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Review Article

Maternal dyslipidemia during pregnancy may increase the risk of preterm birth: A meta-analysis

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ABSTRACT

Epidemiological studies have reported an inconsistent relationship between maternal lipid levels and preterm birth (PTB). We performed this meta-analysis to evaluate the association between maternal dyslipidemia and PTB. Overall, three nested case-control studies and eight cohort studies were eligible. Effect estimates [odds ratio(OR)/relative risk] were pooled using a fixed-effects or a random-effects model. Subgroup and metaregression analyses were conducted to evaluate the sources of heterogeneity. Eleven studies involving 13,025 pregnant women were included. Compared with pregnant women with normal lipid levels, the women with elevated levels of lipids had an increased risk of PTB, and the pooled OR was 1.68 [95% confidence interval (CI): 1.25–2.26)]; meanwhile, women with lower levels of lipids also had a trend of an increased risk of PTB (OR = 1.52, 95% CI = 0.60–3.82). The pooled ORs for elevated levels of total cholesterol, triglycerides, low density lipoprotein-cholesterol, and lower levels of high density lipoprotein-cholesterol were 1.71 (95% CI: 1.05–2.79), 1.55 (95% CI: 1.13–2.12), 1.19 (95% CI: 0.95–1.48), and 1.33 (95% CI: 1.14–1.56), respectively. The present meta-analysis found that maternal dyslipidemia during pregnancy, either the elevated total cholesterol or triglycerides, was associated with an increased risk of PTB. These findings indicate that a normal level of maternal lipid during pregnancy may reduce the risk of PTB.

Introduction

The prevalence of preterm birth (PTB) has been increasing during the past two decades in almost all countries [1]. It is estimated that a total of 15 million babies were born premature in 2010, 5% of whom were younger than 28 gestational weeks [2]. PTB (<37 gestational weeks) is the second most common cause of death in children younger than 5 years nowadays. Moreover, it is also associated with an increased risk of adverse metabolic outcomes in later life among infants and their mothers [3]. Several studies strongly suggested that PTB was associated with type 2 diabetes, hypertension, coronary heart disease, and stroke in offspring [4]. Moreover, mothers who delivered preterm infants also appeared to have excess risk of metabolic diseases later in life [5].

The molecular mechanisms that contribute to PTB are still somewhat unclear, although maternal vascular disturbances and infection/inflammation have been implicated [6–8]. Recently, numerous studies have evaluated the relationship between maternal lipid profiles during pregnancy and the risk of PTB. Serum lipid levels increase gradually as pregnancy proceeds [9,10]. Increased lipid levels contribute toward hormonal and nutritional support of a healthy pregnancy [11]. However, hyperlipidemia is also regarded as an instigator of oxidative stress and inflammation that are related to the incidence of pregnancy complications and adverse pregnancy outcomes, including preeclampsia, PTB, and large for gestational age [12,13]. Recently, a systematic review and meta-analyses demonstrated that women who developed preeclampsia have elevated levels of total cholesterol, nonhigh-density lipoprotein-cholesterol (HDL-C), and triglycerides during all trimesters of pregnancy, as well as lower levels of HDL-C during the third trimester [14]. However, the relationship between maternal dyslipidemia and PTB risk were inconsistent, and the relationship has not been reported by any systematic review or meta-analyses

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before. Therefore, we conducted a meta-analysis to examine the associations of higher and lower levels of maternal lipids during pregnancy with the risk of PTB.

Methods

Search strategy

We conducted a thorough search to identify eligible studies that measured and reported the lipid levels during pregnancy, and patients were followed-up until delivery. The hypothesis was to explore the association between maternal dyslipidemia and PTB risk. The databases included PUBMED, EMBASE, and Cochrane Library up to June 2016. A combination of keywords for preterm birth (preterm birth OR premature birth OR preterm delivery OR preterm infant OR preterm labor), for lipid levels (lipid* OR dyslipidemia OR hyperlipidemia OR hypolipidemia OR cholesterol OR triglyceride OR HDL OR LDL), and for pregnancy (mother* OR maternal OR pregnant OR pregnancy OR gestation*) were used. References from these publications were also manually searched for potentially relevant citations.

