Preplanned Studies

Hematological Parameters in the First Trimester and the Risk of Gestational Diabetes Mellitus — Beijing, China, 2017–2020

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Summary

What is already known about this topic?

Hematological parameters may indicate the presence of chronic low-grade inflammation and increasing viscosity, which are involved in the pathological processes of gestational diabetes mellitus (GDM). However, the association between several hematological parameters in early pregnancy and GDM has yet to be elucidated.

What is added by this report?

Hematological parameters in the first trimester, particularly red blood cell (RBC) count and systematic immune index, have a significant impact on GDM incidence. The neutrophils (NEU) count in the first trimester was particularly pronounced for GDM. The upward trend of RBC, white blood cell (WBC), and NEU counts was consistent across all GDM subtypes.

What are the implications for public health practice?

Early pregnancy hematological parameters are associated with the risk of GDM.

Gestational diabetes mellitus (GDM) is a prevalent high-risk disorder during pregnancy, increasing the risk of adverse pregnancy outcomes (*1*). Previous studies have documented that abnormalities in hematological cells reflect the increasing level of maternal immune dysregulation and viscosity, which may play a role in the pathophysiology of GDM (*2–3*). However, reports of the association between several hematological parameters in early pregnancy and GDM are equivocal. Although some epidemiological studies have demonstrated a positive association between red blood cell (RBC) (*4*), white blood cell (WBC) (*5*), or hemoglobin (Hb) (*6*) in early pregnancy and GDM, inconsistent results were observed in other studies (*7*). To our knowledge, previous studies have not included certain novel immune blood parameters, such as the neutrophil-lymphocyte ratio (NLR). We conducted a retrospective study and used adjusted logistic regression

models to assess the association between increased hematological parameters in early pregnancy and incident GDM, collecting data from the Haidian District Maternal and Child Health Care Hospital on pregnant women between 2017 and 2020. All analyses were performed using the R software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria). The results showed that a quartile increment in Hb, RBC, WBC, platelet (PLT), neutrophils (NEU), NLR, and systemic immune-inflammation index (SII) was positively associated with GDM incident (P_{trend}<0.05) after multivariable adjustment.

This retrospective cohort study was conducted among 29,570 reproductive-aged women with singleton pregnancies who were registered in the obstetric archives between January 2017 and April 2020 and completed their routine prenatal visits in the Maternal and Child Health Care Hospital of Haidian District, Beijing. After excluding participants with chronic diseases (e.g., hypertension, diabetes, or chronic nephritis), infectious diseases [e.g., syphilis, clap, or acquired immune deficiency syndrome (AIDS)], missing values of hematological parameters before 13 gestational weeks, or women who did not undergo a standard oral glucose tolerance test (OGTT) at 24 to 28 gestational weeks, a total of 5,529 participants were finally included (Supplementary Figure S1, available in https://weekly.chinacdc.cn/).

Hematological parameters included blood cell counts [RBC, PLT, and WBC, including neutrophil (NEU) and lymphocyte (LYM)] and hemoglobin concentration, which were tested from fasting blood samples collected in the first trimester and immediately stored at 4–8 °C for 24 h. We further calculated NLR and SII [(neutrophil × platelet)/lymphocyte], indicating the degree of individual inflammatory burden (*8*). Both NLR and SII reflect the balance of adaptive immune and inflammatory factors in the human body. Physical examinations, previous obstetric history, laboratory parameters, and diagnoses were extracted from the electronic medical record system.

Information on physical examinations contained height and weight.

GDM was diagnosed if at least one value of plasma glucose concentration was equal to or exceeded the thresholds of 5.1, 10.0, and 8.5 mmol/L for fasting, 1 h, and 2 h post-glucose load values, respectively, after performing a 75 g OGTT at gestational 24–28 weeks according to the Guidelines for Diagnosis and Treatment of Diabetes in Pregnancy (2014) in China (9). We further distinguished the impact of three subtypes of GDM: isolated fasting hyperglycemia (GDM-IFH), isolated post-load hyperglycemia (GDM-IPH), and combined hyperglycemia (GDM-CH) (10). This study used age-adjusted and multivariable-adjusted logistic regression models to examine the associations between hematological parameters and GDM. The odds ratio (OR) and 95% confidence interval (CI) of having GDM were used to quantify the association. We categorized participants into four groups based on quartile cutoff values of hematological parameters. A linear trend was tested by recoding individual hematological parameters as a continuous variable into the regression model. To provide clinical recommendation (11), the normal ranges of RBC, Hb, WBC, PLT, NEU, and LYM in the first trimester were defined as 3.42–4.55 ($\times 10^{12}$/L), 116–139 (g/L), 5.7–13.6 ($\times 10^9$/L), 174–391 ($\times 10^9$/L), 3.61–10.19 ($\times 10^{12}$/L), and 1.1–3.6 ($\times 10^{12}$/L), respectively. All the regression models were adjusted for the following covariates: age (categorical, <30, ≥30), gestational week (categorical, <9, ≥9), parity (categorical, 0, ≥1), body mass index (BMI) before 20 gestational weeks (categorical, <18.5, 18.5–23.9, 24.0–27.9, ≥28.0), history of adverse pregnancy outcomes (categorical, have, not have), and fasting blood glucose (categorical, <6.1, ≥6.1). All analyses were conducted using R software 4.1.2, and two-sided P<0.05 values were considered statistically significant.

