

Appendices (online only)

– Fig. S1-S3, Tab. S1-S3, Questionnaire (Early Life Plan Cohort Study Questionnaire)

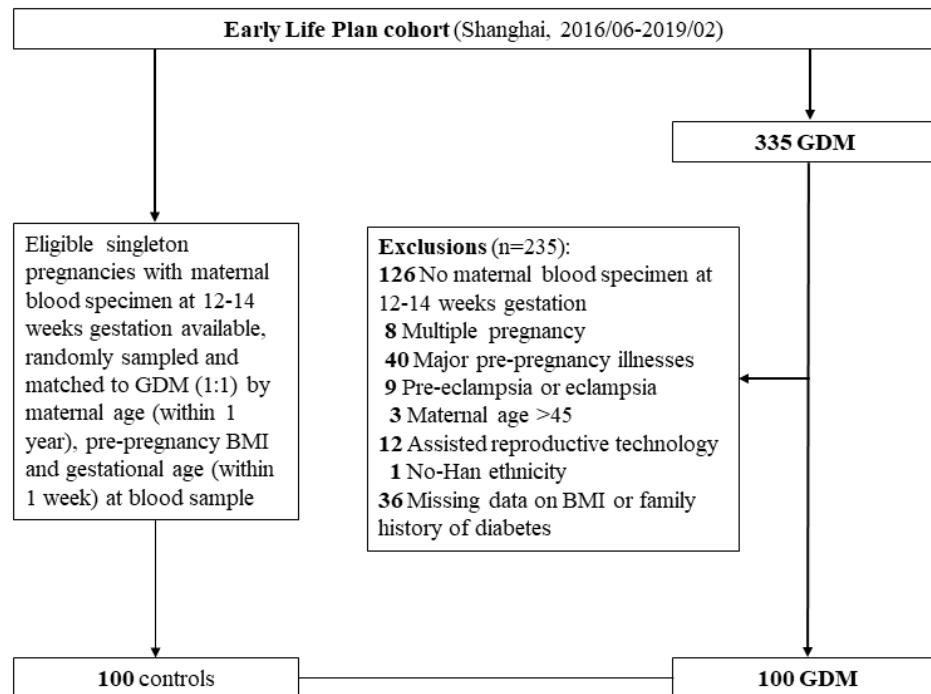


Figure S1. Flowchart in the selection of study subjects on early gestational biomarkers of gestational diabetes mellitus (GDM).

Figure S2. Feature importance of variables for predicting gestational diabetes in random forest models

