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Human milk composition in women with gestational diabetes mellitus: a systematic review and meta-analysis

Xinyu Qin[1†], Siyu Li[1†] and Huiyan Wang[1*]

Abstract

Background Gestational diabetes mellitus (GDM) is a prevalent pregnancy disorder. In recent years, numerous studies have affirmed the augmented risk of obesity and diabetes mellitus in the offspring of affected individuals. Exclusive breastfeeding has been vigorously advocated as an infant feeding practice in various countries. We aimed to test our hypothesis that human milk of women with gestational diabetes differs from that of non-GDM women.

Methods For this systematic review and meta-analysis, we searched the CNKI, PubMed, Web of Science databases, and citations for studies published between Jan 1,2000 and Sep 26, 2024. We included all studies related to human milk macronutrients. We did separate meta-analyses for carbohydrates, proteins, lipids, and energy of the colostrum and mature human milk. All analyses were performed using Revman 5.4.1 (Review Manager). The quality of the evidence was assessed with the NOS scale. Registration does not apply.

Findings Of 377 records identified, 9 records were available, all of which had a moderate to high quality. Compared to non-GDM women, the colostrum of GDM women exhibited a higher protein content (MD = 0.04, 95% CI: 0.00~0.07, P = 0.03), while there were no significant disparities in carbohydrates, lipids, and energy. Simultaneously, the mature human milk of GDM women had a higher protein content (MD = 0.01, 95% CI: 0.00~0.02, P = 0.007) and a higher lipid content (MD = 0.19, 95% CI: 0.08~0.31, P = 0.001), with no significant differences in carbohydrates and energy.

Interpretation There are many factors affecting the composition of human milk and fewer studies have been conducted on the composition of human milk. More high-quality studies are needed to validate the relationship between macronutrients in colostrum and carbohydrate in mature milk content with GDM.

Keywords Gestational diabetes, Human milk, Breastfeeding

Introduction

Gestational diabetes mellitus (GDM), characterized by impaired glucose tolerance first identified during pregnancy, constitutes a significant public health concern, with an approximate global prevalence of 14% [1]. Over the recent decades, the prevalence of GDM has been steadily escalating in numerous countries [2]. GDM not only heightens the risk of major obstetric and perinatal complications, such as preeclampsia, stillbirth, macrosomia, shoulder dystocia, metabolic syndrome, and cardiovascular disease, but it is also associated with long-term health hazards for both women and their infants [3–5]. A burgeoning body of research indicates that infants exposed to GDM have an elevated incidence of obesity and insulin resistance during childhood, along with an increased likelihood of impaired glucose tolerance and type 2 diabetes in adulthood [6–8]. The underlying

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mechanisms accountable for these long-term ramifications of GDM exposure in infants remain elusive. It has been hypothesized that the altered glycolipid metabolism in women with GDM can exert an influence on neonatal well-being [9].

Human milk (HM) furnishes essential nutrients and bioactive factors for infant growth and development [10, 11]. Currently, the definition of the four stages of human milk vary across different literatures. It is generally believed that human milk is divided into four stages: colostrum, transitional milk, mature milk, and late milk. Colostrum refers to the milk secreted within the first week after childbirth, which is characterized by high levels of immunoglobulins and proteins, and low levels of fat and lactose. Transitional milk is the stage between colostrum and mature milk, secreted from day 7 to 14 after childbirth, with a significant increase in milk volume, gradually decreasing protein content, and gradually increasing fat and lactose content. Mature milk is secreted from day 14 after childbirth until the end of the breastfeeding period, with relatively stable components, moderate protein content, and higher levels of fat and lactose. Late milk is secreted after 10 months of childbirth, with gradually decreasing milk volume and nutritional components. Exclusive breastfeeding has emerged as a highly advocated infant feeding approach in various nations. The World Health Organization (WHO) recommends that infants be exclusively breastfed for at least 6 months [12].

Infancy represents a critical period of development [13]. Mother's milk is frequently regarded as the prime nutritional choice for newborns, and it has been demonstrated that breastfeeding offers protection against childhood obesity [14]. Conversely, the early introduction of formula or bottle-feeding has been associated with a more rapid increase in infant weight gain and a subsequent augmented risk of childhood obesity [15]. Considering the substantial impact of HM on neonatal development as well as the potential influence of diabetes mellitus on human milk composition, several studies have contrasted the macronutrients in the milk of GDM women with those of non-GDM women to appraise the alterations in human milk composition associated with this pathology, yet with inconsistent outcomes. Consequently, this study aims to compare the macronutrients in the human milk of GDM women with non-GDM women via systematic analysis and meta-analysis.

Materials and methods

Search strategy and inclusion/exclusion criteria

All studies concerning human milk composition in women with GDM and gestational diabetes mellitus up to Sep 26, 2024 were retrieved through the CNKI, PubMed, and Web of Science databases. The search terms encompassed Diabetes, Gestational (MeSH, from PubMed) and Milk, Human-related terms, namely Diabetes, Gestational, Gestational Diabetes Mellitus, Pregnancy-Induced Diabetes, Gestational Diabetes, Milk, Human, Human Milk, Human Milk Composition, and Gestational Diabetes Mellitus. The detailed search terms employed in each database are presented in Supplementary Table 1. Additionally, the reference lists were manually inspected from eligible studies, review papers, and conference abstracts. Irrelevant articles were excluded by scrutinizing the title, abstract, and full text. In the event that a full text could not be accessed or downloaded from the aforementioned electronic databases, efforts were made to obtain the full text by searching the online scholarly search and full text delivery system or by contacting the corresponding author. Both authors conducted database searches and screened titles and abstracts to determine the potential eligibility of the records, and independently evaluated the eligibility of the full texts, resolving any discrepancies through negotiation. The specific extraction process is depicted in Fig. 1.

The included studies were required to encompass (1) gestational diabetes, excluding other forms of diabetes, and human milk macronutrients, and (2) detailed quantitative data. There were no restrictions imposed on the sample size, medical setting, or geographic location. Case reports, book chapters, conference abstracts, and studies on pregestational diabetes were excluded.

Data extraction

The following information was extracted: (1) The first author's name and the year of publication. (2) The content of the study. (3) The method and instrumentation employed to test the human milk composition. (4) The baseline data of the participants. (5) The number of GDM and non-GDM women in each study. (6) The macronutrient levels of human milk at each time period, including carbohydrates, proteins, lipids, and energy.

