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Original paper

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Feto-Maternal Outcomes of Breastfeeding during Pregnancy: A Systematic Review and Meta-Analysis

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ABSTRACT

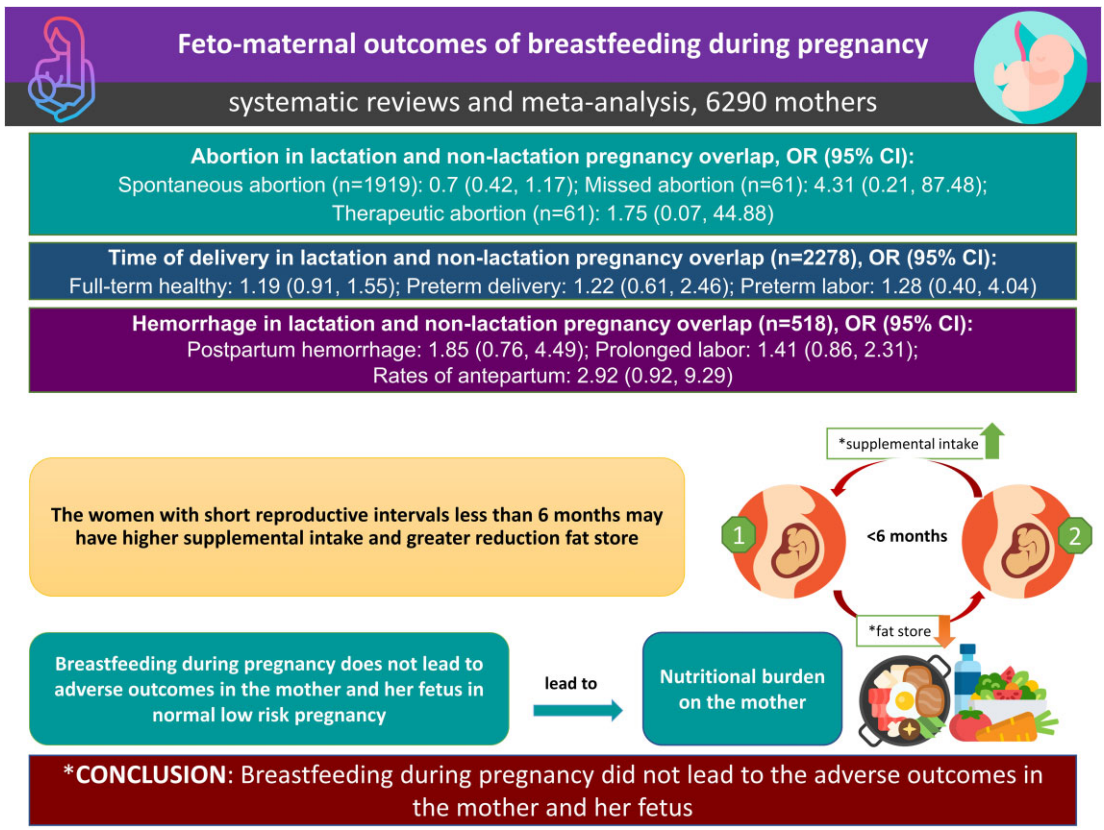
Background: Breastfeeding is beneficial to both mother and infant. However, overlap of lactation with pregnancy and short recuperative intervals may impact mothers nutritionally. We aimed to investigate the possible effects of pregnancy during breastfeeding.

Methods: In October 2018, we searched systematically in nine electronic databases to investigate any association of breastfeeding during pregnancy with fetal and/or maternal outcomes. The study protocol was registered in PROSPERO (CRD41017056490). A meta-analysis was done to detect maternal and fetal outcomes and complications during pregnancy. Quality assessment was performed using the Australian Cancer Council bias tool for included studies.

Results: With 1992 studies initially identified, eight were eligible for qualitative analysis and 12 for quantitative analysis. Our results showed no significant difference in different abortion subtypes between lactating and non-lactating ones. In delivery, no difference between two groups regarding the time of delivery in full-term healthy, preterm delivery and preterm labor. No significant difference was detected in rates of antepartum, postpartum hemorrhage and prolonged labor between two groups. The women with short reproductive intervals may have higher supplemental intake and greater reduction fat store. The present studies showed that breastfeeding during pregnancy does not lead to adverse outcomes in the mother and her fetus in normal low-risk pregnancy, although it may lead to the nutritional burden on the mother.

Conclusion: The present studies showed that breastfeeding during pregnancy did not lead to the adverse outcomes in the mother and her fetus.

KEYWORDS: breastfeeding, pregnancy, maternal health, neonatal outcome, meta-analysis, systematic review



BACKGROUND

Benefits of breastfeeding to both mother and infant include protecting against a variety of diseases and conditions in the infant, decreasing postpartum bleeding and more rapid uterine involution, decreasing menstrual blood loss and increased child spacing and decreasing the risk of breast and ovarian cancer [1, 2]. Exclusive breastfeeding recommendations from the World Health Organization (WHO), UNICEF and the American Academy of Pediatrics recommended that Breastfeeding should begin within one hour of birth, be exclusive for the first six months of life [3, 4]. The WHO highly recommends the practice of breastfeeding until 2 years or more [5]. The longer duration of breastfeeding, the higher possibility of overlapping breastfeeding and pregnancy. Shaaban and Glasier [6] interviewed 2617 parous women attending a hospital in Egypt for antenatal care, and 25.3% of these women reported breastfeeding. According to Briefel, *et al.* [7], the rate of pregnancy in lactating US women was 5%. One-third of all pregnancy occur in lactating women in India [8].

Few researches have been found to investigate the effect of breastfeeding during pregnancy on maternal, pregnancy and child outcomes. In a letter to the editor, Onwudiegwu [9] hypothesized that oxytocin accelerates postpartum uterine involution and stirs uterine contraction, and therefore, oxytocin can cause impaired uteroplacental blood flow, premature labor, low birth weight, abortion, and intrauterine growth retardation and death. Marquis, *et al.* [10] showed that infants of women who keep breastfeeding during pregnancy gained 125 grams less than infants of control groups. Overlap and short recuperative intervals were associated with maternal outcomes of increased supplement intake and reduced-fat stores [11]. However, other studies showed the reverse results. Breastfeeding in late pregnancy has not been linked to an increased risk of small-for-gestational-age (SGA) [12, 13]. Additionally, difference regarding the full-term rate between breastfeeding during pregnancy group and non-breastfeeding during pregnancy group was not identified [13]. Current systematic review and meta-analysis (SR/MA) aimed to investigate health risks and possible adverse effects of pregnancy during breastfeeding on maternal, child and pregnancy outcomes.