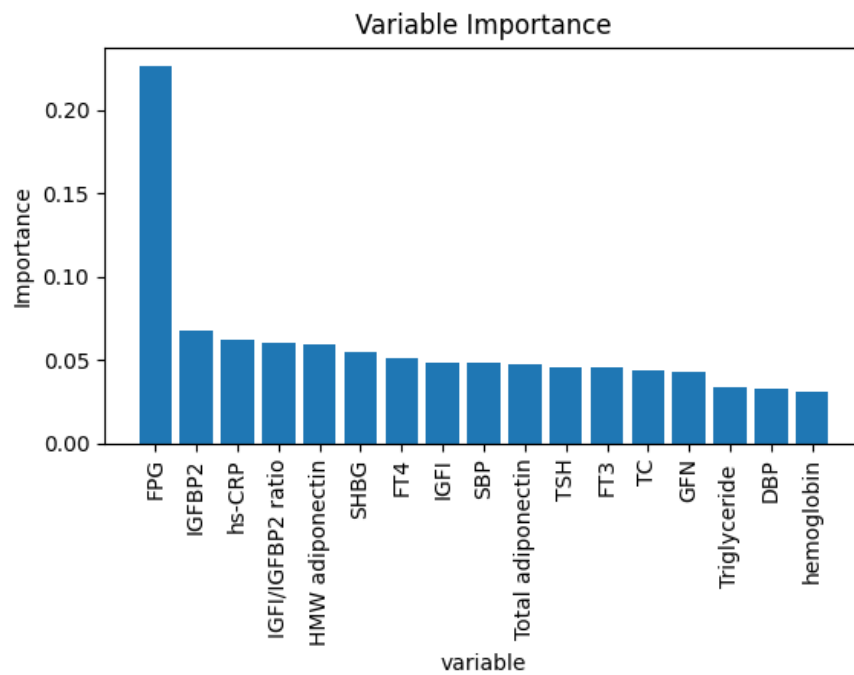


Figure S3. SHAP (SHapley Additive exPlanations) summary plots of features for predicting gestational diabetes in random forest models: the importance (left panel) and impact (right panel) of features by SHAP values, the feature is high (in red) or low (in blue) according to the SHAP value (right panel)

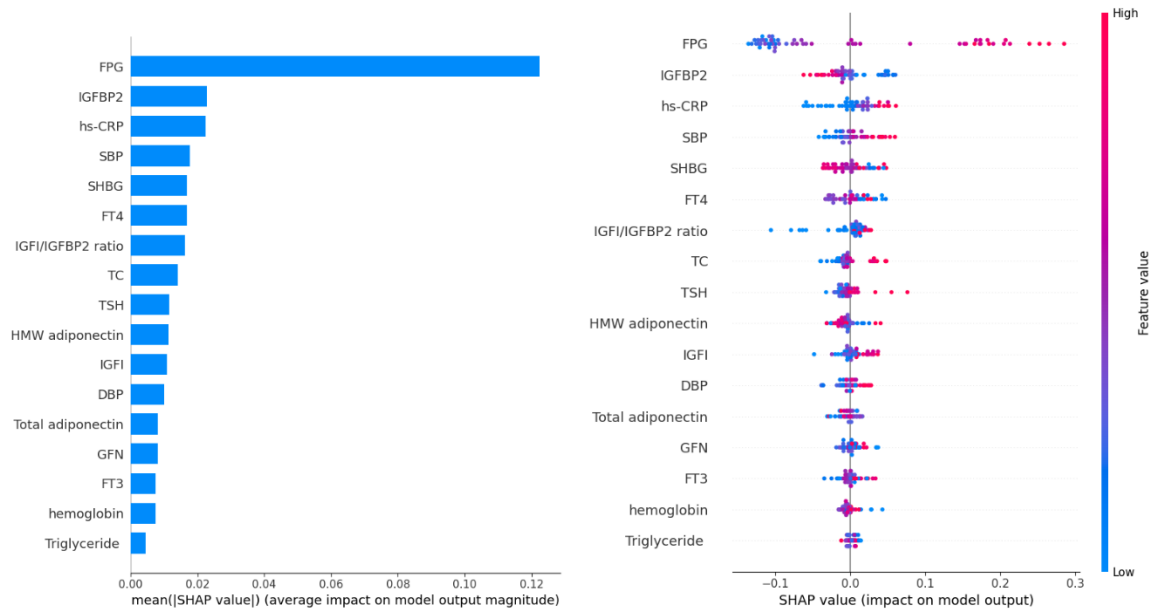


Table S1. Maternal characteristics and early gestational biomarkers in GDM and euglycemic (control) subjects in the training (70 pairs) and testing (30 pairs) sets