Among the 5,529 participants, 1,017 incident GDM cases (18.4%, including 503 GDM-IPH, 339 GDM-IFH, and 175 GDM-CH) were identified. Table 1 shows the baseline characteristics of the pregnant women. The median age of participants was 31 (29 to 34) years, and the median gestational week at enrollment was 12.01. Participants with GDM were more likely to be older, parous, have an abnormal pregnancy history, and have higher levels of fasting plasma glucose and BMI in the first trimester (P<0.05). The hematological parameters in the first trimester, including RBC, Hb, WBC, PLT, LYM, NEU, NLR, and SII, were higher in GDM than in non-GDM women (P<0.05). Results from multivariable-adjusted logistic regressions revealed that, compared with the first quartile, the odds ratios (95% CI) of GDM across the highest quartile of NEU, WBC, RBC, Hb, SII, NLR, and PLT were 1.87 (1.53, 2.29), 1.81 (1.48, 2.21), 1.56 (1.28, 1.91), 1.52 (1.26, 1.84), 1.51 (1.24, 1.84), 1.42 (1.17, 1.74), and 1.36 (1.12, 1.67), respectively (all P_{trend}<0.01, Table 2). For GDM subtypes, increased risks of GDM-IFH, GDM-IPH, and GDM-CH were associated with an increase in RBC, WBC, and NEU count. Elevated LYM, rather than SII or NLR, was only significantly associated with GDM-CH. In addition, Hb and PLT were only significantly associated with GDM-IPH (Table 3). In summary, the results verified that a high level of each hematological parameter was a significant predictor of GDM. According to clinical classification, the risk for GDM was significantly increased with higher WBC [OR=2.03 (1.21, 3.31) for WBC ≥13.7×10^{12}/L], NEU [OR=2.01 (1.33, 2.98) for NEU ≥10.2×10^{12}/L], RBC [OR=1.55 (1.28, 1.87) for RBC ≥4.56×10^{12}/L], and Hb [OR=1.7 (1.34, 2.14) for Hb ≥140 g/L] levels in the first trimester (Supplementary Table S1, available in https://weekly.chinacdc.cn/).

DISCUSSION

This study found that several high-level hematological parameters (Hb concentration, RBC, PLT, and WBC, including NEU count, NLR, and SII) in the first trimester were significantly associated with an increased risk of gestational diabetes mellitus (GDM). Notably, elevated Hb concentration and PLT count, as well as elevated LYM count, could be used as potential biomarkers to identify isolated post-load hyperglycemia and GDM with fasting hyperglycemia, respectively. Our results also provide clinical evidence that elevated RBC and NEU counts in early pregnancy could be novel risk factors and biomarkers of GDM in addition to Hb concentration. To our knowledge, this is the first study to assess the impact of SII, RBC, and other hematological indices in early pregnancy on GDM and to discuss their impact on different GDM subtypes with a moderate sample size. Given that the discovery of symptoms or signs at the early stage of GDM is difficult, combining elevated hematological parameters in the first trimester with clinical risk factors or laboratory indicators may be able to identify women at higher risk as early as possible.

Research evidence suggests that subclinical inflammation may lead to insulin resistance by

TABLE 1. Characteristics among participants in the cohort according to GDM status (*n*=5,529).