Quality assessment

The quality of the included studies was evaluated using the NOS scale, which comprises eight items out of a possible nine stars, where one star represents one point. The article quality was assessed on the following scale: low quality = 0~3 stars; moderate quality = 4~6 stars; high quality = 7~9 stars.

Statistical analysis

The weighted mean difference (MD) and the associated 95% confidence intervals (CI) for the macronutrients in the human milk of women with gestational diabetes mellitus and non-gestational diabetes mellitus were utilized

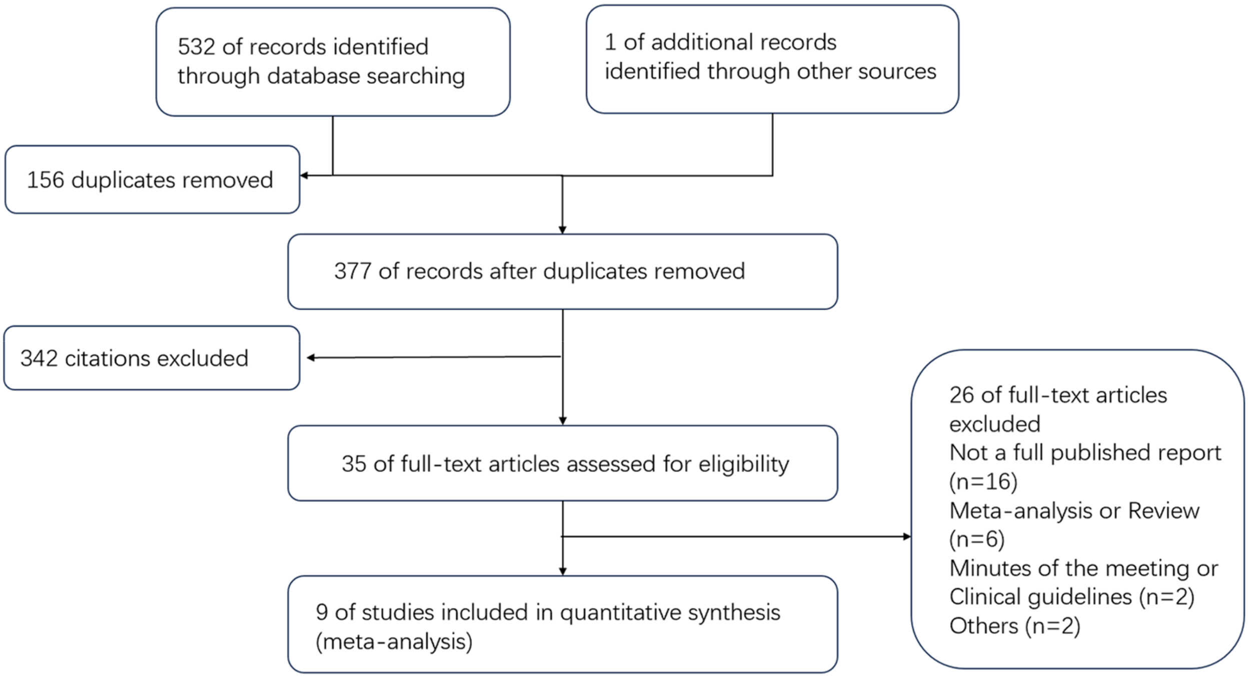

Fig. 1 A flow diagram for selection of studies and specific reasons for exclusion from this meta-analysis

to determine whether there was a disparity in the macronutrients of human milk between women with GDM and non-GDM. The heterogeneity between the studies was estimated by the Q-test and I^2 statistics. Typically, I^2 values of 25%, 50%, and 75% respectively indicate low, moderate, and high levels of heterogeneity [16]. If $I^2 > 50\%$ and $P < 0.05$, a random effects model was employed; otherwise, a fixed-effects model was utilized [17].

Subgroup analyses were employed to explore potential sources of heterogeneity based on participant BMI, test method and instrument, GDM criteria, and study quality. Sensitivity analyses were conducted to assess the stability of the results and potential sources of heterogeneity by excluding one study at a time. All analyses were performed using Revman 5.4.1 (Review Manager), and all tests were two-sided with a significance level of 0.05.

Results

Study characteristics

In total, 533 potentially relevant articles were screened, including 10 from CNKI, 159 from PubMed, 363 from Web of Science, and 1 from the reference list (Fig. 1). After eliminating 156 duplicate papers, 377 articles remained. The titles and abstracts of the 377 relevant articles were then screened, leaving 35 for full-text reading. Of these, 16 were irrelevant, 6 were meta-analyses and reviews, 2 were conference abstracts and treatment guidelines, and 2 were others. Finally, 9 articles with 1057 participants were included for meta-analysis. The nine included articles were case–control studies, and the detailed process of the literature search is presented in Fig. 1.

Among these 9 articles, 2 articles examined the 3 stages of human milk: colostrum, transitional milk, and mature milk; 2 articles examined the 2 stages of colostrum and mature milk; 1 article examined only the colostrum stage; 2 articles examined only the mature milk stage; and 2 articles examined only the lactose component of colostrum. Considering that only 2 studies on the transitional milk stage were involved, the results of the colostrum and mature milk stages will be analyzed in this study as two separate studies. Therefore, a total of 8 data studies were included in the meta-analysis. The main characteristics included in the meta-analysis are presented in Table 1.

