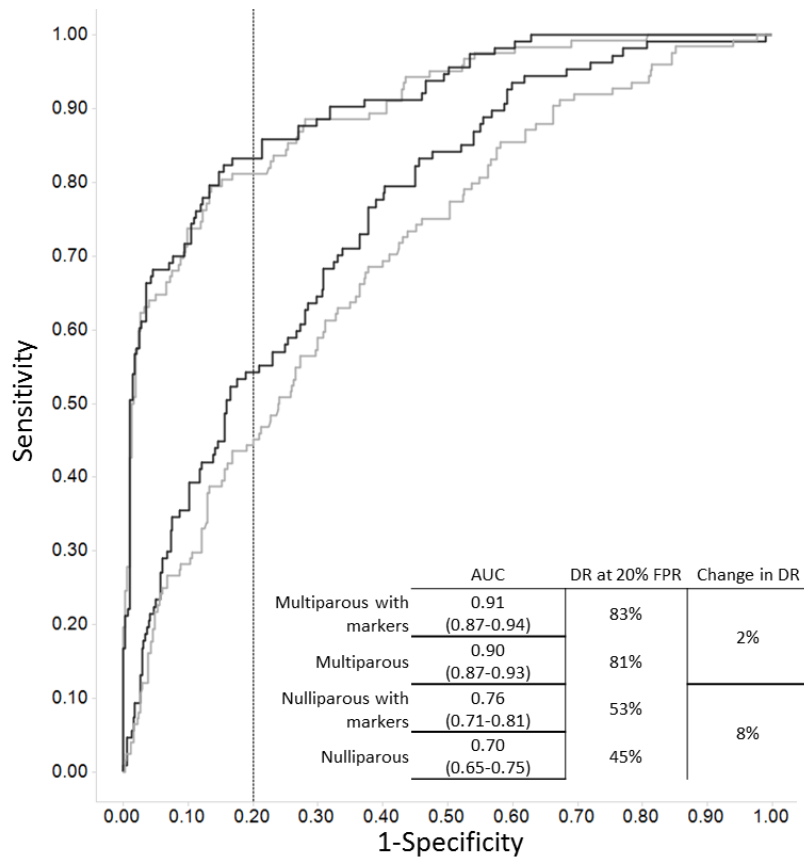


Supplementary Figure S1 ROC curves showing the performance of triglycerides and lipocalin-2 for prediction of GDM within ethnic sub-cohorts

Lipocalin-2 AUC (95% CI): 0.65 (95% CI 0.59-0.71) (Caucasians); 0.54 (95% CI 0.42-0.66) (South Asians); 0.49 (95% CI 0.41-0.57) (East Asians), respectively. Triglycerides AUC (95% CI): 0.68 (95% CI 0.57-0.79) (South Asians); 0.64 (95% CI 0.58-0.70) (Caucasians); 0.60 (95% CI 0.52-0.68) (East Asians).



Supplementary Figure S2 ROC curves demonstrating the contribution of biomarkers to the performance of the novel prediction model according to parity

Contribution of biomarkers to model performance is marginal for multiparous women with a history of previous GDM and/or family history of diabetes (two upper lines). Model performance is however significantly enhanced by the addition of the novel biomarkers in nulliparous women in whom previous GDM or family history of diabetes is not available (two lower lines) Black lines are with biomarkers and grey lines without biomarkers.

Supplementary Table S1 Maternal characteristics and first trimester markers by timing of GDM diagnosis

Variables	GDM early (n=89; 39%)	GDM late (n=138; 61%)
Gestation at diagnosis (weeks)	17.5±3.9	28.2±2.0
Maternal age (years)	33 (30-36)	33 (30-36)
BMI (kg/m²)	25.1 (22.3-29.6)	24.5 (22.8-27.4)
Ethnicity (%)	#	
Caucasian	30 (33.7%)	69 (50%)
East Asian	33 (37.1%)	50 (36.2%)
South Asian	25 (28.1%)	18 (13.0%)
Other	1 (1.1%)	1 (0.8%)
Family history of diabetes mellitus** (%)	59 (66.3%)#	74 (53.6%)
Parity (%)		
Nulliparous	41 (46.1%)	80 (58.0%)
Parous with previous GDM	29 (32.6%)#	16 (11.6%)
Parous with no previous GDM	19 (21.3%)	42 (30.4%)
Polycystic Ovary Syndrome (%)	4 (4.5%)	7 (5.1%)
Previous Macrosomia*** (%)	8 (9.0%)	6 (4.3%)
Aneuploidy and pre-eclampsia markers		
MoM (IQR)		
PAPP-A	0.79 (0.61-1.17)	0.83 (0.57-1.25)
free-hCGβ	1.07 (0.63-1.50)	0.95 (0.66-1.47)
MAP	1.02 (0.96-1.11)	1.02 (0.96-1.09)
UtA PI	1.04 (0.78-1.26)	1.00 (0.83-1.18)
Biochemistry		
MoM (IQR)		
Glucose	1.04 (0.95-1.18)#	1.03 (0.94-1.10)
Cholesterol	0.99 (0.90-1.10)	1.02 (0.91-1.12)
Triglycerides	1.28 (0.97-1.64)#	1.14 (0.90-1.44)
Novel biomarkers		
MoM (IQR)		
Leptin	1.09 (0.83-1.46)	1.12 (0.81-1.53)
Adiponectin	0.85 (0.71-1.05)	0.87 (0.67-1.12)
Lipocalin-2	1.05 (0.80-1.49)	1.18 (0.89-1.40)
PAI-2	1.05 (0.75-1.36)	1.06 (0.74-1.52)