METHODS

Study design

We performed a systematic review followed by a meta-analysis [14]. The Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) statement, which was published in 2009, was used to design this review [15]. Also, we reported our results based on the updated PRISMA checklist [16] (Supplementary Table S1). We registered the study protocol in PROSPERO (CRD41017056490).

We used the PICOS strategy (Participants, Interventions, Comparisons, Outcomes, and Study design) for study searching, substituting intervention (I) with exposure (E) [17]. The population of interest consisted of pregnant mothers. Breastfeeding was considered as the exposure in current study. The control group comprised of mothers who did not breastfeeding. The outcomes were all reported fetal or maternal effects.

We have searched for related articles since inception up to October 2018. Nine databases were used for searching stage, including PubMed, Scopus, WHO Global Health Library (GHL), Virtual Health Library (VHL), Institute of Science Index (ISI), New York Academy of Medicine Grey Literature Report (NYAM), System for Information on Grey Literature in Europe (SIGLE), POPLINE and Cochrane Central Register of Controlled Trials (CENTRAL). Each database detailed search strategy is outlined in Supplementary Table S2.

Our inclusion criteria were original articles which have evidence of investigating any association of breastfeeding during pregnancy with the fetal and/or maternal outcomes. There were no limitations on research design ethnicity, gender, and ethnicity, publishing date, location or the language of articles. A manual search of included studies' references was done to detect any relevant study, by running a comprehensive search to include journal articles and gray literature; we also manually screened reference list of included full texts and explored PubMed for additional articles using 'similar articles' option [18].

Research articles with the following criteria were excluded: *in vitro* studies, animal studies (rats, mouse, dogs), overlapped data, cannot extract data, abstract, case-report, case series, thesis, book chapters, abstract/poster for a conference paper and articles have no full texts (authors' responses, editorials, comments and letters), reviews and meta-analysis. Three reviewers separately performed titles and abstract screening for initial eligibility assessment. We included all the original articles that fulfill our inclusion criteria. Full texts of all included articles were then retrieved and reviewed. All relevant articles were selected for the systematic review and then all data were further screened the meta-analysis. In all screening steps, decision to include or exclude by all three reviewers was considered as conclusive. Any opposite decisions were finally accepted or rejected after discussion. Finally, any disagreements and discrepancies were fixed by consult with senior reviewers. The study selection procedure is represented in the PRISMA flow diagram (Fig. 1).

Data collection

At first, we performed a pilot extraction to test our extracted template design using Microsoft Excel. All the data from included studies were extracted by at least three reviewers. Before the analysis, the double-checking of the data was executed by at least two different authors. Discussion between reviewers and consultation with a senior author was done when there are any disagreements.

Data analysis

The quality of selected studies was assessed by three reviewers using the criteria of the Australian Cancer Council bias tool [19]. The judgment of each reviewer on each domain is categorized as 'low risk', 'high risk' or 'unclear risk' of bias. Any disagreement was resolved by discussions between reviewers and by consultation from a supervisor (NTH) to reach a consensus.

Meta-analyses were performed using Comprehensive Meta-analysis software version 3 (Biostat, NJ, USA). The pooled event rate and odds ratio (OR) was calculated from dichotomous variables. The continuous variables were calculated to compute the pooled mean difference (MD). If studies were considered as heterogeneity, we used a random-effects model following the method of Der Simonian and Laird. Otherwise, we used a fixed-effect model following the Mantel–Haenszel method [20]. We used the Q statistic and I^2 test, which describes the percentage of variability in the effect estimates that is because of heterogeneity beyond sampling error to evaluate the heterogeneity between studies [21, 22]. Heterogeneity was considered significant if the *p*-value of Q statistic was <0.1 and/or I^2 was $>50\%$ [23]. Begg's funnel plot and Egger's regression test were done to evaluate the presence of publication bias, when there were five or more studies in the analysis [24–26]. Egger's regression test *p*-value was <0.05 considered significant for publication bias. When the publication bias was detected, the method of trimming and filling Duvall and Tweedie was achieved by incorporating studies to improve the symmetry [27]. The adjusted pooled effect size and its 95% confidence interval (CI) were computed after the addition of potential missing studies.

RESULTS

Literature search

The electronic search yielded 1992 references from nine databases. A total of 25 relevant articles full texts were screened after duplicates deletion during title/abstract screening. Ultimately, eight studies met the standards for selection. With the addition of 12 more papers in manual search, in the end, we had eight relevant papers qualitative analysis and 12 for quantitative analysis (Fig. 1). There were very few studies supporting specific outcomes included in specific meta-analyses. There were two to five studies in the meta-analysis of maternal outcomes, complications during pregnancy and complications at delivery, nine studies in the meta-analysis of birth weight and three studies in the meta-analysis of neonatal interventions.

Included study characteristics

The description of all included studies is listed in Table 1. Most parts of the study was taken place in low-income nations with small sample sizes. More important, the overlap of lactation was specified differently in each studies makes the interpretation of current study' results with caution.