Study eligibility criteria and study selection

Records identified from the literature search were screened for duplicates. First, title and abstract were screened, and then potentially relevant articles were screened for full-text review. The inclusion criteria were defined as follows: (1) an original study that examined the association between dyslipidemia during pregnancy and PTB risk; (2) one or more of the following maternal lipid parameters were assessed as a predictor variable: total cholesterol, triglycerides, low density lipoprotein-cholesterol (LDL-C) and HDL-C; (3) the associations were presented as a relative risks (RRs) or odds ratio (ORs) with the 95% confidence interval (CI); (4) a cohort study or a case-control study. We excluded duplicate publications and studies that recruited women with a history of PTB, preeclampsia, gestational diabetes, familial hyperlipidemia, or other severe diseases. Our primary outcome was PTB (defined as birth prior to 37 gestational weeks). Where possible, we then subdivided PTB into spontaneous PTB (sPTB) and medically induced PTB (mPTB).

Of the 2471 identified articles, 2381 did not match our selection criteria based on a review of the title and abstract conducted independently by two authors (S.Y. Jiang and J.X. Jiang). These two authors then independently reviewed the full-text version of the remaining 90 articles (Figure 1). Eventually, 79 studies were excluded after an evaluation of the manuscripts. Overall, 11 studies were deemed eligible, including three nested case-control studies [15–17] and eight cohort studies [18–25]. When duplicate data were published, only the most up to date and the one with a larger sample size were included. Any disagreements about study eligibility were resolved by discussion, with arbitration by a third reviewer (Z.Y. Liu) if necessary.

Data abstraction and quality assessment

Data were extracted from the eligible studies by two authors (S.Y. Jiang and J.X. Jiang) using a piloted data extraction form. The extracted data included study characteristics (author, year of publication, study area, and study design); participant characteristics {number of participants, definitions of the PTB and control groups, diagnostic criteria, mean age, ethnicity of pregnant women, mean prepregnancy body mass index [BMI; weight (kg)/height (m^2)], smoking status and mean gestational age at blood sampling}; lipid measurements (fasting status at blood sampling, the effect estimates (i.e., RRs or ORs) and 95% CIs for dyslipidemia and PTB risk).

The quality assessment was performed by applying the Newcastle–Ottawa Scale [26]. Overall, the publications were classified as high quality (scoring $\geq$ 5 points) or low quality (scoring < 5 points). Only studies scoring 5 or more points were included, ensuring only high-quality research articles were included in this meta-analysis.

Data synthesis and analysis

The multivariate-adjusted risk estimates were selected if they were reported in the original publication; otherwise, the unadjusted risk estimates were selected or calculated using the original data. The study-specific risk estimates were obtained for higher and lower levels of total cholesterol, triglycerides, LDL-C, and HDL-C. First, second, and third trimesters were defined as 1–13 gestational weeks, 14–26 gestational weeks, and $\geq$27 gestational weeks, respectively. Effect estimates of elevated levels of total cholesterol were priority selection for estimating the pooled effect of elevated maternal lipid levels, because six studies reported effect estimates of total cholesterol. If it was not provided, the effect estimates of elevated triglycerides were selected. Because most of these studies reported lipid measurements in the second trimester, the effect estimates in the second trimester were selected for analysis if lipid levels were also measured in the other two trimesters. Otherwise, the effect estimates in the first trimester were selected.

The heterogeneity among studies was assessed using the I^2 statistic, defining a significant heterogeneity as $p \leq 0.10$ and/or $I^2 \geq 50\%$ [27]. The fixed-effects model was applied when no significant heterogeneity was presented; otherwise, the random-effects model was applied to provide more conservative estimates [28]. The forest plots for the association between maternal dyslipidemia and PTB risk were generated for higher and lower levels of maternal lipids versus normal lipid levels, respectively. In addition, the associations between elevated levels of total cholesterol, triglycerides, LDL-C, and PTB risk were generated, as well as lower levels of HDL-C. Furthermore, subgroup analysis was carried out stratified by study design, study area, trimester of blood sampling, fasting status at blood sampling, smoking status during pregnancy, PTB subtypes (all PTB, sPTB, and mPTB), major confounders adjusted (gestational age at blood sampling, prepregnancy BMI, or weight). We also applied metaregression to access the covariates effect on the estimated ORs obtained from random-effects meta-analysis to explore the source of heterogeneity. In sensitivity analysis, each study was eliminated in turn from the pooled analysis to assess its effect on pooled effects. Possible publication bias was assessed using Egger's test and Begg's tests. All statistical analyses were performed in statistical package STATA, Version 12.0, software (Stata-Corp LP, College Station, TX, USA). A p value $\leq$0.05 was considered statistically significant.