GDM versus non-GDM human milk macronutrient levels—primary outcome, subgroup analysis, and sensitivity analysis

Overall, 1057 participants from 9 articles were included to compare the human milk macronutrient levels in GDM women with non-GDM women. As depicted in Fig. 2(2.1–2.8), the heterogeneity of the studies was not significant for colostrum protein levels ($I^2 = 31\%$, $P = 0.21$), and mature milk protein ($I^2 = 50\%$, $P = 0.07$) and lipid levels ($I^2 = 54\%$, $P = 0.05$), for which a fixed-effects model was used for statistical analysis. However,

Table 1 The baseline of characteristics of all included studies

Author, Year	*n*	**Age (years)**	BMI(Kg/m^2)	Gestational Age (weeks)	Birth Weight(g)	Pre-pregnancy BMI (Kg/m^2)	Weight gain during Pregnancy (Kg)	Study Quality	Diagnostic Criteria	Test Method
Azulay Chertok 2020 [18]	GDM 13NGT 120	31.50±3.4130.50±4.49	31.10±6.1127.90±7.08	39.10±1.1539.40±1.20	3400.00±440.003600.00±450.00	*NA*	*NA*	High	*NA*	*NMR*
Camille Dugas 2023 [19]	GDM 24NGT 29	33.50±3.6030.00±3.10	30.90±7.7026.80±6.80	38.60±1.0039.40±1.10	3380.00±340.003340.00±390.00	*NA*	*NA*	High	*OGCT*	Chemical Analysis Method
Sabriye Korkut 2022 [20]	GDM 31NGT 61	32.00±6.3027.50±5.30	31.30±6.4027.00±4.10	*NA*	3289.00±649.803126.10±531.00	*NA*	*NA*	High	75g *OGTT*	*MIRIS HMA*
Dana Shapira 2019 [21]	GDM 31NGT 31	34.32±4.0233.40±4.08	*NA*	38.70±0.9039.40±0.88	3261.00±405.103208.70±386.50	24.70±5.8022.50±3.81	10.51±6.2111.55±4.65	High	*OGCT*	*MIRIS HMA*
Kalliopi Dritsa-kou 2016 [22]	GDM 27NGT 183	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	Moderate	*NA*	*MIRIS HMA*
Yacong Cheng 2024 [23]	GDM 52NGT 92	29.77±5.3929.26±5.34	27.09±3.0927.09±3.21	*NA*	*NA*	*NA*	15.86±3.1416.30±3.08	High	75g *OGTT*	*MR*-9030 *HMA*
Hui Ye 2021 [24]	GDM 45NGT 90	29.10±4.7027.60±4.10	26.70±3.8026.40±2.80	*NA*	*NA*	21.70±3.6020.70±2.40	12.70±4.6014.30±4.00	High	75g *OGTT*	*MIRIS HMA*
Song Lin 2020 [25]	GDM 66NGT 112	30.10±4.0029.00±3.90	26.50±4.9026.70±3.30	*NA*	*NA*	21.70±3.4020.80±4.10	*NA*	High	75g *OGTT*	*MIRIS HMA*
Azulay Chertok 2017	GDM 19NGT 31	GDM there years older than NGT		*NA*	*NA*	24.1027.30	*NA*	High	75g *OGTT*	Chemical Analysis Method
Author, Year	*n*	Colostrum				Mature milk				
		Carbohydrates(g/100mL)	Protein(g/100mL)	Lipids(g/100mL)	Energy(kcal/100mL)	Carbohydrates(g/100mL)	Protein(g/100mL)	Lipids(g/100mL)	Energy(kcal/100mL)	
Azulay Chertok 2020 [18]	GDM 13NGT 120	3.15±1.654.16±1.27	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	
Camille Dugas 2023 [19]	GDM 24NGT 29	*NA*	*NA*	*NA*	*NA*	11.50±1.5012.20±1.90	1.30±0.301.20±0.20	6.30±2.00 5.30±1.20	108.00±18.00101.00±13.00	
Sabriye Korkut 2022 [20]	GDM 31NGT 61	5.70±1.604.60±1.50	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	
Dana Shapira 2019 [21]	GDM 31NGT 31	4.40±1.70 5.10±1.60	3.30±1.80 3.20±2.40	2.50±1.50 2.90±1.70	56.30±19.00 61.10±21.10	6.20±1.50 6.30±1.40	1.40±0.50 1.50±0.40	4.10±1.50 4.80±1.90	68.70±13.10 76.90±14.80	

Table 1 (continued)

Kalliopi Dritsa-kou 2016 [22]	GDM 27NGT 183	6.10±0.606.10±1.00	2.40±1.303.00±1.70	2.70±1.002.60±1.00	64.90±8.0057.80±7.90	6.80±0.50 6.90±0.60	1.60±0.702.00±0.90	3.00±0.802.90±1.20	61.50±7.5056.30±8.40
Yacong Cheng 2024 [23]	GDM 52NGT 92	7.32±0.627.55±0.36	1.01±0.100.97±0.093	*NA*	60.08±0.6260.15±10.87	6.65±0.586.62±0.23	0.96±0.020.95±0.02	4.23±0.284.00±0.57	68.28±3.6066.39±5.88
Hui Ye 2021 [24]	GDM 45NGT 90	6.30±1.306.60±1.00	2.60±1.602.50±1.30	1.70±0.701.70±0.80	52.90±8.6053.30±9.50	7.70±0.807.70±0.70	1.30±0.801.30±0.40	3.40±1.203.00±1.30	67.90±10.9063.90±10.30
Song Lin 2020 [25]	GDM 66NGT 112	*NA*	*NA*	*NA*	*NA*	8.45±0.318.14±0.62	1.24±0.211.24±0.21	3.19±1.133.30±1.55	68.50±10.0968.50±14.00
Azulay Chertok 2017	GDM 19NGT 31	4.87±1.706.05±1.33	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