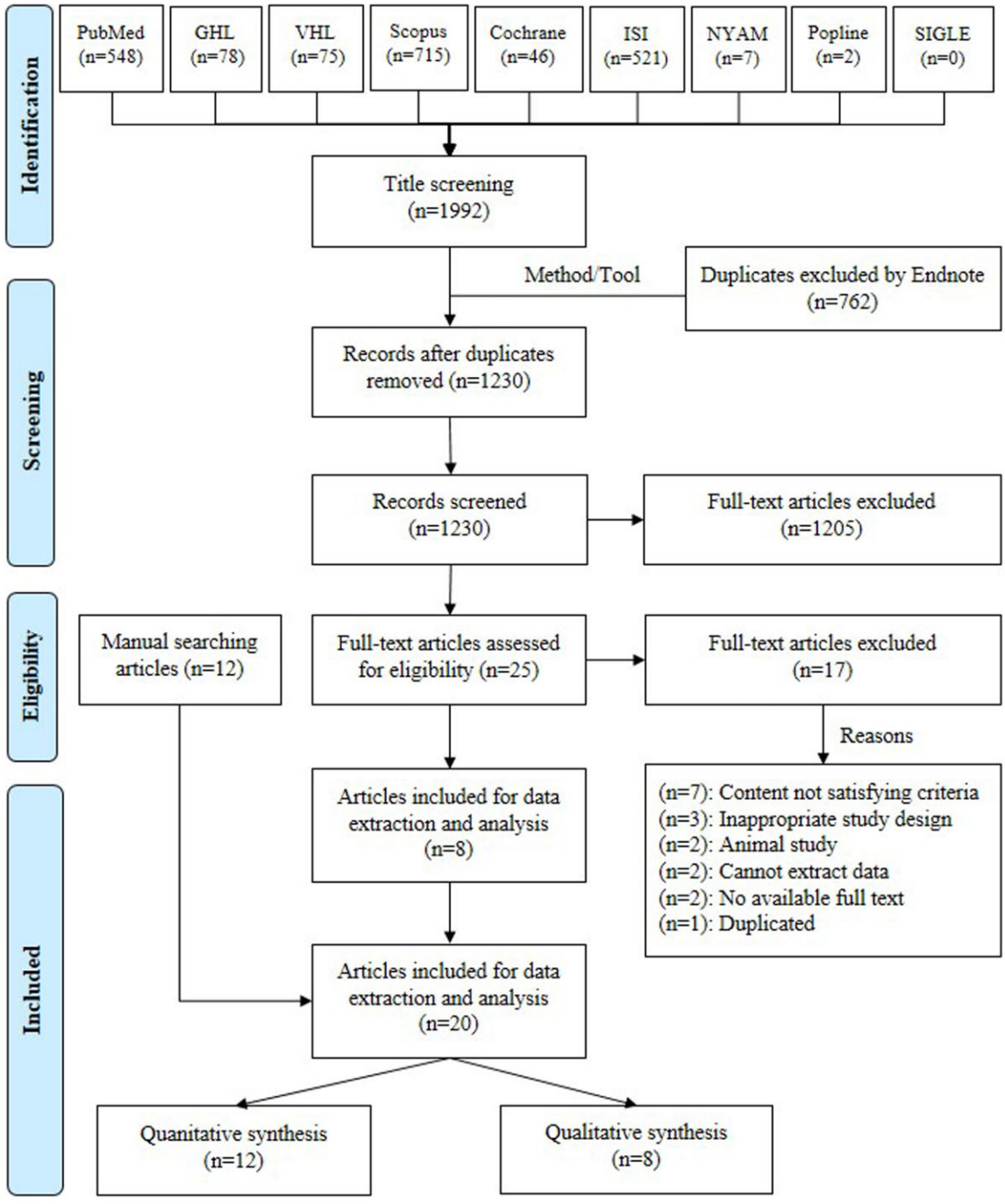


Fig. 1. PRISMA flow diagram of studies' screening and selection.

Maternal characteristics

The mean age of 6290 included mothers was 27.80 years (95% CI: 27.77–27.82) with average heights of 150.36 (95% CI: 147.13–153.58) and 149.48 cm (95% CI: 148.83–150.13) for lactating and non-lactating groups, respectively. Additionally,

Table 1. Characteristic of studies included in quantitative analysis

No.	Author/year/country	B. Definition of the overlap of lactation	Time of data collection	Country of recruitment	Sample size	Outcomes available	Data collection method	Study design	Note
Quantitative synthesis									
1	Shaaban/2015/Egypt [32]	• All successive multiparous women who were pregnant introduced to the enrollment Maternal and Child Health Centers in the first trimester of pregnancy (under 12 weeks pregnant) and be followed until labor. • Qualified subjects were divided into two groups based on the point of time they got pregnant: during breastfeeding or after weaning.	November 2013 to December 2014	Egypt	540	• The prevalence of miscarriage, maternal anemia, hemorrhage, elevated blood sugar, elevated blood pressure, placental separation and eclampsia between the two groups. • Time, method of delivery and onset of complications during delivery. • Fetal status at birth, weight at birth and need for referral to a neonatal care unit.	Interview using structured questionnaire	Prospective-cohort study	Women who did not give lactation to their last child and lived in areas away from recruitments center were excluded.
2	Merchant/1990/Guatemala [37]	• According to the weaning time of the previous child and the concept of indexing the child, pregnancies are divided into two groups: (1) non-overlap if weaning $\leq$ 2 weeks after conception and (2) overlap if weaning $>$ 2 weeks after conception. • Study sample: When there is an overlap, 55.7% only breastfed during the first trimester of pregnancy, 41.1% continued breastfeeding to the second trimester and 3.2% continued to the third trimester.	1969 to 1977	Guatemala	504	• Maternal supplement intake, body store • Fetal growth	Interview Observation Intervention (Supplement provider)	Longitudinal data from a nutrition-supplementation trial	48% of the women provided data on more than one pregnancy to the study sample.
3	Madarshahian/2012/Iran [13]	• The overlap group consisted of women who breastfeed their older children three to five times per day during their current pregnancy, for at least 30 days.	April to December 2008	Iran	320	• Pregnancy problems, nutritional change, gestational age, birth weight • Pattern and duration of breastfeeding	• Interview using questionnaire • Observation	Comparative Study	

(continued)

Table 1. (continued)

No.	Author/year/country	B. Definition of the overlap of lactation	Time of data collection	Country of recruitment	Sample size	Outcomes available	Data collection method	Study design	Note
		• The non-overlapping group included women who stopped breastfeeding at least 3 months before and did not breastfeed during their current pregnancy. • The two groups were matched based on maternal age, parity, medical and midwifery problems and changes in nutritional status during pregnancy.							
4	Albadran/2013/Iraq [33]	• Study population: Pregnant women who breastfed during pregnancy. Case group: pregnant women who breastfed over 24 weeks of pregnancy. Control group: pregnant women who breastfed during 24 weeks of pregnancy. • Exclusion: women less than 18 and over 35; with diseases such as diabetes mellitus, thyroid diseases, sickle cell anemia; with history of recurrent miscarriage and preterm births; multiple pregnancies.	September 2011 to September 2012	Iraq	215 cases 280 controls	Proportion of miscarriage, preterm, full term and birth weighs	Prospective	Case–control study	
5	Ishii/2009/Japan [34]	• Cases: The pregnancy was confirmed before 8 weeks of gestation, and women who were breastfeeding at the time of diagnosis were recruited. In these cases, 38.7% continued breastfeeding to 12 weeks, 27.4% to 28 weeks, 33.6% continued after 28 weeks and 7.9% continued breastfeeding infants even after delivery.	1996 to 2000	Japan	110 cases 774 controls	• Proportion of term and preterm births, miscarriage • Frequency of lactation • Gestational age at weaning	Retrospective review the outcome of each pregnancy from patient records	Retrospective matched control study	All children were continued to breastfeed even after a miscarriage.