Results

Literature search and study characteristics

Figure 1 presents the flowchart of the literature search and selection. There were 2471 studies identified in the initial search, of which 2381 were excluded after screening the title and abstract because of duplication or lack of relevance. Owing to insufficient data, women complicated with diseases, or irrelevant outcomes, 11 studies published were finally included for further analyses, including three nested case-control [15–17] and eight cohort studies [18–25]. The detailed characteristics of the 11 studies [15–25] are listed in Table 1. Six of these studies were conducted in

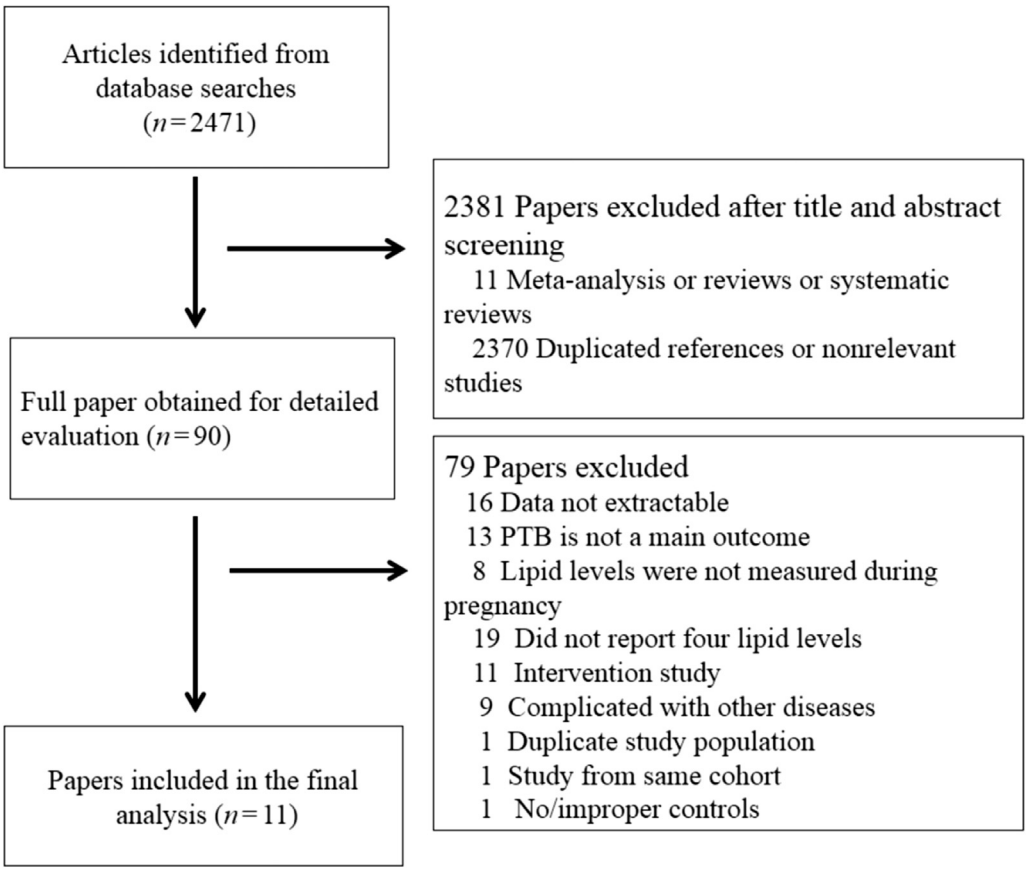

Figure 1. Flow diagram of study selection for the meta-analysis of the association between dyslipidemia during pregnancy and the risk of preterm birth.

North America [15–18,20,24], and the other five studies were performed in Europe [22], Asia [19,25], and Africa [21,23]. Of these 11 included studies, nine [15,18–21,24,25] measured serum lipid levels during the second trimester. Moreover, nine studies [17–22,24,25] defined PTB as gestational age of less than 37 weeks, and the other two defined it as 34–37 weeks or <34 weeks [16], and <30 weeks [15], respectively. A total of 13,025 pregnant women were included in these 11 studies, with 1786 PTB and 11,239 term birth.

Meta-analyses

The overall risk of PTB was increased in pregnant women with higher (OR = 1.68, 95% CI: 1.25–2.26) and lower lipid levels (OR = 1.52, 95% CI: 0.60–3.82) compared with women whose lipid levels were normal (Figure 2), but lower lipid levels did not reach statistical significance. Figure 3 shows study-specific and pooled ORs (95% CIs) of PTB for elevated levels of total cholesterol, triglycerides, and LDL-C, and lower levels of HDL-C. When compared

Table 1
Characteristics of studies included in the meta-analysis of maternal dyslipidemia and preterm birth, January 1973–February 2016.