Variable	Overall (*N*=5,529)	non-GDM (*n*=4,512)	GDM (*n*=1,017)	*P* value*
Age, years [median (IQR)]	31.00 (29.00, 34.00)	31.00 (29.00, 33.00)	32.00 (29.00, 35.00)	<0.001
Parity (%)				
≥1	1,966 (35.6)	1,565 (34.7)	401 (39.4)	0.005
BMI, kg/m², *n* (%)				<0.001
<18.5	190 (3.4)	154 (3.4)	36 (3.5)	
18.5–23.9	3,548 (64.2)	2,998 (66.4)	550 (54.1)	
24.0–27.9	1,450 (26.2)	1,129 (25.0)	321 (31.6)	
≥28.0	341 (6.2)	231 (5.1)	110 (10.8)	
Gestational weeks (mean±SD)	12.01±0.98	12.01±0.98	12.02±0.96	0.868
Adverse pregnancy history, *n* (%)	456 (8.2)	330 (7.3)	126 (12.4)	<0.001
Fasting plasma glucose, mmol/L (mean±SD)	4.91±0.34	4.88±0.33	5.02±0.33	<0.001
OGTT fasting, mmol/L (mean±SD)	4.63±0.38	4.54±0.30	5.01±0.46	<0.001
OGTT 1 hour, mmol/L (mean±SD)	7.69±1.61	7.29±1.32	9.45±1.59	<0.001
OGTT 2 hour, mmol/L (mean±SD)	6.63±1.24	6.32±0.95	7.99±1.43	<0.001
Hematological parameters				
RBC, 10^{12}/L (mean±SD)	4.20±0.31	4.19±0.31	4.25±0.31	<0.001
HB, g/L (mean±SD)	127.78±8.27	127.47±8.22	129.20±8.38	<0.001
WBC, 10^9/L [median (IQR)]	8.60 (7.40, 9.90)	8.50 (7.30, 9.80)	9.00 (7.70, 10.40)	<0.001
PLT, 10^9/L (mean±SD)	237.77±49.62	236.32±49.49	244.20±49.71	<0.001
LYM, 10^9/L [median (IQR)]	1.70 (1.40, 2.00)	1.70 (1.40, 2.00)	1.70 (1.50, 2.00)	0.001
NEU, 10^9/L [median (IQR)]	6.30 (5.20, 7.40)	6.20 (5.20, 7.30)	6.60 (5.50, 7.90)	<0.001
NLR [median (IQR)]	3.72 (3.00, 4.58)	3.71 (3.00, 4.56)	3.80 (3.13, 4.69)	0.005
SII [median (IQR)]	872.14 (678.57, 1113.60)	860.50 (672.19, 1099.820)	914.52 (709.71, 1186.67)	<0.001

Abbreviation: GDM=gestational diabetes mellitus; BMI=body mass index; OGTT=oral glucose tolerance test; RBC=red blood cell count; Hb=hemoglobin concentration; WBC=white blood cell count; PLT=platelet; LYM=lymphocytes; Neu=neutrophil; NLR=Neutrophil-to-lymphocyte ratio; SII=systemic immune-inflammation index, IQR=interquartile range; SD=standard deviation.

* Data are presented as mean±SD, and *P* values were from 2-sample independent *t*-tests; or presented as median (interquartile range), and *P* values were from Mann–Whitney U test; or presented as number (percent), and *P* values were from Chi-squared tests.

† OGTT was tested at 24–28 gestational weeks, and other variables were collected or measured in early pregnancy.

impairing β cell function and affecting insulin signaling directly (*12*). This may explain why classical inflammatory markers, such as WBC count and NLR, as well as the novel inflammation marker, SII, are correspondingly increased in early pregnancy among women with GDM. Additionally, platelet aggregation and glycated platelets have been reported in diabetes, which is correlated to a setting of acute and chronic inflammation with a similar cytokine milieu as that implicated in increased WBC count (*13*). In terms of surrogacy for nutritional improvement, higher RBC and Hb levels are often accompanied by higher blood viscosity, which has been demonstrated to be associated with insulin resistance (*14*). Furthermore, GDM-IFH and GDM-CH reveal impaired β -cell function and a high risk of maternal and neonatal outcomes, rather than GDM-IPH. However, the mechanisms

underlying the link between elevated lymphocytes, rather than NLR or SII, and GDM-CH still need to be established in the future.

This study had several limitations. The participants were recruited from one hospital in China, which may have introduced selection bias and limited the generalizability of our findings. Additionally, this observational study cannot explain the causal relationship between parameters in the early trimester and the risk of GDM, nor can it explain the mechanisms between hematological parameters and the risk of GDM. Further experiments or research are needed to explore these mechanisms. Overall, our results provide evidence that abnormally high routine first-trimester complete blood test results are positively associated with the risk of GDM.