(continued)

Table 1. (continued)

No.	Author/year/country	B. Definition of the overlap of lactation	Time of data collection	Country of recruitment	Sample size	Outcomes available	Data collection method	Study design	Note
		• Control: Women who stopped breastfeeding at least 3 months before having pregnancy and matched with cases in age and score of 1-0-0-1 (number of term births, premature births, abortions and healthy infants, respectively).							
6	Pareja/2015/Peru [12]	Continue breastfeeding until at least the 28th week of pregnancy.	March 2006 to April 2007	Peru	95 cases 150 controls	*Compared the proportion of women who breastfed > 28 weeks of pregnancy, between two groups: SGA and non-SGA*	Interviewing using structured questionnaire Reviewing and extracting information from clinical chart	Case–control study	
7	Marquis/2002/Peru [10][f]	Continue breastfeeding during the third trimester of pregnancy.	July 1998 to January 2000	Peru	133	Compare birth events, newborn characteristics and growth outcomes at 1 month between group overlap and non-overlap	Prospective	Prospective-cohort study	Families of included pregnant women had some indicators of a better economic status compared to those were excluded.
8	Marquis/2003/Peru [38][f]	Continue breastfeeding during the third trimester of pregnancy.	July 1998 to January 2000	Peru	133	Evaluating the link between an overlap with macronutrients and immunological agents in milk, newborn urinary IgA, morbidity of mother and infants.	Prospective	Prospective-cohort study	
9	Merchant/1990/Guatemala [11]	Breastfeeding> 2 weeks after conception.	1969 to 1977	Guatemala	102	• Maternal supplement consumption and fat storage • Birth weight	Prospective	Data from randomized control trial	

(continued)

Table 1. (continued)

No.	Author/year/country	B. Definition of the overlap of lactation	Time of data collection	Country of recruitment	Sample size	Outcomes available	Data collection method	Study design	Note
10	Ayrim/2014/Turkey [29]	All pregnant women who continued breastfeeding during the pregnancy period.	June 2004 to December 2011	Turkey	165	Compared between two groups in body mass index before pregnancy, weight gain during pregnancy, birth weight, Apgar score, obstetric adverse events (anemia, miscarriage, intrauterine growth retardation, preterm delivery).	Retrospective reviewed the clinical records	Cross-sectional study	Intrauterine growth retardation was not observed in two groups.
11	Sengul/2013/Turkey [28]	Women who experienced pregnancy while breastfeeding.	June 2006 to June 2009	Turkey	61	Compared between two groups in terms of pre-pregnancy body mass index, gestational weight gain, birth weight, obstetric complications (missed abortion, intrauterine growth restriction, preterm labor).	Observation	Case–control study	None in the breastfeeding group continued to breastfeed after 20 gestational weeks.
Qualitative synthesis									
12	Hassanabadi/2013/Iran [35]	• Overlap: Women who breastfed their older children during current pregnancy. • Non-overlap: Women who weaned their older children at least 3 months before pregnancy.	July 2009 to April 2010	Iran	320	Birth weight, height, head circumference and pregnancy outcome between two groups	Observation	Case–control study	
13	Shaaban/2008/Egypt [6]	Conceived the present pregnancy during breastfeeding.	June 2006 to June 2007	Egypt	2617	• Prevalence of women who got pregnancy during lactating period • Pregnancy intention • Breastfeeding pattern	Using an interviewer-administered structured questionnaire	Cross-sectional study	29 women (4.4%) conceived in the first 6 months postpartum, 100 women (15.1%) conceived before menstruation resumed.

(continued)

Table 1. (continued)

No.	Author/year/country	B. Definition of the overlap of lactation	Time of data collection	Country of recruitment	Sample size	Outcomes available	Data collection method	Study design	Note
14	Bohler/1996/Himalayas [42]	Breastfeeding concurrent with pregnancy.	April to September 1990	East Bhutan	113	• Average growth rate during weaning • Relation between conceived while lactating and early cessation of lactation	Semi-structured interview	Cross-sectional study	
15	Merchant/1991 Guatemala/[46]	• Short overlap subgroup: women weaned their baby in the first trimester. • Long overlap subgroup: women weaned their baby in the second or third trimester.	1969 to 1977	Guatemalan	504	The effects of breastfeeding during pregnancy on the nutrition implication of mothers, infants and fetuses.	Prospective	Data from randomized control trial	
16	Ismail/2009/Egypt [44]	Breast milk samples from 45 lactating pregnant women, whose duration of pregnancy range from 8–11, 12–15, 16–19 and 20–40 weeks. Only nine women, who were at 8–11 weeks, can be followed up to the third trimester.	Not mention	Egypt	• 45 case and • 45 control	Total chemical composition of milk, protein composition and immune components.	Prospective	Case–control study	
17	Moscone/1993/UK [45]	Overlap criteria was not specified.	September 1985 to Jun 1986	La Leche League	57	Change in flow/frequency of breast milk	Questionnaire by email	Retrospective	
18	Pike/1999/Kenya [30]	Overlap criteria was not specified.	August 1993 to July 1994	Ngisonyoka, Turkana	68		Questionnaire interviewed	Cross-sectional study, prospective	
19	Siega-Riz/1993/Philippines [31]	Women who were lactating during pregnancy.	1983 to 1987	Cebu Longitudinal Health and Nutrition Survey	1367	Patterns of weight gain during pregnancy		Comparative study	
20	Molitoris/2019/USA [36]	Women who were lactating during pregnancy.	2002 to 2015	National Survey of Family Growth	10 661	Risk of miscarriage	Extract data from several waves of the National Survey of Family Growth	Cross-sectional study, retrospective	