	Train set (n=140)	Testing set (n=60)	P Value
GDM	70 (50)	30 (50)	1.00
Age (years)	32.3±3.7	31.5±4.3	0.19
Primiparity	72 (51.4)	35 (58.3)	0.44
Family history of diabetes	2 (1.4)	0 (0.0)	1.00
Family history of hypertension	51 (36.4)	19 (31.7)	0.63
Pre-pregnancy BMI (kg/m ²)	23.6±3.1	23.2±2.9	0.40
Routine blood tests 11-14 weeks			
FPG	5.0±0.4	4.8±0.4	0.027
SBP (mmHg)	118.5±12.5	118.8±12.9	0.86
DBP (mmHg)	72.0±8.5	71.8±8.4	0.89
Triglyceride (mmo/L)	1.5±0.6	1.5±0.6	0.96
TC (mmo/L)	4.7±0.7	4.9±0.9	0.14
hemoglobin (g/L)	123.0±8.5	124.1±7.9	0.37
TSH (uIU/ml)	1.3±0.9	1.4±0.8	0.29
FT4 (pmol/l)	15.3±2.2	15.0±2.2	0.38
FT3 (pmol/l)	4.7±0.6	4.5±0.4	0.21
Blood biomarkers			
Hs-CRP (mg/L)	5.5±5.3	4.2±4.5	0.10
GFN (µg/mL)	377.3±203.6	381.1±201.0	0.90
IGF-I (ng/ml)	50.9±24.3	49.6±18.8	0.72
IGFBP-2 (ng/ml)	81.2±29.3	79.8±28.9	0.75
IGF-I/IGFBP-2 ratio	0.7±0.5	0.7±0.3	0.44
SHBG (nmol/L)	164.2±41.8	159.2±41.8	0.44
Adiponectin			
HMW (ng/ml)	2242.0±1383.8	2482.4±1366.9	0.26
Total (ng/ml)	5642.5±2190.4	6177.6±2327.4	0.12

Data presented are Mean ± SD or n (%).

GDM, gestational diabetes mellitus; GA, gestational age; BMI, body mass index; FPG, fasting plasma glucose; SPB, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TSH, thyroid stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine; OGTT, oral glucose tolerance test.

*P-values in comparisons of the two groups in t-tests for continuous variables and Chi-square tests for categorical variables.

P values in **bold**, p<0.05.

Table S2. Early gestational predictors of gestational diabetes mellitus (GDM)

	OR	P	aOR ^a	P
hs-CRP	1.21 (0.91, 1.61)	0.19	1.23 (0.92, 1.65)	0.16
GFN	1.03 (0.78, 1.36)	0.85	1.07 (0.81, 1.42)	0.64
IGF-I	1.17 (0.88, 1.54)	0.29	1.16 (0.87, 1.54)	0.32
IGFBP-2	0.64 (0.47, 0.86)	0.004	0.64 (0.47, 0.87)	0.005
SHBG	0.75 (0.57, 1.00)	0.052	0.74 (0.55, 0.99)	0.047
HMW adiponectin	0.78 (0.59, 1.04)	0.09	0.78 (0.56, 1.05)	0.10
Total adiponectin	0.88 (0.77, 1.00)	0.06	0.89 (0.78, 1.02)	0.08
IGF-I/IGFBP-2 ratio	1.43 (1.05, 1.95)	0.02	1.42 (1.04, 1.95)	0.03
FPG	2.62 (1.82, 3.76)	<0.001	2.70 (1.85, 3.93)	<0.001
SBP	1.64 (1.22, 2.21)	0.001	1.58 (1.17, 2.14)	0.003
DBP	1.39 (1.04, 1.85)	0.03	1.36 (1.01, 1.82)	0.04
Triglyceride	1.16 (0.89, 1.51)	0.29	1.12 (0.84, 1.49)	0.44
Total Cholesterol	1.29 (0.97, 1.72)	0.08	1.26 (0.95, 1.68)	0.12
Hemoglobin	1.01(0.76, 1.34)	0.95	0.98 (0.74, 1.31)	0.90
TSH	1.19 (0.91, 1.57)	0.21	1.19 (0.90, 1.58)	0.21
FT4	1.02 (0.77, 1.35)	0.92	1.02 (0.77, 1.37)	0.87
FT3	1.24 (0.95, 1.61)	0.12	1.23 (0.94, 1.61)	0.13

Data presented are odds ratios (ORs) per SD increase in each biomarker.

hs-CRP, high sensitivity C reactive protein; GFN, glycosylated fibronectin; IGF-I, insulin-like growth factor-I; IGFBP-2, insulin-like growth factor binding protein 2; SHBG, sex hormone binding globulin; HMW, high molecular weight. FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TSH, thyroid stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine.

