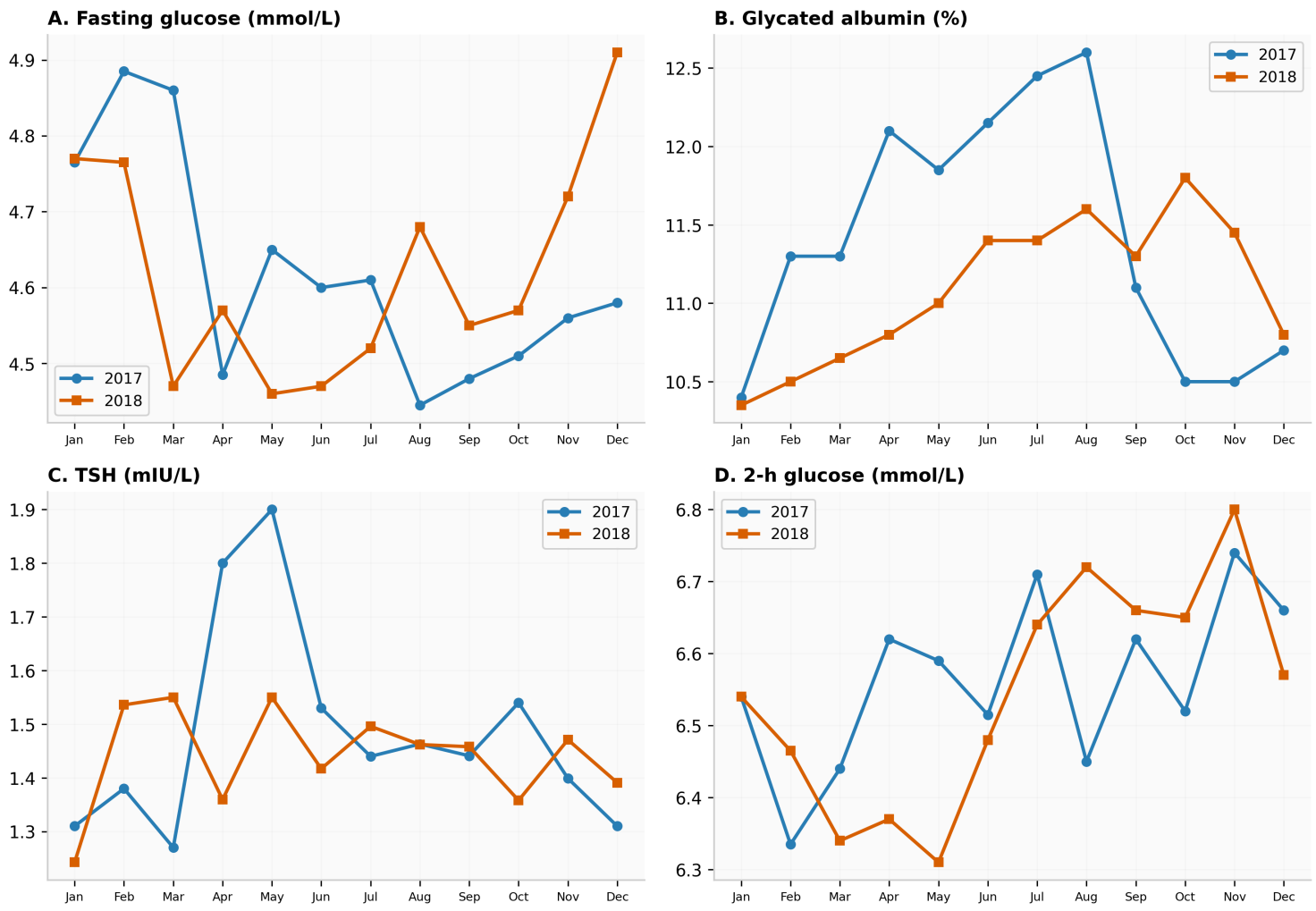


Figure 2

Year-stratified internal replication (2017 vs 2018) of monthly medians for fasting glucose, glycated albumin, TSH, and 2-h glucose.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TableS3monthlyOGTT.csv
- TableS1yearstratifiedcosinor.csv
- SupplementaryMaterial.docx
- SupplementaryFigureS3.png
- SupplementaryFigureS2.png
- SupplementaryFigureS1.png