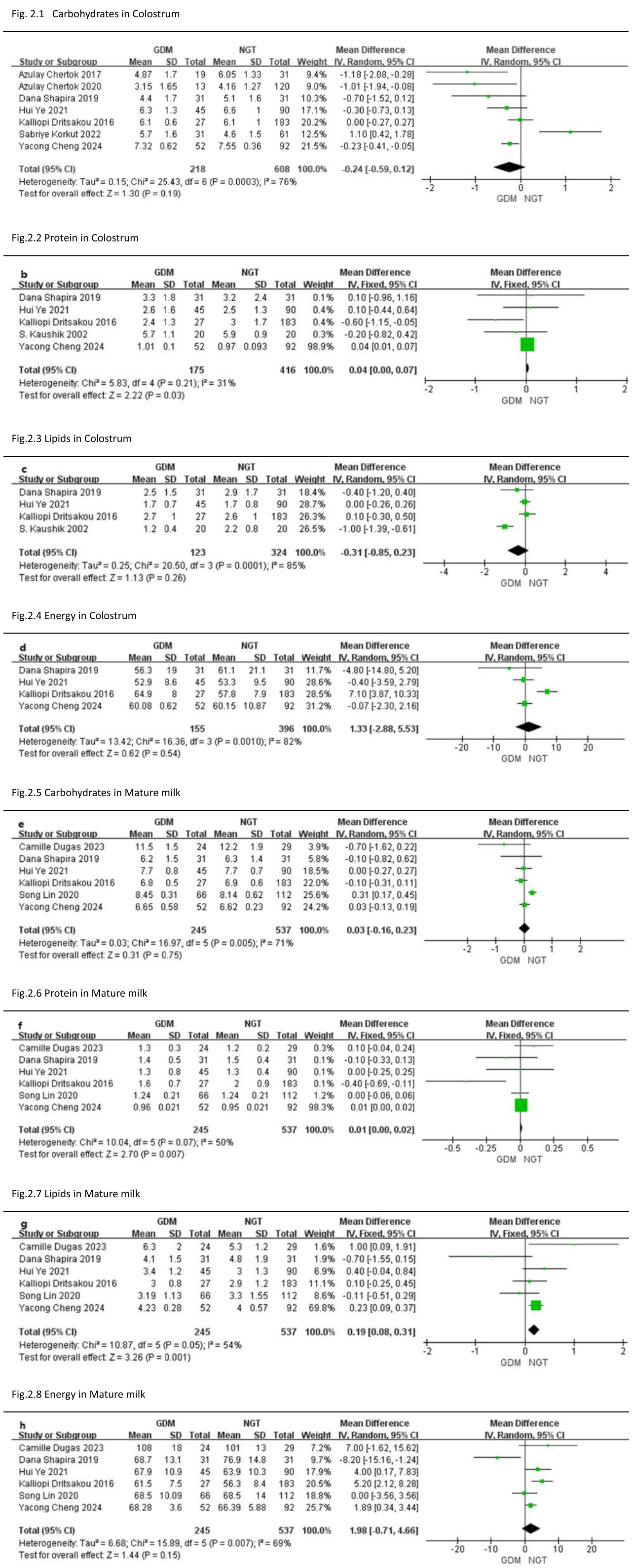

Fig. 2 Forest plots for the human milk composition in pregnant woman with GDM and control during pregnancy (GDM vs. NGT)

for colostrum carbohydrates (I^2=76%, P<0.001), lipids (I^2 = 85%, P < 0.001) and energy (I^2=82%, P=0.001) levels, and for mature milk carbohydrates (I^2=71%, P=0.005) and energy (I^2=69%, P= 0.007) levels, significant heterogeneity was observed, and a random-effects model was used for statistical analysis. Compared to non-GDM women, GDM women had higher protein (MD=0.04, 95% CI: 0.00~0.07, P=0.03) in colostrum, with no significant differences in carbohydrates, lipids, and energy. Meanwhile, GDM women had higher levels of protein (MD=0.01, 95% CI: 0.00~0.02, P=0.007) and lipids (MD=0.19, 95% CI: 0.08~0.31, P=0.001), with no significant differences in carbohydrates and energy in mature milk.

To identify the sources of heterogeneity, subgroup analyses were conducted based on participant BMI, test method and instrumentation, diagnostic criteria, and study quality, respectively. In the subgroup analysis, when adjusted for diagnostic criteria stratified by 75 g OGTT diagnosis, the heterogeneity in colostrum energy was significantly reduced (I^2=0%, P=0.87). Another variable that reduced heterogeneity was study quality (I^2=0%, P=0.66). The subgroup analyses indicated that other factors did not have a significant impact on heterogeneity. The detailed results of the subgroup analysis are presented in Table 2.

A sensitivity analysis was performed using a case-by-case exclusion method. It showed that the results for colostrum protein, lipid, energy, and mature lactose classes were inconsistent with the combined results, while the results of the remaining studies did not significantly differ from the combined results (Table 3). Among them, for the three studies of colostrum protein, lipid, and energy, all of them had fewer participants included in the literature (less than 5).

Discussion

Previously, Komal Manerkar published a meta-analysis on maternal gestational diabetes mellitus and infant nutrition and growth [26], which focused more on the correlation between women with GDM and infant growth. It suggested that human milk from women with GDM was similar in terms of energy, fat, and carbohydrate content, but slightly lower in protein. The present meta-analysis incorporated four newly published articles on human milk in GDM in recent years, and human milk from different periods was analyzed after detailed categorization. This study found that the energy of proteins and lipids in mature human milk of women with GDM during pregnancy was higher than that of non-GDM women; this is inconsistent with the previous study by Komal Manerkar et al. Among the studies included in the meta-analysis, the study by Dana Shapira et al. concluded that mature human milk of non-GDM women had higher levels of lipids [21]. Previously published meta-analyses of published studies have shown that gestational diabetes alters the levels of glucose and lipid metabolism in humans [27–30], and a study by Hong Zhong et al. concluded that women with GDM had higher levels of blood triglycerides and 36 up-regulated lipids and 24 down-regulated lipids in colostrum of women with GDM, which was associated with heavier infant weight [30]. This is in accordance with the results of the present meta-analysis.

In the measurement of human milk carbohydrates, two studies published by Sabriye Korkut and Kalliopi Dritsakou used carbohydrates as a measure. Sabriye Korkut concluded that the carbohydrate content of colostrum was higher in GDM women than in non-GDM women, while Kalliopi Dritsakou's study concluded that there was no significant difference.

In the several studies we included, none mentioned the treatment standards for GDM during pregnancy and the blood glucose control status. Moreover, no studies have shown a correlation between poor glycemic control during pregnancy and the carbohydrate content in the human milk of women with GDM. However, the study by Emily M Nagel suggests that the occurrence of GDM can alter the concentration of human milk metabolites, and the differences in milk composition of mothers with GDM may beneficially regulate infant growth and body composition [31].

Several published studies have indicated that BMI and age can influence the composition of breast milk. In our meta-analysis, although there were differences in BMI and age between the two groups in five studies [18–20, 22], while there were no significant differences in human milk composition after eliminating the effects of age and BMI. In our meta-analysis, subgroup analyses related to age and BMI were performed; however, the results indicated that they were not a source of heterogeneity in this study. This suggests that the human milk composition of women with GDM is higher than that of normal women and is not affected by other factors. The occurrence of GDM can significantly alter the composition of human milk.