^aAdjusted for family history of diabetes and gestational age at blood sampling; other factors were excluded since they did not affect the comparisons ($p > 0.2$).

P values in bold, $p < 0.05$.

Table S3. The selected predictors of GDM by four machine learning algorithms - stepwise logistic regression (LR), Lasso regression, support vector machine (SVM) and random forest

	Stepwise LR	Lasso	SVM	Random forest
Selected predictors	FPG*	FPG*	FPG*	FPG*
	IGFBP-2*	IGFBP-2*	IGFBP-2*	IGFBP-2*
	TSH		TSH	hs-CRP
	FT3		hs-CRP	IGF-I/IGFBP-2 ratio
	Hemoglobin		Hemoglobin	HMW adiponectin

hs-CRP, high sensitivity C reactive pprotein;; IGF-I, insulin-like growth factor-I; IGFBP-2, hinsulin-like growth factor binding protein 2; SHBG, sex hormone binding globulin; HMW, high molecular weight. FPG, fasting plasma glucose; TSH, thyroid stimulating hormone; FT3, free triiodothyronine.

Early Life Plan Cohort Study Questionnaire

I. Basic Information of the Pregnant Woman

1. Study ID: |_|_|-|_|_|_|_|-|_|_|_|_|_|-|_|_|_|_|

2. Education:

- ☐1 Primary School and Below ☐2 Junior High School ☐3 High School
☐4 Associate Degree ☐5 Bachelor's Degree ☐6 Master's Degree
☐7 Doctorate ☐99 Uncertain

3. Marital Status: ☐1 Single ☐2 Married ☐3 Divorced ☐4 Widowed ☐5 Other _____

II. Pregnancy Information

1. First prenatal care consultation date: |_|_|_|_|Year|_|_|Month|_|_|Day

2. Gestational age at first prenatal care visit: |_|_| weeks |_| days (0-6)

Date of last menstruation: |_|_|_|_|Year|_|_|Month|_|_|Day

Gestational age in ultrasound dating: |_|_| weeks |_| days (0-6)

III. Maternal Medical History (Tick/Selection where appropriate)

1. Pre-pregnancy Disease:

- ☐ None ☐ Diabetes ☐ Hypertension ☐ Cardiac Disease
☐ Renal Disease ☐ Autoimmune Disease
☐ Hyperthyroidism ☐ Hypothyroidism ☐ Asthma

2. Family History of Hypertension (first degree relatives):

- ☐ None ☐ Yes ☐99 Uncertain

3. Family History of Diabetes (first degree relatives):

- ☐ None ☐ Yes ☐99 Uncertain

IV. Pregnancy History

(Note: If it is no for any item, filling the corresponding space with 99)

1. Number of Pregnancies (Including Current Pregnancy): |_|_| times (Range: 0-20)

2. Full-Term Deliveries (Prior to Current Pregnancy): |_|_| times (Range: 0-9)

3. Preterm Deliveries: |_|_| times (Range: 0-9)

4. Current Number of Children: |_|_| (Range: 0-9)

V. First Prenatal Care - Examinations

(Note: If it is not available for this item, filling the corresponding space with 9999)

1. Weight at first prenatal care consultation: |_|_|_|_| . |_| kg (Range: 20-180)

2. Height: |_|_|_| cm (Range: 50-200)

3. Blood Pressure (Systolic): |_|_|_| . |_| mmHg (Range: 0-250)

4. Blood Pressure (Diastolic): |_|_|_| . |_| mmHg (Range: 0-180)

VI. Laboratory Tests

(Note: If it is no available for any item, filling in the corresponding space with 99)

(I) Initial (first prenatal care) Consultation

1. Hemoglobin (HB): |_|_|_| g/L (Range: 1-300)

2. Blood Platelet Count (BPC): $\times 10^9/L$ (Range: 0-500) Adjust sequence

3. Urine Protein Test:

☐0 Negative ☐1 Positive, Specify Value: mg/dl (Range: 0-500)