First author, yr (reference)	Country	No. of participants	No. of PTB	Study design	Race[a]	Trimester[b]	Fasting status	Definition of PTB (wk)
Alleman, 2013 [24]	Iowa (USA)	2699	200	Cohort	White (82%)	First and second	Nonfasting	<37
Chatzi, 2009 [22]	Greece	625	74	Cohort	Greek origin (91.0%), Other (9%)	First	Fasting	<37
Edison, 2007 [18]	USA	1058	70	Cohort	White (63%), Black (36%)	Second	Unknown	<37
Catov, 2007 [16]	USA	289	67	Nested case-control	Black (32.8–41.7%), White/Other (58.3–67.2%)	First	Non-fasting	<34 and 34, 37
Kramer, 2009 [17]	Canada	648	207	Nested case-control	White (82.6–84.5%), Black/Other (15.5–17.4%)	Second	Non-fasting	<37
Jelliffe-Pawlowski, 2014 [15]	USA	108	72	Nested case-control	White (27.8–30.6%), Others (52.8–62.5%)	Second	Non-fasting	<30
Lei, 2016 [25]	China	5535	810	Cohort	Yellow	Second	Fasting	<37
Maymunah, 2014 [23]	Nigeria	287	23	Cohort	Black	Second	Fasting	<37
Mudd, 2011 [20]	USA	1309	221	Cohort	Black (33.7%), White/Other (66.3%)	Second	Nonfasting	<37
Niromanesh, 2012 [19]	Iran	180	19	Cohort	Unknown	Second	Fasting	<37
Oluwole, 2012 [21]	Nigeria	287	23	Cohort	Black	Second	Fasting	<37

PTB = preterm birth.
[a] Race proportion of all participants.
[b] Trimester of blood sampling.

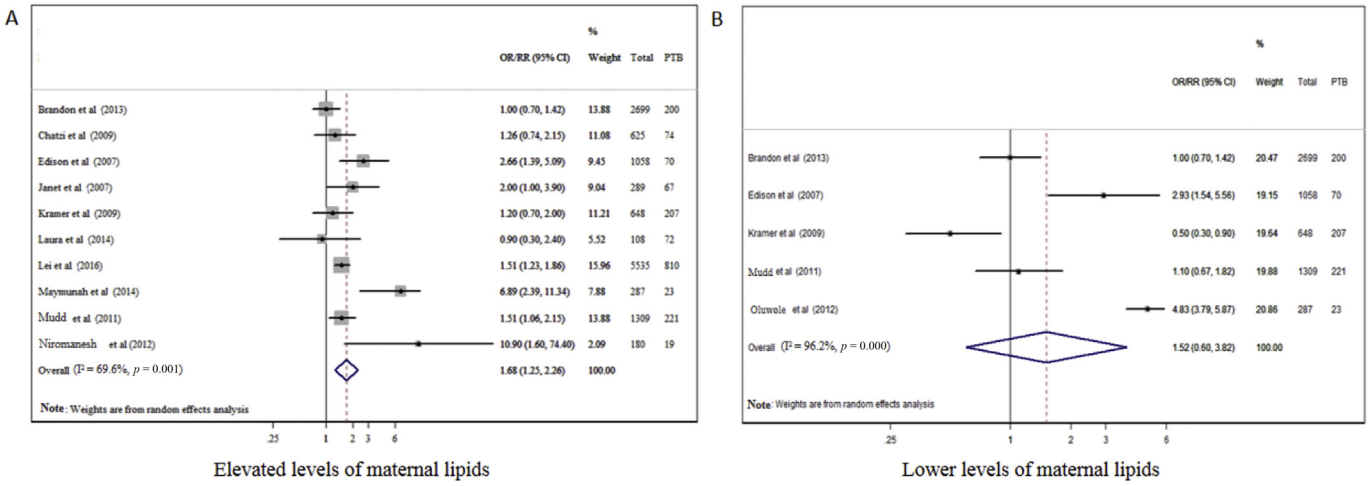

Figure 2. Forest plots for pooled odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) of preterm birth for (A) elevated levels of maternal lipids and (B) lower levels of maternal lipids. PTB = preterm birth; RR = relative risk.