There are no definitive studies on whether the occurrence of mastitis during breastfeeding has an effect on the composition of human milk. Five of the studies included in this meta-analysis explicitly included mastitis and human diseases during breastfeeding as one of the exclusion criteria [20, 21, 23–25], whereas the rest of the studies did not include it as an exclusion criterion. Similarly, with the exception of Yacong Cheng's study [23], none of the remaining studies specified the prenatal glycemic control of the GDM women included in the study.

Table 2 Subgroup analysis for the human milk composition in pregnant woman with GDM and control during pregnancy (GDM vs. NGT)

Carbohydrates in Colostrum							
Subgroup	Study Count (*n*)	Sample Size (*n*)	MD [95% CI]	*P*	χ^2	Heterogeneity Test	
						I^2 (%)	*P*
Combined Results	7	826	-0.24 [-0.59, 0.12]	0.190	25.43	76	< 0.001
BMI							
< 28Kg/m^2	2	279	-0.24 [-0.41, -0.07]	0.005	0.09	0	0.77
≥28Kg/m^2	4	497	0.01 [-0.22, 0.24]	0.930	17.49	1	< 0.001
Not Mentioned	1	50	-1.18 [-2.08, -0.28]	0.010	-	-	-
Diagnostic criteria							
75g *OGTT*	4	421	-0.20 [-0.36, -0.03]	0.020	19.04	1	< 0.001
OGCT	1	62	-0.70 [-1.52, 0.12]	0.100	-	-	-
Not Mentioned	2	343	-0.08 [-0.34, 0.18]	0.550	4.22	76	0.04
Test method							
MIRIS HMA	4	499	-0.01 [-0.22, 0.20]	0.920	14.75	80	0.002
Others	3	327	-0.30 [-0.47, -0.12]	0.001	6.52	69	0.04
Study quality							
High	6	616	-0.24 [-0.39, -0.08]	0.003	23.2	78	< 0.001
Moderate	1	210	0.00 [-0.27, 0.27]	1.000	-	-	-
Energy in Colostrum							
Subgroup	Study Count (*n*)	Sample Size (*n*)	MD [95% CI]	*P*	χ^2	Heterogeneity Test	
						I^2 (%)	*P*
Combined Results	4	551	1.33 [-2.88, 5.53]	0.54	16.36	8200	0.001
BMI							
< 28Kg/m^2	2	279	-0.18 [-2.00, 1.65]	0.85	0.03	0	0.87
≥28Kg/m^2	2	272	5.98 [2.91, 9.05]	< 0.001	4.93	80	0.03
Not Mentioned							
Diagnostic criteria							
75g *OGTT*	2	279	-0.18 [-2.00, 1.65]	0.85	0.03	0	0.87
OGCT	1	62	-4.80 [-14.80, 5.20]	0.35	-	-	-
Not Mentioned	1	210	7.10 [3.87, 10.33]	< 0.001	-	-	-
Test method							
MIRIS HMA	3	407	2.91 [0.70, 5.12]	0.01	12.9	84	0.002
Others	1	144	-0.07 [-2.30, 2.16]	0.95	-	-	-
Study quality							
High	3	341	-0.33 [-2.12, 1.47]	0.72	0.82	0	0.66
Moderate	1	210	7.10 [3.87, 10.33]	< 0.001	-	-	-
Carbohydrates in Mature milk							
Subgroup	Study Count (*n*)	Sample Size (*n*)	MD [95% CI]	*P*	χ^2	Heterogeneity Test	
						I^2 (%)	*P*
Combined Results	6	782	0.03 [-0.16, 0.23]	0.75	16.97	71	0.005
BMI							
< 28Kg/m^2	3	457	0.17 [0.07, 0.27]	< 0.001	8.26	76	0.020
≥28Kg/m^2	3	325	-0.13 [-0.32, 0.07]	0.2	1.57	0	0.460
Not Mentioned							
Diagnostic criteria							
75g *OGTT*	3	457	0.17 [0.07, 0.27]	< 0.001	8.26	76	0.020
OGCT	2	115	-0.33 [-0.90, 0.24]	0.25	1.02	2	0.310
Not Mentioned	1	210	-0.10 [-0.31, 0.11]	0.35	-	-	-
Test method							
MIRIS HMA	4	585	0.15 [0.05, 0.26]	0.004	12.41	76	0.006
Others	2	197	0.01 [-0.15, 0.17]	0.93	2.37	58	0.120

Table 2 (continued)