☐99 Not Tested

4. Urine Glucose:

☐0 None (-) ☐1 <50mg/dl (+) ☐2 50-300mg/dl (++)

☐3 301-500mg/dl (+++) ☐4 >500mg/dl (+++ and above) ☐99 Not Tested

5. TSH: uIU/ml (0-50)

6. FT4: pmol/l (0-80)

7. FT3: pmol/l (0-80)

8. TPOAb: IU/ml (0-150)

9. Fasting Blood Glucose (FBG): mmol/l (1.5-30)

10. Triglycerides (TG): mmol/l (0.1-20)

11. Total Cholesterol (TC): mmol/l (0.5-20)

12. High-Density Lipoprotein Cholesterol (HDL): mmol/l (0-20)

13. Low-Density Lipoprotein Cholesterol (LDL): mmol/l (0-20)

(II) Mid-Pregnancy (Note: If there is no medical history of this item, fill in the corresponding space with 9999) - around 24-28 weeks

Oral glucose tolerance test (OGTT):

1. OGTT (Fasting): mmol/l (1.5-30)

2. OGTT (1h): mmol/l (1.5-30)

3. OGTT (2h): mmol/l (1.5-30)

VII. Pregnancy Complications (Note: If there is not available, filling in 99)

1. Diagnosis of Thyroid Disorders Post-Pregnancy:

☐ No ☐ Hyperthyroidism ☐ Hypothyroidism

2. Diagnosis of Gestational Hypertension Post-Pregnancy?

☐ No ☐ Yes

2.1 Please specify the diagnosis type on the medical record:

☐1 Gestational Hypertension ☐2 Preeclampsia

☐3 Severe Preeclampsia ☐4 Eclampsia ☐5 Chronic Hypertension with Superimposed Preeclampsia

☐6 Pregnancy Complicated by Chronic Hypertension ☐ Other Special: Please Specify _____

2.2 Gestational Hypertension Diagnosis at Gestational Weeks: weeks (4-45) days (0-6)

3. Diagnosis of Gestational Diabetes Mellitus (GDM):

☐ No ☐ Yes

3.1 Use of Insulin: ☐ No ☐ Yes

3.2 Use of Oral Hypoglycemic Agents: ☐ No ☐ Yes

3.3 Dietary and Lifestyle Adjustment: ☐ No ☐ Yes

3.4 Gestational Diabetes Mellitus Diagnosis at Gestational Weeks: weeks (4-45) days (0-6)

VIII. Delivery information

(Note: If the information is not available, filling in 999 in the corresponding space)

1. Date of hospitalization at the time of delivery: Year Month Day

2. Admission weight: kg (20-180) (if not measured, fill in 9999)

3. Gestational age at delivery: weeks (4-45 weeks) days (0-6 days)

4. Mode of delivery

☐1 Vaginal delivery ☐2 Cesarean section

IX. Newborn Information

(Note: If the medical history does not contain the item, fill in 9 in the corresponding blank)

1. Birth outcome:

☐1 Live birth ☐2 Stillbirth ☐3 Neonatal death

2. Sex:

☐1 Male ☐2 Female ☐3 Other special, please copy appearance description: _____

3. Birth weight: |__|_|_|_|_| g (300-8000) (if not measured, fill in 9999)

4. 1-minute APGAR: |__|_|_| (range: 0-10, no decimals) (if not measured, fill in 99)

5. 5-minute APGAR: |__|_|_| (range: 0-10, no decimals) (if not measured, fill in 99)

6. 10-minute APGAR: |__|_|_| (range: 0-10, no decimals) (if not measured, fill in 99)

7. Head circumference |__|_|_| . |__|_| cm (range: 20-45) (if not measured, fill in 999)

8. Length |__|_|_| . |__|_| cm (range: 25-75) (if not measured, fill in 999)

9. Congenital anomalies: ☐0 None ☐1 Yes