Conflicts of interest: No conflicts of interest.

TABLE 2. Odds ratio and 95% confidence intervals for GDM according to quartiles of hematological markers in early pregnancy.

Variable	ORs (95% CIs) for GDM				P_{trend}*
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
SII	<680	680–872	873–1,110	≥1,111	
Cases/total (%)	211/1,383 (15.26)	229/1,382 (16.57)	277/1,382 (20.04)	300/1,382 (21.71)	
Model 1[†]	1 (ref.)	1.11 (0.90, 1.36)	1.4 (1.15, 1.70)***	1.55 (1.27, 1.88)***	<0.001
Model 2[§]	1 (ref.)	1.11 (0.90, 1.36)	1.35 (1.10, 1.64)***	1.48 (1.22, 1.81)***	<0.001
Model 3[¶]	1 (ref.)	1.12 (0.91, 1.38)	1.35 (1.11, 1.65)***	1.51 (1.24, 1.84)***	<0.001
NLR	<3.01	3.01–3.72	3.73–4.58	≥4.59	
Cases/total (%)	218/1,390 (15.68)	268/1,383 (19.38)	253/1,376 (18.39)	278/1,380 (20.14)	
Model 1	1 (ref.)	1.29 (1.06, 1.58)*	1.22 (1.00, 1.50)*	1.37 (1.12, 1.66)***	0.002
Model 2	1 (ref.)	1.29 (1.06, 1.57)*	1.21 (0.99, 1.48)	1.39 (1.14, 1.69)***	0.001
Model 3	1 (ref.)	1.31 (1.07, 1.60)**	1.24 (1.01, 1.52)*	1.42 (1.17, 1.74)***	0.001
RBC	<4.00	4.00–4.19	4.20–4.39	≥4.40	
Cases/total (%)	203/1,397 (14.53)	253/1,427 (17.73)	253/1,340 (18.88)	308/1,365 (22.56)	
Model 1	1 (ref.)	1.27 (1.04, 1.56)*	1.39 (1.13, 1.70)**	1.73 (1.43, 2.11)***	<0.001
Model 2	1 (ref.)	1.24 (1.01, 1.52)*	1.31 (1.07, 1.61)**	1.56 (1.28, 1.91)***	<0.001
Model 3	1 (ref.)	1.25 (1.02, 1.54)*	1.32 (1.07, 1.62)**	1.56 (1.28, 1.91)***	<0.001
HB	<124	124–128	129–133	≥134	
Cases/total (%)	252/1,600 (15.75)	219/1,346 (16.27)	234/1,255 (18.65)	312/1,328 (23.49)	
Model 1	1 (ref.)	1.04 (0.86, 1.27)	1.24 (1.02, 1.51)*	1.67 (1.38, 2.01)***	<0.001
Model 2	1 (ref.)	1.01 (0.83, 1.23)	1.16 (0.95, 1.41)	1.52 (1.26, 1.84)***	<0.001
Model 3	1 (ref.)	1.02 (0.83, 1.24)	1.16 (0.95, 1.41)	1.52 (1.26, 1.84)***	<0.001
WBC	<7.5	7.5–8.6	8.7–9.9	≥10.0	
Cases/total (%)	205/1,448 (14.16)	237/1,436 (16.5)	252/1,307 (19.28)	323/1,338 (24.14)	
Model 1	1 (ref.)	1.20 (0.98, 1.47)	1.46 (1.19, 1.78)***	1.96 (1.61, 2.38)***	<0.001
Model 2	1 (ref.)	1.18 (0.97, 1.45)	1.39 (1.14, 1.71)***	1.79 (1.47, 2.19)***	<0.001
Model 3	1 (ref.)	1.20 (0.98, 1.47)	1.41 (1.16, 1.71)***	1.81 (1.48, 2.21)***	<0.001
PLT	<205	205–234	235–269	≥270	
Cases/total (%)	213/1,416 (15.04)	247/1,367 (18.07)	266/1,393 (19.10)	291/1,353 (21.51)	
Model 1	1 (ref.)	1.25 (1.02, 1.53)*	1.33 (1.09, 1.62)**	1.53 (1.26, 1.86)***	<0.001
Model 2	1 (ref.)	1.23 (1.01, 1.51)*	1.25 (1.03, 1.53)*	1.37 (1.12, 1.67)**	0.001
Model 3	1 (ref.)	1.23 (1.01, 1.51)*	1.25 (1.02, 1.53)*	1.36 (1.12, 1.67)**	0.001
LYM	<1.41	1.41–1.70	1.80–2.00	≥2.01	
Cases/total (%)	243/1,498 (16.22)	298/1,664 (17.91)	249/1,295 (19.23)	227/1,072 (21.18)	
Model 1	1 (ref.)	1.14 (0.94, 1.37)	1.23 (1.01, 1.50)	1.39 (1.13, 1.70)***	0.002
Model 2	1 (ref.)	1.12 (0.93, 1.35)	1.17 (0.96, 1.43)	1.25 (1.01, 1.53)*	0.074
Model 3	1 (ref.)	1.12 (0.93, 1.35)	1.16 (0.96, 1.42)	1.23 (1.00, 1.51)*	0.102
NEU	<5.21	5.21–6.30	6.40–7.40	≥7.41	
Cases/total (%)	196/1,399 (14.01)	252/1,472 (17.12)	248/1,323 (18.75)	321/1,335 (24.04)	
Model 1	1 (ref.)	1.28 (1.04, 1.56)*	1.43 (1.17, 1.76)***	1.99 (1.63, 2.42)***	<0.001
Model 2	1 (ref.)	1.26 (1.02, 1.54)*	1.37 (1.12, 1.69)**	1.85 (1.51, 2.26)***	<0.001
Model 3	1 (ref.)	1.27 (1.03, 1.56)*	1.39 (1.13, 1.71)**	1.87 (1.53, 2.29)***	<0.001