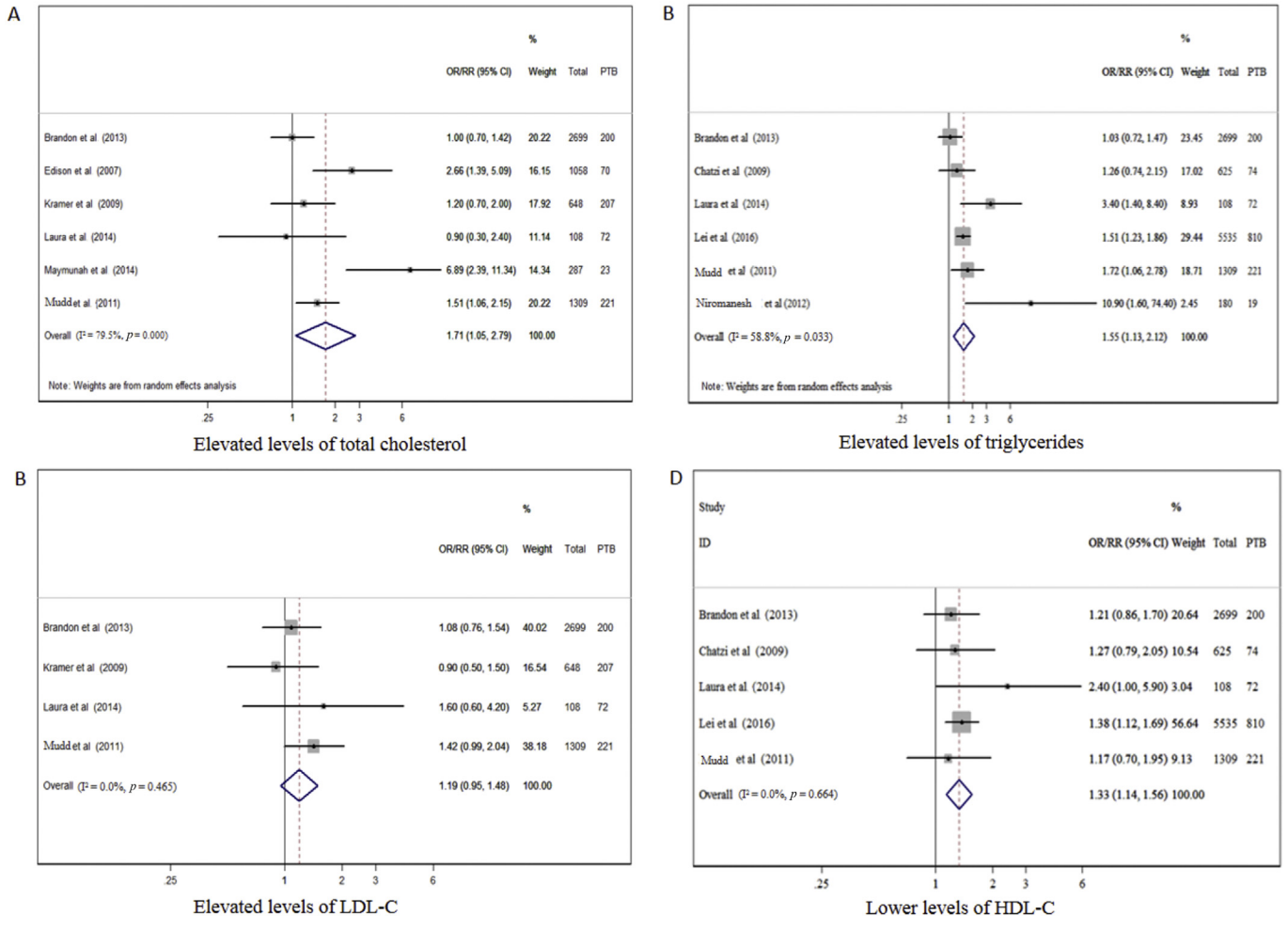

Figure 3. Forest plots for pooled odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) of preterm birth (PTB) for (A) elevated levels of total cholesterol, (B) triglycerides, (C) low density lipoprotein-cholesterol (LDL-C), and (D) lower levels of high density lipoprotein-cholesterol (HDL-C). RR = relative risk.

with normal lipid levels, the pooled PTB ORs were 1.71 (95% CI: 1.05–2.79) for elevated total cholesterol, 1.55 (95% CI: 1.13–2.12) for elevated triglycerides, 1.19 (95% CI: 0.95–1.48) for elevated LDL-C, and 1.33 (95% CI: 1.14–1.56) for lower HDL-C, respectively.

