

Supplemental files for

Association of maternal folate and vitamin B₁₂ in early pregnancy with gestational diabetes mellitus: a prospective cohort study

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Running title: Folate, vitamin B₁₂ and gestational diabetes

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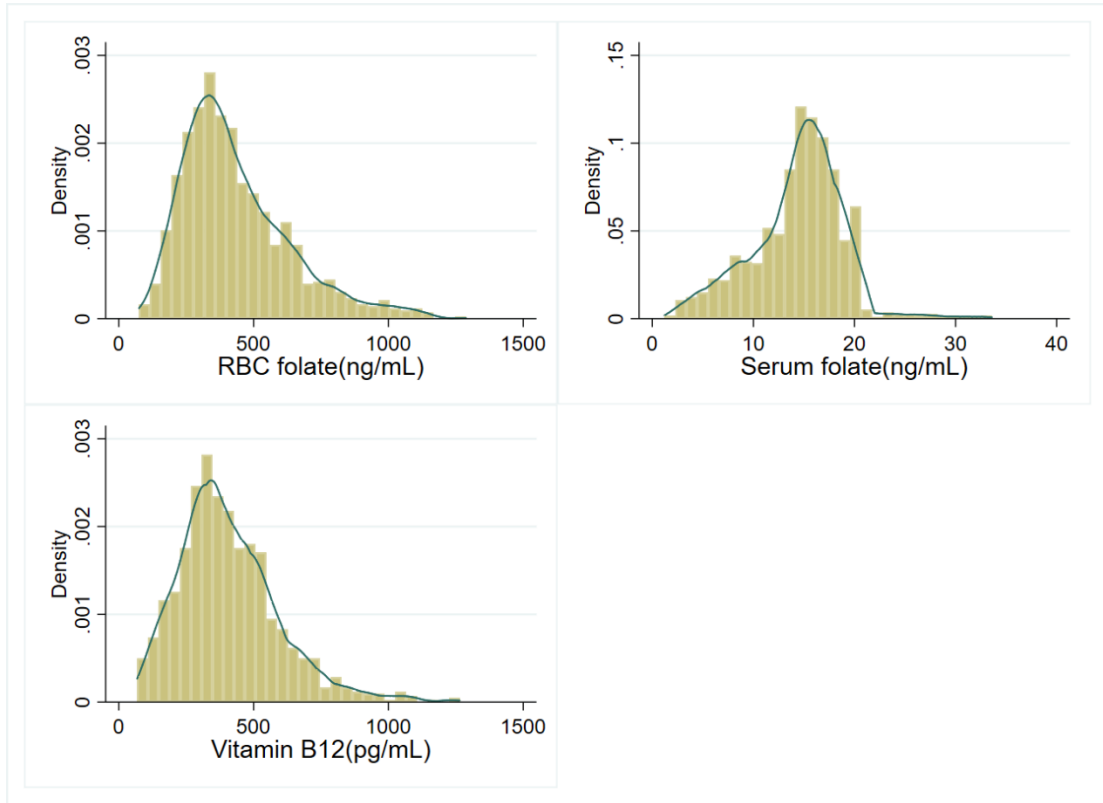
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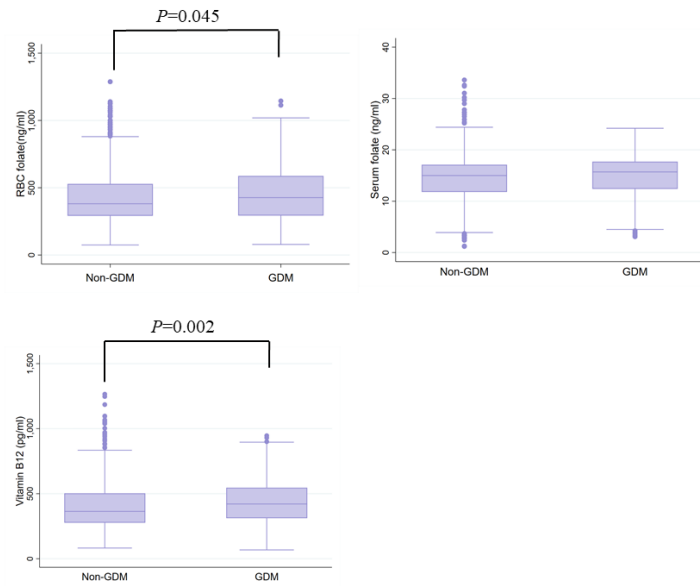
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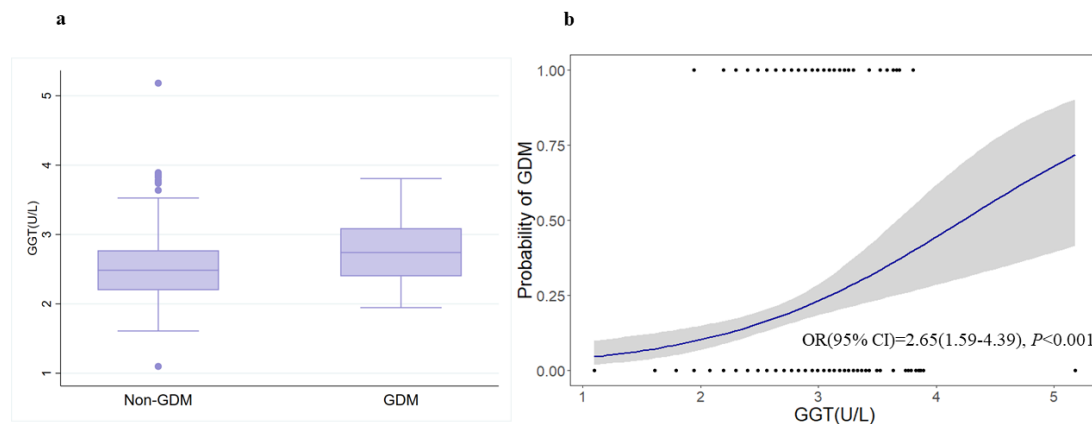
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Supplemental Figure S1. The distribution RBC folate (ng/mL), serum folate(ng/mL) and serum vitamin B₁₂ (pg/mL) concentration.