Values are presented as medians (IQR), numbers (percentages) or means ± SD, as appropriate. *First or second degree relative with type 2 diabetes and/or sister with GDM. **Birthweight >4000 grams. Values as medians (IQR). # p-value < 0.05 early vs. standard GDM.

Supplementary Table S2 Biomarker concentrations and MoM values stratified by GDM status and ethnicity

Markers	Controls			GDM		
	Caucasians (n=530)	East Asians (n=134)	South Asians (n=54)	Caucasians (n=108)	East Asians (n=91)	South Asians (n=47)
Traditional biomarkers						
Concentrations						
Glucose (mmol/L)	4.2 (3.9-4.6)	4.3 (4.0-4.7)‡	4.3 (4.0-4.6)	4.4 (4.0-4.8)*	4.5 (4.1-5.0)	4.4 (4.2-5.2)*
Cholesterol (mmol/L)	4.7 (4.2-5.2)	4.6 (4.1-5.2)	4.7 (4.1-5.2)	4.8 (4.3-5.3)	4.6 (4.2-4.9)	4.8 (4.2-5.4)
Triglycerides (mmol/L)	1.1 (0.9-1.4)	1.3 (1.1-1.7)‡	1.3 (1.0-2.3)‡	1.3 (1.1-1.8)	1.6 (1.2-2.1)*	1.7 (1.3-2.3)*
Median MoM (IQR)						
Glucose	1.01 (0.92-1.09)	1.01 (0.93-1.10)	1.01 (0.93-1.08)	1.03 (0.94-1.11)*	1.04 (0.94-1.13)	1.02 (0.95-1.19)*
Cholesterol	1.00 (0.90-1.12)	0.99 (0.89-1.12)	1.01 (0.86-1.14)	1.03 (0.90-1.13)	0.98 (0.91-1.07)	1.03 (0.89-1.18)
Triglycerides	0.99 (0.82-1.22)	0.97 (0.77-1.26)	0.97 (0.81-1.18)	1.17 (0.93-1.52)*	1.16 (0.86-1.46)*	1.25 (0.98-1.68)*
Novel biomarkers						
Concentrations						
Leptin (ng/mL)	13.3 (8.8-20.5)	12.7 (8.4-17.3)‡	21.8 (13.6-28.4)‡	21.9 (11.3-32.8)*	15.1 (9.4-20.6)*	24.0 (14.6-31.8)
Adiponectin (µg/mL)	24.5 (19.4-30.5)	18.1 (13.2-24.4)‡	17.6 (12.7-25.1)‡	18.8 (15.3-25.4)*	15.5 (11.2-20.1)*	15.0 (12.3-18.7)*
Lipocalin 2 (ng/mL)	87.2 (65.9-111.6)	73.7 (55.1-94.9)‡	64.8 (47.2-109.0)‡	105.9 (73.9-141.7)*	70.9 (57.9-95.8)	76.0 (51.9-91.5)
PAI-2 (ng/mL)	38.3 (30.0-53.7)	38.2 (29.1-47.6)	36.5 (28.4-49.4)	40.5 (28.3-60.1)	40.7 (31.3-51.3)	39.5 (27.0-53.0)
Median MoM (IQR)						
Leptin	1.02 (0.73-1.38)	1.04 (0.74-1.44)	1.10 (0.71-1.38)	1.18 (0.85-1.63)*	1.04 (0.78-1.42)	1.07 (0.70-1.32)
Adiponectin	1.01 (0.81-1.23)	0.97 (0.73-1.31)	1.00 (0.76-1.42)	0.86 (0.69-1.07)*	0.87 (0.67-1.07)*	0.86 (0.74-1.06)*
Lipocalin-2	1.00 (0.79-1.26)	0.99 (0.75-1.32)	0.84 (0.70-1.44)	1.25 (0.95-1.54)*	0.98 (0.84-1.32)	1.04 (0.79-1.34)
PAI-2	0.94 (0.77-1.30)	1.00 (0.76-1.26)	0.95 (0.75-1.30)	1.01 (0.73-1.54)*	1.06 (0.80-1.38)	0.98 (0.73-1.35)

Markers presented as absolute concentrations or MoM values. Values as medians (IQR). * p-value < 0.05 compared to respective control group. ‡ p-value < 0.05 compared to Caucasians.

Women with ethnicity defined as “other” were excluded from this analysis (n=16).