Table S1. Age, pre-pregnancy BMI and race between women with future T2D and no T2D

	No T2D (n=100)	Future T2D (n=100)	P-value
Age, Mean (SD)	33.48 (4.95)	34.06 (5.40)	0.242
Pre-pregnancy BMI, Mean (SD)	32.18 (7.37)	33.79 (8.68)	0.298
Race, n (%)			1.000
Non-Hispanic white	16 (16%)	16 (16%)	
Asian	36 (36%)	36 (36%)	
Non-Hispanic black	10 (10%)	10 (10%)	
Hispanic	36 (36%)	36 (36%)	
Other	2 (2%)	2 (2%)	

Normal distribution was checked through histogram and Q-Q plot. Data are presented as Mean (SD) for continuous variables that are approximately normally distributed. Chi-square test was used for categorical variables (n, %), student's t-test was used for continuous variables (Mean, SD). BMI, body mass index; T2D, type 2 diabetes.

Table S2. Lactation-related clinical variables in future T2D, no T2D and all women

	Future T2D (n=100)	**No T2D (n=100)**	**All (n=200)**	**p-value (T2D vs. no T2D)**
Prolactin (ng/ml), Median (IQR)	54.68 (29.66-113.72)	74.31 (39.61-132.8)	60.88 (34.85-126.24)	0.104
Quartile 1	<=29.66 ng/ml	<=39.61 ng/ml	<=34.85 ng/ml	
Quartile 2	>29.66-54.68 ng/ml	>39.61-74.31 ng/ml	>34.85-60.88 ng/ml	
Quartile 3	>54.68-113.72 ng/ml	>74.31-132.80 ng/ml	>60.88-126.24 ng/ml	
Quartile 4	>113.72 ng/ml	>132.80 ng/ml	>126.24 ng/ml	
Pre-pregnancy BMI, kg/m^2, Mean (SD)	33.79 (8.68)	32.18 (7.37)	32.99 (8.07)	0.298
Glucose tolerance at 6-9 weeks postpartum, n (%)				**<0.001**
Normal	34 (34%)	72 (72%)	106 (53%)	
Impaired	66 (66%)	28 (28%)	94 (47%)	
LIR 2-month score, Median (IQR)	1.72 (0.97-2.00)	1.86 (1.00-2.00)	1.82 (1.00-2.00)	0.661
Total lactation duration, months, Median (IQR)	5.60 (2.00-11.99)	7.08 (2.71-12.00)	6.02 (2.20-12.00)	0.305

Normal distribution was checked through histogram and Q-Q plot. Data are presented as Mean (SD) for continuous variables that are approximately normally distributed. Data are presented as Median (IQR) for continuous variables with asymmetrical distributions. Chi-square test was used for categorical variables (n, %), student's t-test was used for continuous variables (Mean, SD), and Mann-Whitney U test was used for continuous variables (Median, IQR). BMI, body mass index; LIR, lactation intensity/duration ratio; T2D, type 2 diabetes.

Table S3. Clinical characteristics in different quartiles of prolactin levels in women with normal prolactin levels (n=131)