Table 2. Basic characteristics of pregnant women in included studies

No.	Author/ publication year/country	Age (years)						Gravidity/parity						Month of pregnancy when BMI is measure						BMI						Average weight gain					
		Case			Control			Case			Control			Case			Control			Case			Control			Case			Control		
		Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*
1	Ismail/2009/ Egypt [44]	(18–36) [e]	–	45	a (combined)		45			-																					
2	Shaaban/2008/ Egypt [6]	28.09	5.84	2617	a (combined)			2.83 [c] 0.79 [d]	1.7 1.2	2617 2617	a a																				
3	Shaaban/2015/ Egypt [32]	28.8	6.18	270	30.5	5.2	270	2.39 [d]	1.54	270	2.64	1.18	270																		
4	Merchant/ 1990/ Guatemala [37]	30.2	6.8	249	28.7	6.7	252	5.4 [d]	2.8	253	5.8	3	247																		
5	Madarshahian/ 2012/Iran [13]	28.4	4.6	80	29.6	5.7	240	2.9 [d]	1.3	80	2.8	1	240																		
6	Albadran/ 2013/Iraq [33]	27.6	0.28	215	27.9	0.27	280	3.3 2.2	1.6 1.6	215 215	3.5 2.5	1.7 1.7	280 280																		
7	Ishii/2009/ Japan [34]	28.7	3.4	110	29.1	2.9	774	-																							
8	Pareja/2015/ Peru [12]	27.3	6.01	227	a (combined)			2.26 [c] 1.93 [d]	1.51 1.3	228 228	a a															10.71	5.27	128	Note: There are two subgroups: SGA and non-SGA. Combined mean and SD of both subgroups = 10.27 ± 5.27 (n = 128)		
9	Marquis/2002/ Peru [10] [f]	25.9	5.5	68	25.9	4.7	65	2.1 [d]	1.3	68	2.1	1.1	65				1 mo postnatally			26.2	3.8	68	25.9	3.6	65						
10	Marquis/ 2003/Peru [38] [f]	35	–	44	a (combined)		29			–							1 mo postpartum			26.2	0.5	68	25.9	0.4	65						
11	Bohler/1995/ Himalayas [41]	26.8	–	98	a (combined)			–																							
12	Bohler/1996/ Himalayas [42]	29.6	–	40	26.8	–	40	4.0	–	40	2.8	–	40																		
13	Ayrim/2014/ Turkey [29]	24.3	4.9	45	23.2	3.3	120	-									Not mentioned, even no word 'BMI' are found			25.4	4.4	45	26.4	3.7	120	7	3.4	45	13	5.6	120

(continued)

Table 2. (continued)

No.	Author/ publication year/country	Age (years)						Gravidity/parity						Month of pregnancy when BMI is measure						BMI						Average weight gain					
		Case			Control			Case			Control			Case			Control			Case			Control			Case			Control		
		Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*	Mean	SD	*N*
14	Sengul/2013/ Turkey [28]	25.3	4.9	39	23.2	3.3	22	2.5 [c] 1.4 [d]	0.9 0.9	39 39	2.3 1.3	0.7 0.6	22 22		Not mentioned, even no word 'BMI' are found					26.4	4.4	39	25.7	3.7	22	10.6	3.6	39	11.8	3	22
15	Pike/1999/ Kenya [30]	28.09	5.63	68	a (combined)										Pre-pregnancy and third trimester					Monthly changes in maternal weight gain (kg) for each gestational trimester			Tri 1 Tri 2 Tri 3			2.20 −0.21 0.32		20 22 34	0.56 1.11 0.42		20 22 34
16	Siega-Riz/ 1993/ Philippines [31]														(Not state clear) Pre-pregnancy, first + second + third trimester					Monthly total weight gain between women who were lactating during pregnancy			Tri 1 and 2 Tri 3			0.88 1.24					
17	Moscone/ 1993/UK [45]	29	4.14	57	a (combined)																										

Values are mean and standard error of the mean.
[a]Combined mean and standard deviation of the two groups.
[b]One month postpartum.
[c]Gravidity.
[d]Parity.
[e]Range.
[f]Basic characteristics of participants were similar in two studies, data in Marquis/2002/Peru were used in analysis.

the mean gravidity for all mothers was 2.32 pregnancies with an average parity of 2.83 and 2.91 babies for lactating and non-lactating groups, respectively. In the same context, the mean calf circumference of 133 infants was 33 cm in lactating mothers and 32.6 cm in non-lactating mothers. Regarding to maternal body mass index (BMI), mean of BMI in lactating was 26.04 kg/m^2 and 26.16 kg/m^2 in non-lactating mothers. Nevertheless, the average maternal weight gain was significantly different with a mean of 8.79 kg vs. 12.46 kg in lactating and non-lactating groups, respectively [28, 29]. Pike [30] showed that breastfeeding during first trimester affected negatively second trimester weigh gain ($p < 0.01$), but not third trimester. On the other hand, Siega-Riz and Adair [31] found no consistent difference in the weight gain between overlap and non-overlap group irrespective of the duration of overlap. However, during the third trimester, mean weekly weight gain was significant higher in women with overlap group than women with no overlap.

Quality assessment

The quality assessment results are summarized in Supplemental Table S3. We had five case–control studies with an overall risk of bias rated 'high' for three, medium for one and low for one studies. On the other hand, among 11 cohort studies, eight of them were of 'high' risk of bias as well as two 'moderate' risk and one 'low' risk of bias.

Maternal outcomes and complications during pregnancy

Pooling three studies [32–34] of 1919 mothers showed no significant difference between lactating and non-lactating ones of spontaneous abortion [OR (95% CI) = 0.7 (0.42–1.17), $p = 0.18$] (Fig. 2). The study of Şengül, *et al.* [28] with 61 pregnant women also showed no significant difference between two groups regarding missed abortion [OR (95% CI) = 4.31 (0.21–87.48), $p = 0.3$] and therapeutic abortion [OR (95% CI) = 1.75 (0.07, 44.88), $p = 0.73$]. Additionally, a significant difference in prevalence of anemia, as well as hemoglobin level between lactating and non-lactating mother were also identified. Other reported pregnancy complications are summarized in Supplementary Table S4.