Study quality							
High	5	572	0.16 [0.06, 0.25]	0.002	12.18	67	0.020
Moderate	1	210	-0.10 [-0.31, 0.11]	0.35	-	-	-
Energy in Colostrum							
Subgroup	Study Count (*n*)	Sample Size (*n*)	MD [95% CI]	*P*	χ^2	Heterogeneity Test	
						I^2 (%)	*P*
Combined Results	4	551	1.33 [-2.88, 5.53]	0.54	16.36	8200	0.001
BMI							
$<$28Kg/m^2	2	279	-0.18 [-2.00, 1.65]	0.85	0.03	0	0.87
≥28Kg/m^2	2	272	5.98 [2.91, 9.05]	$<$0.001	4.93	80	0.03
Not Mentioned							
Diagnostic criteria							
75g *OGTT*	2	279	-0.18 [-2.00, 1.65]	0.85	0.03	0	0.87
OGCT	1	62	-4.80 [-14.80, 5.20]	0.35	-	-	-
Not Mentioned	1	210	7.10 [3.87, 10.33]	$<$0.001	-	-	-
Test method							
MIRIS HMA	3	407	2.91 [0.70, 5.12]	0.01	12.9	84	0.002
Others	1	144	-0.07 [-2.30, 2.16]	0.95	-	-	-
Study quality							
High	3	341	-0.33 [-2.12, 1.47]	0.72	0.82	0	0.66
Moderate	1	210	7.10 [3.87, 10.33]	$<$0.001	-	-	-
Lipids in Mature milk							
Subgroup	Study Count (*n*)	Sample Size (*n*)	MD [95% CI]	*P*	χ^2	Heterogeneity Test	
						I^2 (%)	*P*
Combined Results	6	782	0.19 [0.08, 0.31]	0.001	10.87	54	0.050
BMI							
$<$28Kg/m^2	3	457	0.21 [0.08, 0.34]	0.001	3.3	39	0.190
≥28Kg/m^2	3	325	0.10 [-0.21, 0.40]	0.53	7.13	72	0.030
Not Mentioned							
Diagnostic criteria							
75g *OGTT*	3	457	0.21 [0.08, 0.34]	0.001	3.3	39	0.190
OGCT	2	115	0.09 [-0.53, 0.72]	0.77	7.13	86	0.008
Not Mentioned	1	210	0.10 [-0.25, 0.45]	0.57	-	-	-
Test method							
MIRIS HMA	4	585	0.06 [-0.16, 0.27]	0.61	6.09	51	0.110
Others	2	197	0.25 [0.11, 0.39]	$<$0.001	2.68	63	0.100
Study quality							
High	5	572	0.20 [0.08, 0.33]	0.001	10.56	62	0.030
Moderate	1	210	0.10 [-0.25, 0.45]	0.57	-	-	-
Energy in Mature milk							
Subgroup	Study Count (*n*)	Sample Size (*n*)	MD [95% CI]	*P*	χ^2	Heterogeneity Test	
						I^2 (%)	*P*
Combined Results	6	782	1.98 [-0.71, 4.66]	0.15	15.89	69	0.007
BMI							
$<$28Kg/m^2	3	457	1.88 [0.55, 3.21]	0.006	2.25	11	0.320
≥28Kg/m^2	3	325	3.39 [0.71, 6.07]	0.01	12.66	84	0.002
Not Mentioned							
Diagnostic criteria							
75g *OGTT*	3	457	1.88 [0.55, 3.21]	0.006	2.25	11	0.320
OGCT	2	115	-2.20 [-7.61, 3.21]	0.43	7.24	86	0.007
Not Mentioned	1	210	5.20 [2.12, 8.28]	$<$0.001	-	-	-

Table 2 (continued)

Test method							
MIRIS HMA	4	585	2.38 [0.47, 4.30]	0.01	14.51	79	0.002
Others	2	197	2.05 [0.53, 3.58]	0.008	1.31	24	0.25
Study quality							
High	5	572	1.65 [0.35, 2.94]	0.01	11.55	65	0.020
Moderate	1	210	5.20 [2.12, 8.28]	$<$0.001	-	-	-

Table 3 Sensitivity analyses using a case-by-case exclusion method

Author，Year	MD [95% CI]							
	Colostrum Carbohydrates	Colostrum Protein	Colostrum Lipids	Colostrum Energy	Mature milk Carbohydrates	Mature milk Protein	Mature milk Lipids	Mature milk Energy
Chertok 2017	-0.14 [-0.49, 0.22]	-	-	-	-	-	-	-
Chertok 2020 [18]	-0.16 [-0.52, 0.21]	-	-	-	-	-	-	-
Dugas 2023 [19]	-	-	-	-	0.06[-0.12, 0.25]	0.01[0.00, 0.02]	0.18[0.06, 0.30]	1.58[-1.24, 4.39]
Shapira 2019 [21]	-0.18[-0.57, 0.20]	0.04[0.00, 0.07]	0.03[-0.19, 0.25]	2.14[-2.36, 6.63]	0.04[-0.17, 0.24]	0.01[0.00, 0.02]	0.21[0.09, 0.33]	2.87[0.91, 4.82]
Hui Ye 2021 [24]	-0.30[-0.73, 0.13]	0.04[0.00, 0.07]	-0.00[-0.36, 0.36]	1.75[-4.40, 7.91]	0.03[-0.20, 0.26]	0.01[0.00, 0.02]	0.18[0.06, 0.30]	1.47[-1.76, 4.71]
Kalliopi Dritsakou 2016 [22]	-0.32[-0.80, 0.17]	0.04[0.01, 0.07]	-0.04[-0.29, 0.21]	-0.33[-2.12, 1.47]	0.07[-0.15, 0.29]	0.01[0.00, 0.02]	0.20[0.08, 0.33]	1.14[-1.89, 4.17]
Korkut 2022 [20]	-0.34[-0.61, -0.07]	-	-	-	-	-	-	-
Song Lin 2020 [25]	-	-	-	-	-0.03[-0.14, 0.09]	0.01[0.00, 0.02]	0.22[0.10, 0.34]	2.38[-0.84, 5.61]
Yacong Cheng 2024 [23]	-0.28[-0.81, 0.25]	-0.20[-0.56, 0.16]		1.60[-4.92, 8.11]	0.03[-0.13, 0.19]	-0.00[-0.06,0.05]	0.11[-0.10, 0.32]	1.82[-2.21, 5.85]
Results	-0.24[-0.59, 0.12]	0.04[0.00, 0.07]	-0.00[-0.21, 0.21]	1.33[-2.88, 5.53]	0.03[-0.16, 0.23]	0.01[0.00, 0.02]	0.19[0.08, 0.31]	1.98[-0.71, 4.66]

Numerous studies have shown that the protein of mature milk decreases compared to colostrum, but the fat and lactose content gradually increases. Among the studies included in this meta-analysis, the time of mature milk specimens selected for each study was different (14 days/30 days/42 days/2 months), and this meta-analysis found no significant difference in lactose and energy between the mature milk of the GDM group and the non-GDM group, which may be related to the different collection times. Therefore, more high-quality studies are needed to clarify the lactose and energy levels of mature milk in the two groups.

These studies still have some methodological limitations, which may be the source of heterogeneity, including (1) the nadir criteria of the subjects, (2) different sampling times of mature milk, and (3) different detection indexes. In addition, the results of our subgroup analysis also showed that the different clinical characteristics of the study subjects and different diagnostic criteria may also be the source of heterogeneity in this meta-analysis.

Our meta-analysis shows that the energy from lipids and proteins in the mature milk of women with GDM is higher than that in the human milk of normal women. This suggests that women with GDM can promote the recovery of postpartum glucose and lipid metabolism by extending the duration of breastfeeding, allowing the excess lipids in their bodies to be excreted through human milk. This finding is similar to the results of a prospective cohort study published in 2018 [32], in which Ep G concluded that the duration of breastfeeding is independently associated with a reduced incidence of diabetes. The study by Fanzhu Xue also supports the idea that the excess carbohydrates and lipids in the bodies of women with gestational diabetes can be excreted through human milk [33], and therefore, a longer breastfeeding period can facilitate the recovery of glucose and lipid metabolism. Therefore, we should encourage all mothers, especially those with GDM, to breastfeed for as long as possible, as this has a positive impact on the recovery of postpartum glucose and lipid metabolism and long-term prognosis.