We detected significant heterogeneity in most of the meta-analyses, with I^2 values ranging from 58.8% to 96.2% ($p \leq 0.05$; Figures 2 and 3), except for the elevated levels of LDL-C and PTB analysis ($p = 0.465$, $I^2 = 0\%$) and lower levels of HDL-C analysis

($p = 0.664$, $I^2 = 0\%$). Table 2 presents the associations between elevated levels of maternal lipids and PTB among subgroups stratified by different study characteristics. Elevated maternal lipids was associated with greater odds of PTB risk particularly in cohort studies (OR = 1.86, 95% CI: 1.28–2.71, $p = 0.001$), studies from Africa or Asia (OR = 4.08, 95% CI: 1.08–15.46, $p = 0.038$), studies where blood was sampled in the second trimester (OR = 1.74, 95% CI: 1.22–2.50, $p = 0.002$), studies where blood was sampled at fasting status (OR = 2.61, 95% CI: 1.22–5.56, $p = 0.013$), and studies that excluded women who smoked during pregnancy (OR = 2.62, 95% CI: 1.28–5.37, $p = 0.009$). The association of elevated levels of lipids with the risk of sPTB (OR = 1.67, 95% CI: 1.05–2.68, $p = 0.031$) was stronger than that of elevated levels of lipids with the risk of mPTB (OR = 1.11, 95% CI: 0.64–1.91, $p = 0.715$). A positive association was found in studies that were unadjusted for gestational age (OR = 2.15, 95% CI: 1.32–3.48, $p = 0.002$), but the association did not reach statistical significance in studies that adjusted for gestational age (OR = 1.29, 95% CI: 0.90–1.85, $p = 0.168$). When compared with the studies unadjusted for maternal BMI or weight (OR = 1.76, 95% CI: 1.17–2.64, $p = 0.006$), the association was slightly weaker after adjusting for maternal BMI or weight (OR = 1.62, 95% CI: 1.04–2.54, $p = 0.034$).

Metaregression analyses were also summarized to identify potential factors that could explain the heterogeneity for elevated levels of maternal lipids and PTB risk analyses. The results indicated that the study area might be a potential source of heterogeneity ($p = 0.091$) (Table 3). When we excluded the two studies [16,23] that defined PTB as <34 weeks or <30 weeks, the risk of PTB of women with elevated levels of lipids became higher (OR = 1.74, 95% CI: 1.24–2.42). On the basis of Egger's test, publication bias was not present in most of the meta-analyses with p values ranging from 0.091 to 1.000. The funnel plots showed that the publication bias might be present for studies with lower levels of maternal lipids (Supplementary Figures 1 and 2). The sensitivity analysis suggested that the pooled results did not change markedly even if the most influential study was omitted (Supplementary Figures 3 and 4).

Table 2
Subgroup analysis stratified by potential modifying factors of the association between elevated maternal lipid levels and preterm birth.

Studies included	*N*	OR (95% CI)	p^c	I^2 (%)	p^d
Study design					
Cohort	7	1.86 (1.28–2.71)	0.001	78.0	<0.0001
Nested case-control	3	1.36 (0.92–2.02)	0.126	2.8	0.357
Study area					
North America or Europe	7	1.38 (1.08–1.77)	0.011	36.6	0.149
Others	3	4.08 (1.08–15.46)	0.038	88.4	<0.0001
Trimester					
First	3	1.28 (0.97–1.68)	0.079	4.4	0.352
Second	8	1.74 (1.22–2.50)	0.002	75.4	<0.0001
Fasting[a]					
Nonfasting or unknown	6	1.42 (1.05–1.91)	0.022	46.8	0.094
Fasting	4	2.61 (1.22–5.56)	0.013	83.7	<0.0001
Smoking					
No	5	2.62 (1.28–5.37)	0.009	80.5	<0.0001
Yes	5	1.29 (1.04–1.59)	0.020	9.6	0.352
PTB subtypes					
All PTB	7	1.61 (1.11–2.34)	0.012	75.7	<0.0001
sPTB	4	1.67 (1.05–2.68)	0.031	44.2	0.146
mPTB	2	1.11 (0.64–1.91)	0.715	28.1	0.238
GA[b] adjusted					
Yes	5	1.29 (0.90–1.85)	0.168	49.4	0.095
No	5	2.15 (1.32–3.48)	0.002	77.0	0.002
Maternal BMI or weight adjusted					
Yes	4	1.62 (1.04–2.54)	0.034	41.1	0.165
No	6	1.76 (1.17–2.64)	0.006	79.4	<0.0001