Shaaban, *et al.* [32] reported a significantly higher percentage of high blood pressure in the non-lactating pregnant group (15.6% compared to 12.2% in the lactating groups, $p = 0.003$). On the other hand, this study reported increased percentage of mothers suffering from placental separation in the lactating group [OR (95% CI) = 3.79 (1.38–10.35), $p = 0.009$] and vaginal bleeding in the same group [OR (95% CI) = 3.56 (1.29–9.80), $p = 0.01$]. In another study, Ayrim, *et al.* [29] showed no difference

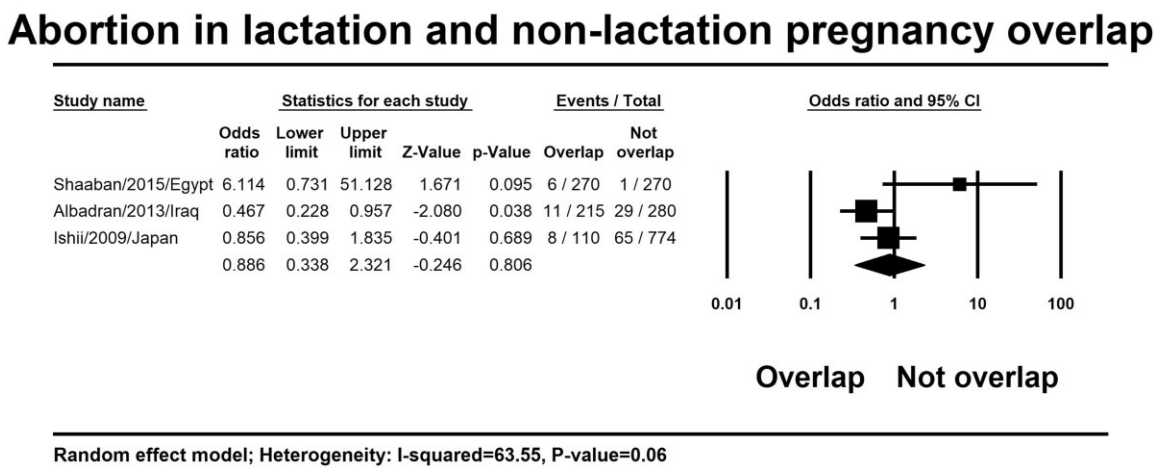


Fig. 2. Meta-analysis of spontaneous abortion between lactating and non-lactating pregnant.

in hyperemesis gravidarum percentage between the two groups with OR (95% CI) [2.79 (0.54–14.34), $p = 0.203$]. Hassanabadi and Madarshahian [35] also found no significant effect of previous child lactation during pregnancy on the average weight ($p = 0.45$), height ($p = 0.15$) and head circumference ($p = 0.31$) of the newborn and pregnancy outcomes were similar between groups.

Maternal outcomes and complications at delivery

Five studies [13, 28, 32–34] (2278 participants) had compared the time of delivery between lactating and non-lactating groups which showed no difference in full-term healthy [OR (95% CI) = 1.19 (0.91–1.55), $p = 0.22$] (Fig. 3A), preterm delivery [OR (95% CI) = 1.22 (0.61–2.46), $p = 0.57$] (Fig. 3B) and preterm labor [OR (95% CI) = 1.28 (0.40–4.04), $p = 0.68$] (Fig. 3C).

One study [32] with 518 mothers showed no difference in rates of antepartum hemorrhage with [OR (95% CI) = 2.92 (0.92–9.29), $p = 0.07$]. Similarly, there was no significant difference in both postpartum hemorrhage [OR (95% CI) = [1.85 (0.76–4.49), $p = 0.17$] and prolonged labor with [OR (95% CI) = 1.41 (0.86–2.31), $p = 0.17$] (Fig. 4A).

In a recently published article of 10 661 pregnancies from the National Survey of Family Growth, Molitoris [36] showed that the miscarriage rate was significant higher in mothers who exclusively breastfed during pregnancy (35%) than in those who practiced complementary breastfeeding during pregnancy (14%) or did not breastfeed (15%). After adjusting for maternal characteristic and other characteristic related to pregnancy, the risk of miscarriage remained greater in mothers exclusively breastfed compared to those did not breastfeed.

Baby outcomes and complications

The average newborn weight of non-lactating group in six studies [10, 13, 29, 32, 33, 37] was 3197 g with non-significant difference from lactating group in babies' weight with mean difference [MD (95% CI) = 0.04 (−0.062, 0.142), $p = 0.44$]. Birth weight was significantly higher in non-lactating group for gestational age at birth with MD [−0.19 (−0.36, −0.01), $p = 0.03$] (Fig. 4B).

Neonatal interventions

One study [32] compared the transfer of neonates into Pediatric Care Unit to non-lactating group with [OR (95% CI) = 1.26 (0.89–1.78), $p = 0.2$]; however, it revealed no statistical significance. In the same context, Şengül, *et al.* [28] compared Apgar score of babies at first- and fifth-minute between lactation and non-lactation group and showed no statistical significant (first-minute: 7.03 ± 0.39 compared to 7.0 ± 0.44; fifth-minute 8.94 ± 0.24 compared to 8.91 ± 0.29).

Other outcomes

Four studies have investigated maternal nutritional status and supplement intake in cases of concurrent pregnancy and breastfeeding. Siega-Riz, *et al.* [31] found that weight gain during the 3rd trimester of women with any overlap of pregnancy was higher than in women with no overlap. In 1990, Merchant, *et al.* [37] examined maternal and fetal health effects during breastfeeding while being pregnant. It was noticed that women with short reproductive intervals (<6 months) have higher supplement intake and greater reduction in fat stores. However, this association did not persist after pregnancy and disappeared 3 months postpartum. Shaaban, *et al.* [32] concluded that there is an association between pregnancy during breastfeeding and an increase in overall complications of pregnancy as; maternal anemia, prolonged labor, delayed fetal growth, cesarean section delivery and low birth weight infants. In the same context, Merchant, *et al.* [11] further examined the consequence of different maternal nutrition status in case of reproductive stress of short birth intervals. The results showed that the overlap of breastfeeding and pregnancy along with short birth intervals found to be stressful for mothers. The results demonstrated that overlap of breastfeeding and pregnancy along with short birth intervals results in increased maternal intake of supplements and reduced-fat stores. Again, fetal growth was not affected and all full-term births did not show any significant reduction in weight. The aforementioned results suggested that fetal growth was protected at the cost of concurrent depletion of maternal nutritional status (Supplementary Table S5). Marquis, *et al.* [38] have examined the effect of the overlap between