Conclusions

In our meta-analysis, differences in human milk composition were found between women with GDM and those without GDM. Specifically, compared with non-GDM women, GDM women had higher levels of protein and lipids in their mature milk. Moreover, the differences in human milk composition among GDM women were not related to factors such as age and BMI. Due to the limitations of our meta-analysis, more high-quality studies are needed to verify the relationship between the macronutrient content of colostrum and the carbohydrate content of mature milk with GDM.

Abbreviations

GDM Gestational diabetes mellitus
CNKI China National Knowledge Infrastructure
HM Human milk
WHO The World Health Organization
OGTT Oral Glucose Tolerance Test

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Authors' contributions

HYW defined the research program and obtained ethics committee approval. XYQ and SYL searched and screened literatures, performed the meta-analysis and wrote the manuscript. HYW critically assessed the manuscript, revised the manuscript and approved it. All authors read, reviewed and approved the final manuscript.

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Data availability

All data are available from CNKI, Pubmed and Web of Science.

Declarations

Ethics approval and consent to participate

Ethical approval is not required since there were no ethical issues involved in this paper. The reasons are as follows: this paper is a secondary analysis of published literatures, which are available in public databases, do not cause harm to humans, and does not involve sensitive personal information or commercial interests.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, Hoegfeldt CA, Elise Powe C, Immanuel J, Karuranga S, Divakar H, Levitt N, Li C, Simmons D, Yang X; IDF Diabetes Atlas Committee Hyperglycaemia in Pregnancy Special Interest Group. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes Res Clin Pract. 2022;183:109050. https://doi.org/10.1016/j.diabres.2021.109050. Epub 2021. PMID: 34883186.
2. Lappe V, Greiner GG, Linnenkamp U, Viehmann A, Adamczewski H, Kaltheuner M, Weber D, Schubert I, Icks A. Gestational diabetes in Germany-prevalence, trend during the past decade and utilization of follow-up care: an observational study. Sci Rep. 2023;13(1):16157. https://doi.org/10.1038/s41598-023-43382-6.PMID:37758812;PMCID:PMC10533812.
3. Farahvar S, Walfisch A, Sheiner E. Gestational diabetes risk factors and long-term consequences for both mother and offspring: a literature review. Expert Rev Endocrinol Metab. 2019;14(1):63–74. https://doi.org/10.1080/17446651.2018.1476135. Epub 2018 Jun 5 PMID: 30063409.
4. Mora-Ortiz M, Rivas-García L. Gestational Diabetes Mellitus: Unveiling Maternal Health Dynamics from Pregnancy Through Postpartum Perspectives. Open Res Eur. 2024;5(4):164. https://doi.org/10.12688/openreseurope.18026.1.PMID:39355538;PMCID:PMC11443192.
5. Wang XY, Cleary EM, Thung SF, Venkatesh KK, Buschur EO. Gestational Diabetes. 2024 Aug 28. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, de Herder WW, Dhatariya K, Dungan K, Hofland J, Kalra S, Kaltsas G, Kapoor N, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, Levy M, McGee EA, McLachlan R, New M, Purnell J, Sahay R, Shah AS, Singer F, Sperling MA, Stratakis CA, Trence DL, Wilson DP, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000–. PMID: 34370430.
6. Jiang H, Zhang K, Zhang X. Mendelian randomization analysis of the association between childhood overweight or obesity and gestational diabetes mellitus. Diabetes Obes Metab. 2024 Sep 30. https://doi.org/10.1111/dom.15975. Epub ahead of print. PMID: 39344835.
7. Malik N, Ahmad A, Ashraf H. Metabolic Profile of Offspring of Mothers with Gestational Diabetes Mellitus. Indian J Endocrinol Metab. 2024;28(2):192–196. https://doi.org/10.4103/ijem.ijem_211_23. Epub 2024 Apr 29. PMID: 38911115; PMCID: PMC11189277.
8. Leth-Møller M, Hulman A, Kampmann U, Hede S, Ovesen PG, Knorr S. Effect of gestational diabetes on fetal growth rate and later overweight in the offspring. J Clin Endocrinol Metab. 2024:dgae428. https://doi.org/10.1210/clinem/dgae428. Epub ahead of print. PMID: 38916475.
9. Frankevich N, Chagovets V, Tokareva A, Starodubtseva N, Limonova E, Sukhikh G, Frankevich V. Dietary Regulation of Lipid Metabolism in Gestational Diabetes Mellitus: Implications for Fetal Macrosomia. Int J Mol Sci. 2024;25(20):11248. https://doi.org/10.3390/ijms252011248.PMID:39457029;PMCID:PMC11508696.
10. Andreas NJ, Kampmann B, Mehring L-D. Human breast milk: A review on its composition and bioactivity. Early Hum Dev. 2015;91(11):629–35. https://doi.org/10.1016/j.earlhumdev.2015.08.013. Epub 2015 Sep 12 PMID: 26375355.
11. Ballard O, Morrow AL. Human milk composition: nutrients and bioactive factors. Pediatr Clin North Am. 2013;60(1):49–74. https://doi.org/10.1016/j.pcl.2012.10.002.PMID:23178060;PMCID:PMC3586783.
12. World Health Organization. Global strategy for infant and young child feeding. World Health Organization. 2002.
13. Thompson AL, Bentley ME. The critical period of infant feeding for the development of early disparities in obesity. Soc Sci Med. 2013;97:288–96. https://doi.org/10.1016/j.socscimed.2012.12.007. Epub 2012 Dec 17. PMID: 23312304; PMCID: PMC3812266.
14. Muraglia M, Faienza MF, Tardugno R, Clodoveo ML, Matias De la Cruz C, Bermúdez FG, Munizaga MG, Valencia L, Corbo F, Orellana-Manzano A. Breastfeeding: science and knowledge in pediatric obesity prevention. Front Med (Lausanne). 2024;11:1430395. https://doi.org/10.3389/fmed.2024.1430395. PMID: 39399112; PMCID: PMC11466875.
15. Lanigan J. Prevention of overweight and obesity in early life. Proceedings of the Nutrition Society. 2018;77(3):247–56. https://doi.org/10.1017/S0029665118000411.
16. Cui L, Liu X, Tian Y, Xie C, Li Q, Cui H, et al. Flavonoids, flavonoid subclasses,and esophageal cancer risk: a meta-analysis of epidemiologic studies. Nutrients. 2016; 8
17. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst. 1959;22:719–48.
18. Azulay Chertok IR, Haile ZT, Shuisong N, Kennedy M. Differences in Human Milk Lactose and Citrate Concentrations Based on Gestational Diabetes Status. Breastfeed Med. 2020;15(12):798–802. https://doi.org/10.1089/bfm.2020.0051. Epub 2020 Oct 19 PMID: 33074745.