Abbreviation: GDM=gestational diabetes mellitus; RBC=red blood cell count; Hb=hemoglobin concentration; WBC=white blood cell count; PLT=platelet; LYM=lymphocyte; Neu=neutrophils; NLR=Neutrophil-to-lymphocyte ratio; SII=systemic immune-inflammation index; CIs=confidence intervals; ORs=odds ratios; ref.=reference.
* P value <0.05.
[†] Model 1: adjusted for age.
[§] Model 2: adjusted for age and body mass index.
[¶] Model 3: adjusted for age, body mass index, gestational week, parity, adverse pregnancy history, and fasting plasma glucose.
** P value <0.01.
[††] P trend values were obtained from the logistic regression models by using individual hematological parameters treated as continuous variables, where standard deviation (SD) was used as a unit to quantify the elevation of each parameter.
*** P value <0.001.

TABLE 3. Associations of hematological markers with different gestational diabetes mellitus status.

Variable	GDM-IPH vs. NGT			GDM-IFH vs. NGT			GDM-CH vs. NGT		
	Model 1[†] OR (95% CI)	Model 2[§] OR (95% CI)	Model 3[¶] OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
SII									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	1.26 (0.95, 1.67)	1.27 (0.96, 1.69)	1.29 (0.97, 1.71)	1.03 (0.74, 1.44)	1.02 (0.73, 1.43)	1.02 (0.73, 1.44)	0.88 (0.55, 1.38)	0.88 (0.55, 1.39)	0.89 (0.56, 1.40)
Quartile 3	1.47 (1.12, 1.93)**	1.46 (1.11, 1.93)**	1.47 (1.12, 1.94)**	1.43 (1.04, 1.97)*	1.35 (0.99, 1.87)	1.36 (0.99, 1.87)	1.17 (0.76, 1.80)	1.06 (0.69, 1.64)	1.06 (0.68, 1.64)
Quartile 4	1.71 (1.31, 2.24)***	1.71 (1.31, 2.25)***	1.75 (1.34, 2.30)***	1.46 (1.07, 2.01)*	1.37 (1.00, 1.89)	1.38 (1.00, 1.90)*	1.32 (0.87, 2.02)	1.17 (0.77, 1.79)	1.20 (0.78, 1.84)
P_{trend}	<0.001	<0.001	<0.001	0.002	0.007	0.008	0.026	0.126	0.125
NLR									
Quartile 1	ref.	ref.	ref.	ref.	ref.	1 ref.	ref.	ref.	ref.)