BMI = body mass index; CI = confidence interval; GA = gestational age; OR = odds ratio; PTB = preterm birth; mPTB = medically induced preterm birth; sPTB = spontaneous preterm birth.
[a] Fasting status at blood sampling.
[b] Gestational age at blood sampling.
[c] p value for pooled ORs.
[d] p value for I^2.

Table 3
Univariate metaregression analysis results of the association between elevated maternal lipid levels and preterm birth.

Studies included	*N*	Exp (β)	95% CI	p	I^2 (%)	Adj. R^2 (%)
Study design						
Nested case-control	3	Ref				
Cohort	6	1.45	0.48–4.39	0.453	72.70	−23.07
Study area						
North America or Europe	7	Ref				
Others	3	2.20	0.85–5.68	0.091	70.09	5.07
Trimester						
First	3	Ref				
Second	7	1.16	0.33–4.10	0.796	72.97	−28.81
Fasting[a]						
Nonfasting or unknown	6	Ref				
Fasting	3	1.68	0.64–4.43	0.251	71.18	−13.08
Smoking						
No	4	Ref				
Yes	5	0.54	0.23–1.29	0.143	67.91	26.22
PTB subtypes						
All PTB	6	Ref				
sPTB	3	1.32	0.41–4.21	0.598	72.37	−28.55
Adjusted for GA[b]						
Yes	5	Ref				
No	4	1.59	0.64–3.95	0.270	68.38	19.78
Adjusted for maternal BMI or weight						
Yes	4	Ref				
No	5	1.17	0.40–3.36	0.746	72.76	−33.10

BMI = body mass index; CI = confidence interval; GA = gestational age; PTB = preterm birth; Ref = reference; sPTB = spontaneous preterm birth.
[a] Fasting status at blood sampling.
[b] Gestational age at blood sampling.

Discussion

The present meta-analysis found that maternal hyperlipidemia was significantly associated with an increased risk of PTB. Positive association was also found between maternal hypolipidemia and PTB risk, but this did not reach statistical significance. Moreover, it is indicated that dyslipidemia might have a U-shaped relation with PTB risk. In subgroup meta-analysis, elevated levels of total cholesterol and triglycerides, and lower levels of HDL-C were respectively related to an increased risk of PTB.

Lipid metabolism undergoes a major adjustment during pregnancy. Serum total cholesterol, triglyceride, LDL-C, and HDL-C levels increase gradually as pregnancy proceeds [9,10]. The most dramatic damage in the lipid profile in normal pregnancy is observed in serum hypertriglyceridemia, which may be as high as 2- to 3-fold in the third trimester over the levels in nonpregnant women [29]. Increases in cholesterol levels during pregnancy promote the accumulation of maternal fat stores to serve as a source of calories for the mother and the fetus during the later stages of pregnancy and lactation [30,31]. Moreover, cholesterol is also necessary for uteroplacental vascularization, placental steroid synthesis, and placental transport functions [32,33]. However, hyperlipidemia is also regarded as an instigator of inflammation and oxidative stress [34,35]. It is well established that inflammation represents a highly significant risk factor in PTB [36]. So, we hypothesized that maternal hyperlipidemia has a positive association with PTB risk. In this meta-analysis, we found that maternal hyperlipidemia during pregnancy—either the elevated total cholesterol or triglycerides—was associated with an increased risk of PTB. The pooled effects were supported by the findings of several other studies, the format of whose data did not permit pooling.