19. Dugas C, Laberee L, Perron J, St-Arnaud G, Richard V, Perreault V, Leblanc N, Marc I, Di Marzo V, Doyen A, Veilleux A, Robitaille J. Gestational Diabetes Mellitus, Human Milk Composition, and Infant Growth. Breastfeed Med. 2023;18(1):14–22. https://doi.org/10.1089/bfm.2022.0085. Epub 2022 Nov 21 PMID: 36409543.
20. Korkut S, Köse Çetinkaya A, Işık Ş, Özel Ş, Gökay N, Şahin A, Alyamaç DE. Macronutrient Composition of Colostrum in Mothers with Gestational Diabetes Mellitus. Breastfeed Med. 2022;17(4):322–5. https://doi.org/10.1089/bfm.2021.0209. Epub 2022 Feb 10 PMID: 35143337.
21. Shapira D, Mandel D, Mimouni FB, Moran-Lev H, Marom R, Mangel L, Lubetzky R. The effect of gestational diabetes mellitus on human milk macronutrients content. J Perinatol. 2019;39(6):820–3. https://doi.org/10.1038/s41372-019-0362-5. Epub 2019 Mar 27 PMID: 30918340.
22. Dritsakou K, Liosis G, Valsami G, Polychronopoulos E, Skouroliakou M. The impact of maternal- and neonatal-associated factors on human milk's macronutrients and energy. J Matern Fetal Neonatal Med. 2017;30(11):1302–8. https://doi.org/10.1080/14767058.2016.1212329. Epub 2016 Aug 2 PMID: 27405688.
23. Yacong C. Research on the Impact of Pregnancy Complications and Delivery Methods on the Nutritional Components of Colostrum and Mature Milk Postpartum [D]. Chengde Medical College. 2024. https://doi.org/10.27691/d.cnki.gcdyx.2024.000346.
24. Hui Ye. Research on the Impact of Gestational Diabetes Mellitus on the Nutritional Composition and Microbial Diversity of Breast Milk at Different Lactation Stages Postpartum [D]. Fujian Medical University. 2021. https://doi.org/10.27020/d.cnki.gfjyu.2021.000686.
25. Lin S, Ye H, Zhu H, et al. Research on the Impact of Gestational Diabetes Mellitus and Dietary Intake on Milk Composition at 42 Days Postpartum [J]. Journal of Coastal Prevention and Health. 2020;26(06):104–6.
26. Manerkar K, Harding J, Conlon C, McKinlay C. Maternal gestational diabetes and infant feeding, nutrition and growth: a systematic review and meta-analysis. Br J Nutr. 2020;123(11):1201–15. https://doi.org/10.1017/S0007114520000264. Epub 2020 Jan 22 PMID: 31964432.
27. Ma X, Lu Y, Huang C, Guo Z, Xiang Z, Gao H, Zhao K, Zhao Y, Li Y. Analysis of human milk oligosaccharides from women with gestational diabetes mellitus. Anal Biochem. 2024;696:115689. https://doi.org/10.1016/j.ab.2024.115689. Epub ahead of print. PMID: 39426696.
28. Yao D, Shen C, Zhang X, Tang J, Yu J, Tu M, Panpipat W, Chaijan M, Zhang H, Xu X, Liu Y, Cheong LZ. Untargeted metabolomics study of mature human milk from women with and without gestational diabetes mellitus. Food Chem. 2024;460(Pt 3):140663. https://doi.org/10.1016/j.foodchem.2024.140663. Epub 2024 Jul 30. PMID: 39142199.
29. Dou Y, Luo Y, Xing Y, Liu H, Chen B, Zhu L, Ma D, Zhu J. Human Milk Oligosaccharides Variation in Gestational Diabetes Mellitus Mothers. Nutrients. 2023;15(6):1441. https://doi.org/10.3390/nu15061441.PMID:36986171;PMCID:PMC10059845.
30. Zhong H, Zhang J, Xia J, Zhu Y, Chen C, Shan C, Cui X. Influence of gestational diabetes mellitus on lipid signatures in breast milk and association with fetal physical development. Front Nutr. 2022;10(9). https://doi.org/10.3389/fnut.2022.924301.PMID:36034909;PMCID:PMC9402091.
31. Nagel EM, Peña A, Dreyfuss JM, Lock EF, Johnson KE, Lu C, Fields DA, Demerath EW, Isganaitis E. Gestational Diabetes, the Human Milk Metabolome, and Infant Growth and Adiposity. JAMA Netw Open. 2024Dec 2;7(12): e2450467. https://doi.org/10.1001/jamanetworkopen.2024.50467. Erratum.In:JAMANetwOpen.2025;8(1):e2459711.doi:10.1001/jamanetworkopen.2024.59711.PMID:39666338;PMCID:PMC11638796.
32. Ep G, Ce L, Y L, et al. Lactation Duration and Progression to Diabetes in Women Across the Childbearing Years: The 30-Year CARDIA Study[J]. JAMA internal medicine, 2018, 178(3).
33. Fanzhu, Xue. Evaluation of the Impact of Different Feeding Methods on Postpartum Body Mass Index and Glycolipid Metabolism Recovery in Women with Gestational Diabetes Mellitus, as well as Newborn Birth Weight [J]. Diabetes New World, 2023, 26(4): 52–54+66.

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