Quartile 2	1.30 (0.99, 1.71)	1.31 (1.00, 1.72)	1.32 (1.01, 1.74)*	1.18 (0.85, 1.63)	1.18 (0.85, 1.63)	1.19 (0.86, 1.64)	1.48 (0.98, 2.26)	1.53 (1.00, 2.35)	1.54 (1.01, 2.37)*
Quartile 3	1.33 (1.02, 1.75)*	1.32 (1.01, 1.74)*	1.35 (1.03, 1.78)*	1.17 (0.85, 1.62)	1.16 (0.84, 1.6)	1.18 (0.85, 1.63)	1.03 (0.65, 1.62)	1.05 (0.66, 1.67)	1.07 (0.67, 1.71)
Quartile 4	1.43 (1.10, 1.88)**	1.43 (1.10, 1.88)**	1.47 (1.12, 1.92)**	1.36 (1.00, 1.87)	1.39 (1.01, 1.90)*	1.42 (1.04, 1.95)*	1.18 (0.76, 1.84)	1.25 (0.80, 1.96)	1.28 (0.81, 2.01)
P_{trend}	0.006	0.006	0.005	0.039	0.024	0.026	0.586	0.389	0.405
RBC									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	1.16 (0.88, 1.52)	1.15 (0.88, 1.51)	1.17 (0.89, 1.53)	1.23 (0.88, 1.72)	1.19 (0.86, 1.67)	1.21 (0.87, 1.69)	1.83 (1.15, 2.97)*	1.72 (1.08, 2.80)*	1.74 (1.09, 2.84)*
Quartile 3	1.28 (0.98, 1.69)	1.28 (0.98, 1.69)	1.30 (0.99, 1.71)	1.41 (1.02, 1.96)*	1.31 (0.94, 1.83)	1.31 (0.94, 1.83)	1.72 (1.07, 2.82)*	1.44 (0.89, 2.37)	1.46 (0.89, 2.40)
Quartile 4	1.62 (1.25, 2.11)***	1.61 (1.24, 2.11)***	1.62 (1.24, 2.11)***	1.70 (1.24, 2.35)***	1.48 (1.07, 2.05)*	1.49 (1.08, 2.06)*	2.22 (1.41, 3.58)***	1.62 (1.02, 2.64)*	1.64 (1.02, 2.67)*
P_{trend}	<0.001	<0.001	<0.001	0.001	0.024	0.027	<0.001	0.059	0.063
HB									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	0.98 (0.75, 1.29)	0.99 (0.75, 1.30)	1.00 (0.76, 1.31)	1.10 (0.80, 1.51)	1.05 (0.76, 1.44)	1.05 (0.76, 1.44)	1.11 (0.70, 1.75)	0.99 (0.63, 1.58)	1.00 (0.63, 1.59)
Quartile 3	1.12 (0.85, 1.46)	1.11 (0.85, 1.46)	1.12 (0.85, 1.46)	1.39 (1.02, 1.89)*	1.25 (0.92, 1.72)	1.25 (0.91, 1.71)	1.31 (0.84, 2.06)	1.05 (0.66, 1.66)	1.06 (0.67, 1.69)
Quartile 4	1.71 (1.34, 2.19)***	1.72 (1.34, 2.21)***	1.73 (1.35, 2.23)***	1.43 (1.05, 1.94)*	1.26 (0.92, 1.72)	1.25 (0.91, 1.71)	2.00 (1.33, 3.03)**	1.49 (0.98, 2.28)	1.52 (1.00, 2.34)
P_{trend}	<0.001	<0.001	<0.001	0.007	0.074	0.086	0.004	0.197	0.161

TABLE 3. (Continued)