Clinical characteristics	**Quartile 1 <=27.14 (n=32)**	**Quartile 2 >27.14-41.07 (n=33)**	**Quartile 3 >41.07-59.06 (n=33)**	**Quartile 4 >59.06-97.57 (n=33)**	**P-value**
Age, Mean (SD)	32.9 (5.4)	34.3 (5.0)	32.6 (5.0)	34.3 (4.7)	0.383
Pre-pregnancy BMI, kg/m^2, Mean (SD)	35.7 (9.7)	32.3 (8.9)	34.4 (7.0)	34.0 (8.8)	0.463
Race, n (%)					0.134
Non-Hispanic white	4 (12.5%)	10 (30.3%)	4 (12.1%)	4 (12.1%)	
Asian	9 (28.1%)	14 (42.4%)	11 (39.4%)	13 (39.4%)	
Non-Hispanic black	6 (18.8%)	3 (9.1%)	6 (6.1%)	2 (6.1%)	
Hispanic	13 (40.6%)	5 (15.2%)	10 (42.4%)	14 (42.4%)	
Other	0 (0.0%)	1 (3.0%)	2 (0.0%)	0 (0.0%)	
Prenatal 3-hr 100 g OGTT z-score sum, Mean (SD)	0.2 (2.5)	0.3 (2.8)	0.7 (2.9)	1.3 (3.0)	0.389
GDM treatment, n (%)					0.263
Insulin or oral medicine	15 (46.9%)	16 (48.5%)	9 (27.3%)	15 (45.5%)	
Diet	17 (53.1%)	17 (51.5%)	24 (72.7%)	18 (54.5%)	
Baseline variables (6-9 weeks post-delivery)					
BMI, kg/m^2, Mean (SD)	36.0 (8.9)	32.9 (8.2)	34.4 (6.5)	32.9 (7.8)	0.334
LIR 2-month intensity score, Median (IQR)	0.7 (1.4)	1.3 (1.5)	1.7 (1.2)	1.9 (0.8)	**<0.001**
Total lactation duration, months, Median (IQR)	1.2 (2.2)	4.1 (7.0)	5.0 (9.9)	8.0 (9.0)	**<0.001**
FPG, mg/dl, Mean (SD)	101.3 (10.3)	101.5 (11.1)	94.0 (8.7)	99.8 (11.3)	**0.013**
2h-PG, mg/dl, Mean (SD)	119.1 (24.0)	110.1 (29.0)	121.5 (27.2)	132.9 (38.5)	**0.027**
Fasting insulin, mU/ml, Mean (SD)	33.3 (19.0)	28.2 (15.5)	29.6 (17.1)	27.4 (17.5)	0.533
HOMA-IR, Median (IQR)	8.6 (6.3)	6.5 (5.3)	6.3 (5.1)	6.0 (6.4)	0.334
Fasting TAG, mg/dl, Median (IQR)	125.5 (116.0)	108.0 (104.0)	102.0 (84.5)	98.0 (108.5)	0.954
Fasting HDL-C, mg/dl, Mean (SD)	47.4 (12.5)	51.2 (11.8)	47.9 (15.0)	48.4 (9.4)	0.616
Leptin, Mean (SD)	38.3 (16.1)	34.4 (17.5)	37.0 (16.0)	29.6 (17.3)	0.900
Adiponectin, Median (IQR)	6.4 (2.5)	6.6 (3.6)	6.5 (3.9)	6.5 (3.9)	

Normal distribution was checked through histogram and Q-Q plot. Data are presented as Mean (SD) for continuous variables that are approximately normally distributed. Data are presented as Median (IQR) for continuous variables with asymmetrical distributions. Chi-square test was used for categorical variables (n, %), One-way ANOVA was used for continuous variables (Mean, SD), and Kruskal-Wallis test was used for continuous variables (Median, IQR).

2h-PG, 2-hour post-load plasma glucose; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high density lipoprotein-cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LIR, lactation intensity/duration ratio; TAG, triglyceride.

Table S4. Clinical characteristics in different quartiles of prolactin levels in women with abnormal prolactin levels (n=69)