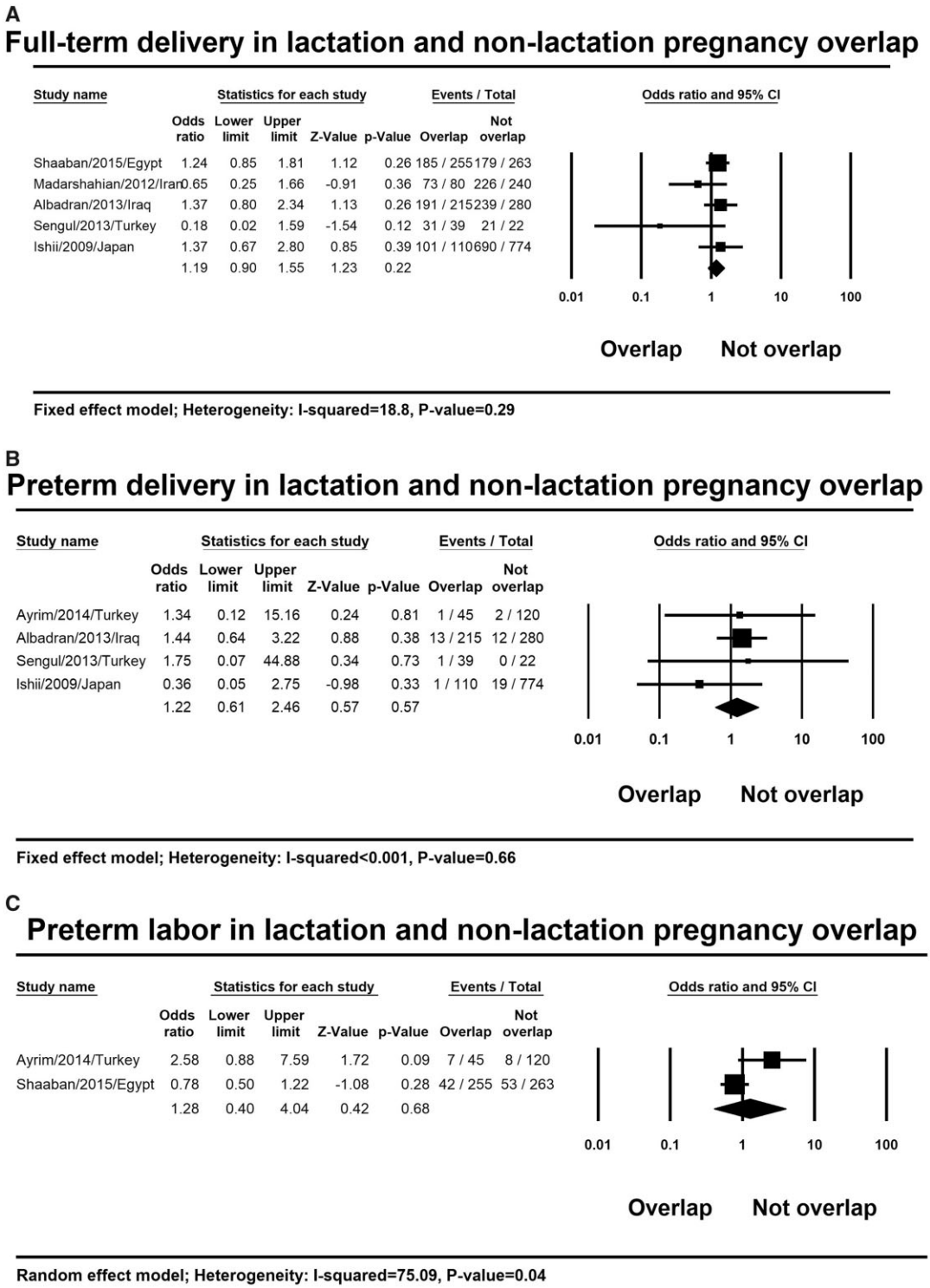


Fig. 3. Meta-analysis of full-term healthy (**A**), preterm delivery (**B**) and preterm labor (**C**) between lactating and non-lactating pregnant.