Variable	GDM-IPH vs. NGT			GDM-IFH vs. NGT			GDM-CH vs. NGT		
	Model 1[†]	Model 2[§]	Model 3[¶]	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
WBC									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	1.28 (0.98, 1.68)	1.28 (0.98, 1.68)	1.30 (0.99, 1.70)	1.01 (0.72, 1.41)	0.98 (0.71, 1.37)	0.98 (0.70, 1.37)	1.46 (0.87, 2.49)	1.40 (0.83, 2.39)	1.42 (0.84, 2.42)
Quartile 3	1.39 (1.06, 1.83)*	1.39 (1.06, 1.83)*	1.41 (1.07, 1.86)*	1.27 (0.92, 1.77)	1.20 (0.87, 1.67)	1.21 (0.87, 1.68)	2.29 (1.42, 3.79)***	2.01 (1.24, 3.36)**	2.03 (1.24, 3.39)**
Quartile 4	1.72 (1.32, 2.25)***	1.72 (1.31, 2.25)***	1.73 (1.32, 2.27)***	1.80 (1.33, 2.45)***	1.60 (1.17, 2.19)**	1.59 (1.17, 2.18)**	3.37 (2.14, 5.47)***	2.62 (1.65, 4.28)***	2.68 (1.68, 4.39)***
P_{trend}	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
PLT									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	1.38 (1.05, 1.82)*	1.40 (1.07, 1.86)*	1.41 (1.07, 1.86)*	1.17 (0.85, 1.61)	1.14 (0.83, 1.57)	1.14 (0.83, 1.57)	1.09 (0.68, 1.74)	1.03 (0.64, 1.65)	1.03 (0.64, 1.66)
Quartile 3	1.45 (1.10, 1.90)**	1.45 (1.11, 1.91)**	1.46 (1.11, 1.92)**	1.12 (0.81, 1.55)	1.03 (0.75, 1.43)	1.03 (0.74, 1.43)	1.44 (0.93, 2.25)	1.21 (0.78, 1.90)	1.21 (0.77, 1.90)
Quartile 4	1.62 (1.24, 2.12)***	1.62 (1.23, 2.13)***	1.62 (1.23, 2.13)***	1.36 (1.00, 1.86)	1.17 (0.85, 1.61)	1.15 (0.84, 1.59)	1.66 (1.09, 2.58)*	1.21 (0.78, 1.90)	1.22 (0.78, 1.91)
P_{trend}	<0.001	<0.001	<0.001	0.044	0.369	0.362	0.001	0.140	0.106
LYM									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	1.08 (0.84, 1.38)	1.09 (0.85, 1.39)	1.09 (0.85, 1.40)	1.16 (0.86, 1.58)	1.13 (0.84, 1.54)	1.13 (0.84, 1.54)	1.32 (0.84, 2.11)	1.26 (0.79, 2.02)	1.25 (0.79, 2.01)
Quartile 3	1.09 (0.84, 1.42)	1.09 (0.84, 1.42)	1.09 (0.83, 1.41)	1.26 (0.92, 1.73)	1.19 (0.87, 1.64)	1.17 (0.85, 1.62)	1.74 (1.10, 2.77)*	1.52 (0.96, 2.43)	1.51 (0.95, 2.42)
Quartile 4	1.14 (0.87, 1.50)	1.13 (0.85, 1.49)	1.11 (0.84, 1.46)	1.37 (0.99, 1.91)	1.20 (0.86, 1.68)	1.19 (0.85, 1.67)	2.42 (1.55, 3.83)***	1.82 (1.16, 2.91)*	1.83 (1.16, 2.92)**
P_{trend}	0.513	0.598	0.678	0.074	0.400	0.458	<0.001	0.009	0.010
NEU									
Quartile 1	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
Quartile 2	1.16 (0.88, 1.52)	1.15 (0.88, 1.52)	1.16 (0.88, 1.53)	1.13 (0.81, 1.59)	1.11 (0.79, 1.56)	1.11 (0.79, 1.56)	2.33 (1.42, 3.94)***	2.25 (1.37, 3.82)**	2.29 (1.39, 3.89)**
Quartile 3	1.4 (1.07, 1.83)*	1.39 (1.06, 1.83)*	1.41 (1.07, 1.85)*	1.32 (0.95, 1.85)	1.25 (0.90, 1.76)	1.26 (0.90, 1.77)	1.91 (1.13, 3.32)*	1.73 (1.02, 3.01)*	1.75 (1.03, 3.06)*
Quartile 4	1.64 (1.26, 2.14)***	1.62 (1.25, 2.13)***	1.65 (1.26, 2.16)***	1.99 (1.46, 2.72)***	1.81 (1.32, 2.49)***	1.81 (1.32, 2.5)***	3.64 (2.26, 6.08)***	2.99 (1.84, 5.02)***	3.07 (1.89, 5.18)***
P_{trend}	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Abbreviation: OGTT=oral glucose tolerance test; RBC=red blood cell count; Hb=hemoglobin concentration; WBC=white blood cell count; PLT=platelet; LYM=lymphocytes; Neu=neutrophils; NLR=Neutrophil-to-lymphocyte ratio; SII=systemic immune-inflammation index; NGT=normoglycaemia; GDM-IPH, fasting glucose values ≥5.1 mmol/L with normal post-load glucose values, GDM-IPH, post-load glucose values ≥10.0 mmol/L at 1 h and/or ≥8.5 mmol/L at 2 h with normal fasting glucose values; GDM-CH, fasting blood glucose values ≥5.1 mmol/L and post-load glucose values ≥10.0 mmol/L at 1 h and/or ≥8.5 mmol/L at 2 h.

* P value <0.05.

† Model 1: adjusted for age.

§ Model 2: adjusted for age and body mass index.

¶ Model 3: adjusted for age, body mass index, gestational week, parity, adverse pregnancy history, and fasting plasma glucose.