Supplemental Figure S2. Comparison of RBC folate, serum folate and vitamin B₁₂ between GDM and non-GDM. RBC folate and vitamin B₁₂ levels of GDM were significantly higher than that of non-GDM [426.44 (293.15, 587.61) vs 380.95 (291.44, 528.53) (ng/mL), $P=0.045$; 421.00 (312.00, 546.00) vs 364.00 (277.00, 503.00) (pg/mL), $P=0.002$].



Supplemental Figure S3. The comparison of GGT at early pregnancy between GDM and non-GDM is based on a subgroup of study subjects (n=458). To explore the potential mechanisms of how higher vitamin B₁₂ associated with an increased risk of GDM, the γ -glutamyl transferase level (GGT), one of impaired liver function markers measured in routine antenatal care, was analyzed with GDM risk. Figure a showed the GGT level in GDM was significantly higher than non-GDM [2.7 (2.3, 3.1) vs 2.4 (2.1, 2.7), $P < 0.001$]; Figure b depicted the probability of GDM fitted by logistical regression, high GGT concentration was significantly associated with GDM risk, OR(95% CI)=2.65(1.59-4.39), $P < 0.001$.

Supplemental Table S1. Association of folate/vitamin B₁₂ in early pregnancy with GDM risk

Variables	Group	GDM/Total (%)	Model 1 [†]			Model 2 [‡]		
			OR	95% CI	<i>P</i>	OR	95% CI	<i>P</i>
RBC folate/ vitamin B ₁₂			0.97	0.83-1.15	0.79	0.923	0.77-1.09	0.36
	Q1(<0.69)	47/257(18.2)		Ref			Ref	
	Q2(0.69-1.55)	88/538(16.3)	0.87	0.59-1.29	0.49	0.83	0.55-1.24	0.36
	Q3(≥1.55)	45/263(17.1)	0.92	0.58-1.44	0.72	0.80	0.50-1.28	0.37
	Trend test				0.72			0.37
Serum folate/ vitamin B ₁₂ [*]			0.99	0.98-0.99	0.027	0.98	0.97-0.99	0.009
	Q1(<28.98)	62/310(20.0)		Ref			Ref	
	Q2(28.98-48.23)	73/444(16.4)	0.78	0.54-1.14	0.21	0.76	0.52-1.13	0.18
	Q3(≥48.23)	45/304(14.8)	0.69	0.45-1.05	0.09	0.63	0.41-0.98	0.042
	Trend test				0.08			0.041

* the ratio of serum folate to vitamin B₁₂ concentrations was determined by dividing folate concentrations (ng/mL) by vitamin B₁₂ concentrations (pg/mL) and multiplying by 1000; † univariate model; ‡ adjusted for age, preconceptional-BMI, family history of diabetes, smoking exposure and drinking status;

Table S2. Association of maternal serum folate levels at mid-gestation with GDM risk (N=458)

Variable	Group	GDM (%)	Model 1 [†]			Model 2 [‡]		
			OR	95% CI	<i>P</i>	OR	95% CI	<i>P</i>
Serum folate (ng/ml)			1.08	1.03-1.13	0.001	1.08	1.03-1.14	0.002
	Q1(<5.1)	16/138(11.5)		Ref			Ref	
	Q2(5.1-10.7)	23/140(16.4)	1.49	0.75-2.39	0.24	1.48	0.72-3.06	0.28
	Q3(≥10.7)	34/136(25.0)	2.81	1.32-4.87	0.005	2.54	1.28-5.03	0.007
Serum folate change*			0.94	0.90-0.98	0.017	0.95	0.90-0.99	0.019

This analysis was conducted based on a subgroup of our study subjects (n=458);

* The levels at early pregnancy minus the levels at mid-gestation;

† Univariate model;

‡ Adjusted for age, preconceptional-BMI, family history of diabetes, smoking exposure and drinking status.