Clinical characteristics	Quartile 1 >100-124.16 (n=17)	Quartile 2 >124.16-165.38 (n=17)	Quartile 3 >165.38-201.44 (n=17)	Quartile 4 >201.44-560.03 (n=18)	P-value
Age, Mean (SD)	34.0 (5.5)	35.2 (5.1)	34.4 (5.3)	33.1 (5.9)	0.716
Pre-pregnancy BMI, kg/m^2, Mean (SD)	32.7 (3.8)	28.1 (4.6)	33.2 (8.4)	29.5 (6.8)	**0.049**
Race, n (%)					0.673
Non-Hispanic white	4 (23.5%)	2 (11.8%)	2 (11.8%)	2 (11.1%)	
Asian	5 (29.4%)	7 (41.2%)	5 (29.4%)	8 (44.4%)	
Non-Hispanic black	0 (0.0%)	2 (11.8%)	1 (5.9%)	0 (0.0%)	
Hispanic	8 (47.1%)	6 (35.3%)	8 (47.1%)	8 (44.4%)	
Other	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	
Prenatal 3-hr 100 g OGTT z-score sum, Mean (SD)	0.7 (2.2)	0.2 (2.2)	0.7 (3.0)	0.03 (3.3)	0.832
GDM treatment, n (%)					0.686
Insulin or oral medicine	7 (41.2%)	7 (41.2%)	8 (47.1%)	5 (27.8%)	
Diet	10 (58.8%)	10 (58.8%)	9 (52.9%)	13 (72.2%)	
Baseline variables (6-9 weeks post-delivery)					
BMI, kg/m^2, Mean (SD)	32.1 (3.7)	28.1 (3.8)	34.1 (7.8)	29.7 (5.2)	**0.009**
LIR 2-month intensity score, Median (IQR)	2.0 (0.3)	2.0 (0.3)	2.0 (0.2)	1.9 (0.7)	0.736
Total lactation duration, months, Median (IQR)	11.5 (10.8)	9.1 (6.0)	11.4 (7.5)	12.0 (10.9)	0.491
FPG, mg/dl, Mean (SD)	95.8 (8.2)	95.8 (9.7)	95.0 (8.1)	94.2 (8.4)	0.943
2h-PG, mg/dl, Mean (SD)	117.2 (27.7)	118.5 (30.9)	105.0 (35.5)	125.1 (28.7)	0.288
Fasting insulin, mU/ml, Mean (SD)	23.3 (10.2)	19.1 (10.4)	28.7 (13.6)	22.5 (11.5)	0.119
HOMA-IR, Median (IQR)	5.3 (2.4)	3.9 (3.1)	5.6 (6.2)	4.7 (2.9)	0.143
Fasting TAG, mg/dl, Median (IQR)	104.0 (111.0)	92.0 (42.5)	125.0 (108.5)	86.5 (47.8)	0.388
Fasting HDL-C, mg/dl, Mean (SD)	48.4 (13.2)	60.9 (10.0)	53.4 (18.5)	55.3 (12.6)	0.079
Leptin, Mean (SD)	28.8 (13.2)	22.9 (12.9)	31.4 (13.4)	31.4 (16.5)	0.256
Adiponectin, Median (IQR)	7.3 (3.3)	6.7 (3.8)	7.4 (3.2)	7.7 (3.9)	0.997

Normal distribution was checked through histogram and Q-Q plot. Data are presented as Mean (SD) for continuous variables that are approximately normally distributed. Data are presented as Median (IQR) for continuous variables with asymmetrical distributions. Chi-square test was used for categorical variables (n, %), One-way ANOVA was used for continuous variables (Mean, SD), and Kruskal-Wallis test was used for continuous variables (Median, IQR).

2h-PG, 2-hour post-load plasma glucose; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high density lipoprotein-cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LIR, lactation intensity/duration ratio; TAG, triglyceride.

Table S5 Prolactin-correlated metabolites subjected to MetaBridge analysis

Metabolites	Correlation coefficients	p-value	FDR
PC ae C36:1	0.269	0.000	0.017
SM (OH) C22:1	0.239	0.001	0.018
lysoPC a C17:0	0.243	0.001	0.019
lysoPC a C18:2	0.253	0.000	0.021
lysoPC a C18:1	0.244	0.001	0.024
PC ae C36:0	0.222	0.002	0.037
SM (OH) C24:1	0.216	0.002	0.042
SM C16:0	0.203	0.004	0.042
Met	0.210	0.003	0.043
SM C24:0	0.213	0.002	0.044
lysoPC a C20:3	0.199	0.005	0.044
lysoPC a C16:0	0.200	0.004	0.045
PC aa C36:1	0.203	0.004	0.046
PC aa C34:1	0.207	0.003	0.047
SM (OH) C16:1	0.204	0.004	0.049
SM (OH) C14:1	0.193	0.006	0.051
SM C18:0	0.193	0.006	0.054
lysoPC a C16:1	0.188	0.008	0.060
PC ae C36:2	0.187	0.008	0.060
lysoPC a C18:0	0.184	0.009	0.061
PC ae C38:0	0.184	0.009	0.063
SM (OH) C22:2	0.177	0.012	0.075
PC ae C34:1	0.178	0.012	0.075
PC aa C28:1	0.173	0.014	0.084
PC ae C38:2	0.170	0.016	0.086
SM C24:1	0.171	0.016	0.088
PC ae C34:0	0.161	0.023	0.121
PC ae C40:2	0.158	0.025	0.128
Orn	0.155	0.028	0.138
lysoPC a C26:1	0.152	0.031	0.148
PC ae C34:2	0.151	0.033	0.150
SM C26:0	0.146	0.039	0.153
PC aa C36:2	0.146	0.039	0.156
PC ae C40:3	0.147	0.038	0.157
PC aa C40:2	0.147	0.037	0.160
lysoPC a C20:4	0.148	0.036	0.160
PC ae C36:3	0.143	0.043	0.161
PC ae C38:3	0.142	0.044	0.161
Lys	0.143	0.043	0.163