** P value <0.01.

*** P value <0.001.

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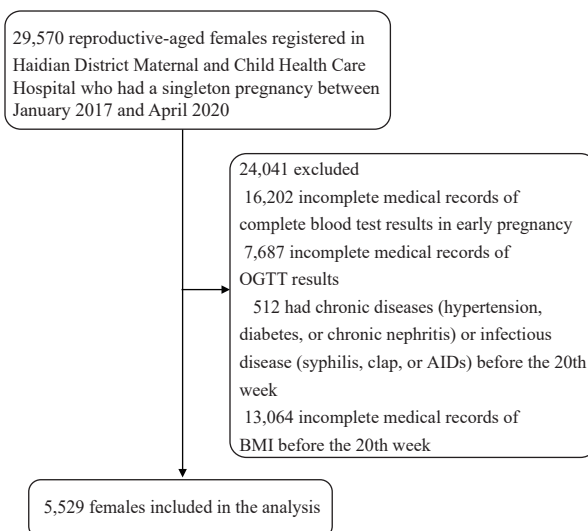[&] Joint first authors.

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SUPPLEMENTARY MATERIAL

29,570 reproductive-aged females registered in Haidian District Maternal and Child Health Care Hospital who had a singleton pregnancy between January 2017 and April 2020

24,041 excluded
 16,202 incomplete medical records of complete blood test results in early pregnancy
 7,687 incomplete medical records of OGTT results
  512 had chronic diseases (hypertension, diabetes, or chronic nephritis) or infectious disease (syphilis, clap, or AIDs) before the 20th week
 13,064 incomplete medical records of BMI before the 20th week

5,529 females included in the analysis

SUPPLEMENTARY FIGURE S1. Participant enrollment flowchart.
Abbreviation: OGTT=oral glucose tolerance test; AIDS=acquired immune deficiency syndrome; BMI=body mass index.

SUPPLEMENTARY TABLE S1. Associations of hematological parameters with GDM according to clinical classification.

Variable	Model 1		Model 2		Model 3	
	OR (95% CI)	*P* value	*OR (95% CI)*	*P* value	*OR (95% CI)*	*P* value
RBC <3.42×10^{12}/L	0.49 (0.08, 1.70)	0.338	0.53 (0.08, 1.84)	0.390	0.49 (0.08, 1.70)	0.338
RBC ≥4.56×10^{12}/L	1.55 (1.28, 1.87)	<0.001	1.40 (1.15, 1.70)	0.001	1.55 (1.28, 1.87)	<0.001
Hb <116 g/L	0.75 (0.55, 1.01)	0.068	0.81 (0.59, 1.09)	0.176	0.75 (0.55, 1.01)	0.068
Hb ≥140 g/L	1.70 (1.34, 2.14)	<0.001	1.57 (1.24, 1.99)	<0.001	1.70 (1.34, 2.14)	<0.001
WBC <5.7×10^9/L	0.89 (0.59, 1.31)	0.577	0.96 (0.63, 1.42)	0.853	0.89 (0.59, 1.31)	0.577
WBC ≥13.7×10^9/L	2.03 (1.21, 3.31)	0.006	1.81 (1.07, 2.98)	0.022	2.03 (1.21, 3.31)	0.006
PLT <174×10^9/L	0.64 (0.48, 0.85)	0.002	0.68 (0.51, 0.90)	0.008	0.64 (0.48, 0.85)	0.002
PLT ≥392×10^9/L	1.00 (0.29, 2.71)	0.996	0.76 (0.22, 2.11)	0.634	1.00 (0.29, 2.71)	0.996
LYM <1.1×10^9/L	1.07 (0.74, 1.51)	0.706	1.14 (0.79, 1.61)	0.475	1.14 (0.78, 1.60)	0.486
LYM ≥3.61×10^9/L	5.34 (0.64, 44.89)	0.095	5.24 (0.62, 44.06)	0.099	5.98 (0.71, 50.35)	0.075
NEU <3.60×10^9/L	0.70 (0.38, 1.20)	0.226	0.73 (0.39, 1.24)	0.272	0.70 (0.38, 1.20)	0.226
NEU ≥10.2×10^9/L	2.01 (1.33, 2.98)	0.001	1.90 (1.25, 2.83)	0.002	2.01 (1.33, 2.98)	0.001

Abbreviation: OGTT=oral glucose tolerance test; RBC=red blood cell count; Hb=hemoglobin concentration; WBC=white blood cell count; PLT=platelet; LYM=lymphocyte; GDM=gestational diabetes mellitus.