Vrijkotte et al [12] reported that every unit increase in triglycerides was linearly associated with an increased risk of PTB (OR = 1.69, $p = 0.006$). Additionally, an intervention study found that a cholesterol-lowering diet that normalized maternal total cholesterol and LDL-C levels reduced PTB rate in low-risk pregnancies (RR = 0.10, 95% CI: 0.01–0.77) [37]. In the subgroup analyses, we found that the association between hyperlipidemia and PTB risk was weaker in the studies conducted in North America or in Europe than in those conducted in other areas. In addition, the results of metaregression analyses indicated that the study area might be a potential source of heterogeneity. Part of the discrepancy might be explained by the racial difference. It is reported that PTB rates are in the range of 16–18% in Black women compared with 5–9% in White women [38]. Black ethnicity was associated with an increased risk of PTB when compared with Whites (OR = 2.0, 95% CI: 1.8–2.2) [39]. Stronger association between hyperlipidemia and PTB risk was found at the second trimester compared with that at the first trimester. Because maternal serum lipid levels increase gradually as pregnancy proceeds [9,10], pregnant women might be more likely to have hyperlipidemia. We also found that the association becomes stronger in studies sampling blood at fasting status. Current national guidelines recommend that blood for lipid profiles be drawn after an 8–2-hour fast [40]. Because serum lipid levels can increase substantially after a meal, fasting levels provide a more stable estimate for risk assessment. In addition, elevated maternal lipid levels had a stronger association with sPTB compared with mPTB. The causes of mPTB are more complex [41], which might weaken the association. Furthermore, maternal obesity is a growing public health concern worldwide and is now becoming the most common risk factor associated with pregnancy complications and adverse birth outcomes [42]. Previous studies indicated an increased risk of PTB associated with maternal obesity [43]. As such, it remains to be clarified whether PTB is caused by obesity or by hyperlipidemia itself. When studies were pooled separately according to the adjustment of prepregnancy BMI or weight, the pooled ORs remained statistically significant, and the association was slightly weaker in studies adjusted for prepregnancy BMI or weight. Therefore, hyperlipidemia during pregnancy might be the risk factor of PTB that is independent of maternal prepregnancy BMI or weight. Additionally, individuals may also develop hyperlipidemia, even in the absence of obesity [44]. Marques-Vidal et al [45] reported that normal weight obese (defined as an excessive body fat associated with a normal BMI) women had higher lipid levels and a higher prevalence of dyslipidemia than lean women. However, the hyperlipidemia of these normal weight individuals might be less severe compared with obese individuals. Hence, pregnant women with normal weight also should also pay attention to their serum lipid levels in order to implement PTB prevention.

Meanwhile, this meta-analysis also found that lower levels of maternal lipids during pregnancy might be also associated with an increased PTB risk, although this did not reach statistical significance. Lower levels of maternal lipids during pregnancy might affect the normal accumulation of maternal fat stores to serve as a source of calories for the mother and fetus. In addition, it might affect the placental vascularization and cause shallow placentation, which is associated with sPTB risk [7,8]. Furthermore, this association might be explained directly by the lack of nutrients, resulting in diminished fetal growth or duration of gestation or indirectly through other associated factors such as smoking, poor diet, or medical illness [21,46,47]. However, owing to the small number of studies, subgroup and metaregression analyses were not performed to define the possible source of heterogeneity. Further studies are still needed to reveal the mechanisms that may link lower lipids during pregnancy with PTB.

This study has several strengths. First of all, we performed a thorough quality assessment of the included studies, and their quality was good. Furthermore, this meta-analysis also included a separate analysis of four lipid parameters and PTB risk. Moreover, we were able to perform subgroup and metaregression analyses to illustrate that study area might be the potential factor that influences the association of hyperlipidemia with PTB. Additionally, robust results were observed from sensitivity analysis. However, we could not completely rule out several limitations in our study. First, a moderate or high heterogeneity exists in the current study. Second, in the course of a normal pregnancy, all lipid and lipoprotein components increased substantially. These increases were particularly marked during the third trimester when triglyceride stores were needed to provide a ready source of energy and fatty acids to the fetus [48]. It should be noted, however, that there are no reference standards defined for lipid parameters during the three trimesters to identify maternal hyperlipidemia and hypolipidemia. Third, only 11 studies were included in our meta-analysis, and only five studies provided the effect estimates of lower lipids. OR and RR value were pooled because of the limited number of articles, which may result in the overestimation of effects between dyslipidemia and PTB. In addition, we were unable to perform subgroup and metaregression analyses to illustrate the potential factors that might influence the association of lower levels of lipids because of the limited number of articles. Therefore, more studies are needed in order to identify the association between maternal lipid levels and PTB risk.

In conclusion, the present meta-analysis found that elevated levels of lipids during pregnancy, either the elevated total cholesterol or triglycerides, were associated with a higher risk of PTB. These findings indicate that a normal level of maternal lipid during pregnancy may reduce the risk of PTB. However, further large-sample, well-designed, prospective epidemiological studies, especially at the first and third trimesters, are needed to confirm our findings.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tjog.2016.07.012.

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