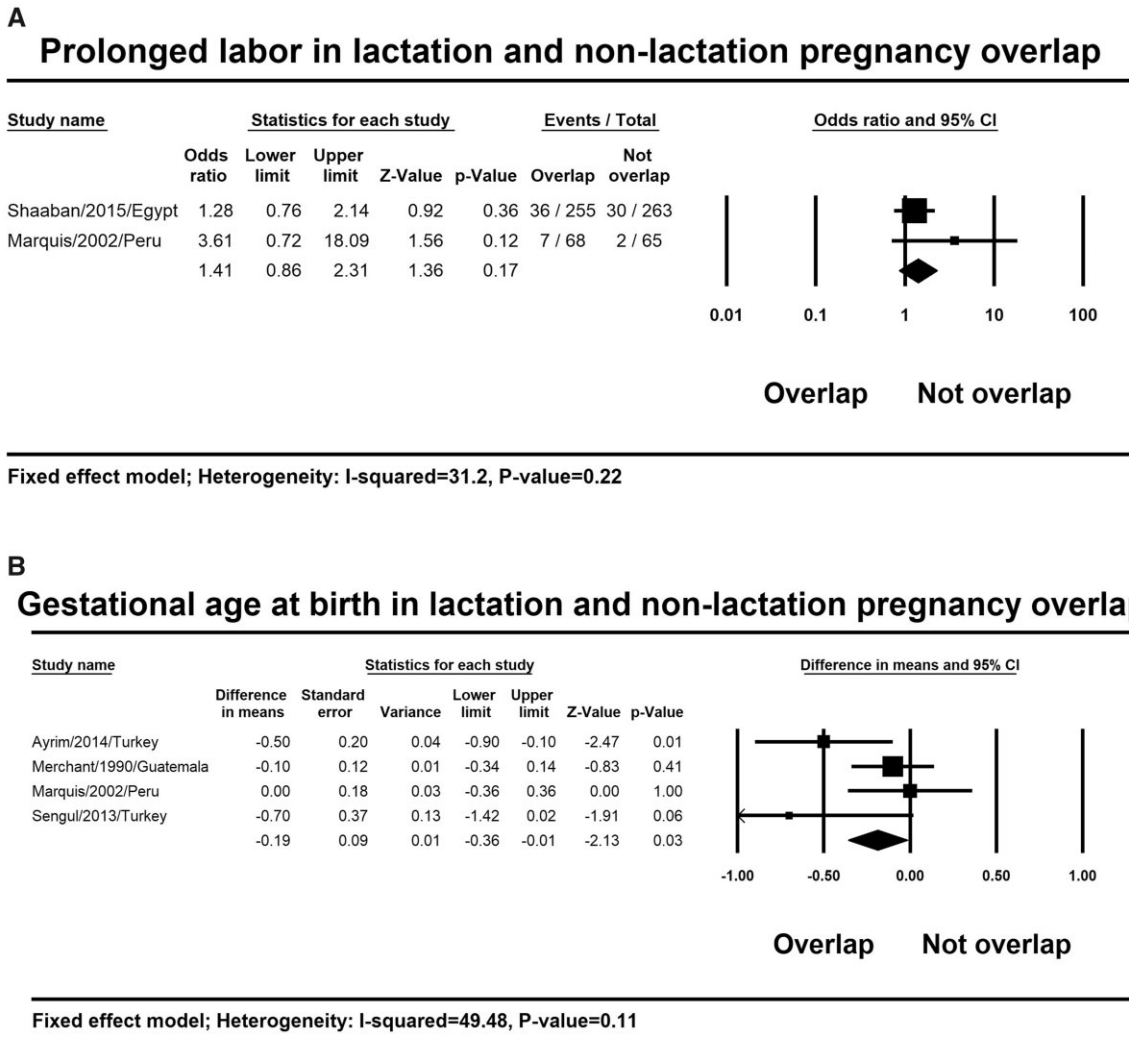


Fig. 4. Meta-analysis of delivery problems (**A**) and gestational age at birth (**B**) between lactating and non-lactating pregnant.

pregnancy and breastfeeding on colostrum composition and morbidities' rate among both mother and offspring. In the second day postpartum, lactose and lysozyme components were higher and lactoferrin component was lower in breastfeeding group (BFG) compared to non-breastfeeding group (NBFG), respectively. One month postpartum, BFG showed a decreased IgA concentration as compared to NBFG. Moreover, infants of BFG were a five-time more susceptible to develop a cough, for at least 7 days, compared to NBFG (Supplementary Table S5).

Meta-analysis result of two studies showed significant higher prevalence of intrauterine growth restriction (IUGR) in women who got pregnant during lactation compared with those occurred after weaning [OR (95% CI) = 3.59 (1.91–6.71), $p = 0.000$] [32]. In another study, Ishii [34] reported one case of artificial induced preterm labor due to IUGR. On the other hand, a case–control study found no evidence of the association between breastfeeding during late pregnancy and elevated risk of SGA [12]. These studies identified IUGR or SGA using the

same criterion 'fetal birth weight less than 10th percentile after adjusting for gestational age'.

DISCUSSION

Breastfeeding is considered as the most effective intervention of ensuring child survival and health. Exclusive breastfeeding until 6 months and continuing up to 2 years are recommended by both WHO and UNICEF [3]. On the other hand, WHO endorses inter-birth interval minimum of 2 years to ensure a healthy outcomes for both mother the infant [5]. In different regions of the world, pregnant women breastfeeding their older children is a common phenomenon. However, the actual effect of a lactation-pregnancy overlap remains uncertain. Our current effort to conduct a comprehensive systematic literature searches failed to identify a desired number of related studies. There were a limited original studies evaluated maternal and infant outcomes when pregnancy occurs during lactation. In meta-analyses for specific outcomes, there were only from two to five studies with small sample sizes went to the final analysis. Moreover, the majority of included studies was conducted in developing countries where poor nutrition of pregnant and lactating women is not an uncommon problem. This significant challenge regarding insufficient available data makes it hard to have an unambiguous conclusions. Future researches should fill these gaps.

It has been reported that lactation overlapped with pregnancy in 50.2% of the pregnancies among rural women [37]. This concurrency may have an impact on maternal and fetal outcomes. Our meta-analysis aimed to explore all the evidence in the literature to find out whether there is an association between breastfeeding during pregnancy and possible undesired maternal and neonatal outcomes.

Meta-analysis for the abortion outcome has demonstrated no significant increase in overall rates of abortions in lactating women, which is similar to previous reports in the literature. Ishii, *et al.* [34] reported there is no significant difference regarding spontaneous abortion between breastfeeding (7.3%) and non-breastfeeding group (8.4%). In the same context, Lawrence, *et al.* [39] similarly concluded that breastfeeding does not cause abortions and it should be continued even if the mother is pregnant. In addition, a recommendation from the American Academy of Pediatrics mentioned that breastfeeding should continue for at least 12 months, and subsequently for as long as mutually desired [4]. Moreover, our analysis did not find any significant relationship between concurrent pregnancy in women and the risk of adverse maternal outcomes and delivery complications.

The result from Shaaban, *et al.*'s [32] study showed a significant increase in the rates of IUGR among babies of lactating women, the incidence of IUGR was as high as 16.7% in newborn of lactating women compared to 4.8% in the non-lactating women. This increased rate of IUGR and a possible SGA neonate may be explained by the depletion of maternal nutritional stores. In low-income countries, a chronic poor diet causes micronutrient deficiency in pregnant women [40]. Concurrent breastfeeding would constitute an additional burden on the mother's stores. These theories may explain the significant decrease in the mean hemoglobin levels in lactating women that we found in our meta-analysis (Supplementary Table S5). Pareja, *et al.* [12], like the current investigation, found no link between late-pregnancy nursing and the risk of a SGA baby. Also, data from nine studies showed no significant difference between birth weight and length between lactating and non-lactating group. The occurrence of a new pregnancy was associated with early cessation of breastfeeding was showed in the study of Bohler, *et al.* [41]. Another study measured the growth rate of 113 children during the first 3 years of life. Results showed that there was a significant reduction in growth rate during the last months before weaning breastfeeding between children from mothers' subsequent pregnancy and children from non-pregnant mothers ($p = 0.04$) [42]. Similarly, a systematic review found that an overlap of breastfeeding and pregnancy does not affect the pregnancy outcomes and birth weights [43].

Ismail, *et al.* [44] investigated the effect of pregnancy during breastfeeding on the chemical composition of mothers' milk. It reported a significant decrease in solids, fat and lactose and an increase in protein, non-protein nitrogen and sodium in lactating pregnant mother's milk compared to non-lactating ones. For the time of weaning in lactating

children, Moscone and Moore [45] found that the majority of weaning from breastfeeding initiated by the infant took place during the second trimester. The middle 3 months of pregnancy corresponds to a period of diminution in volume of breastmilk which reported by 70% of pregnant women. However, the infants born were healthy and appropriate for gestational age. Despite pregnancy during breastfeeding is common and often unintended. Another research was conducted by Shaaban and Glasier [6] found that 66.3% of lactating pregnant noticed a decrease in the amount or frequency of breastfeeding.

Merchant, *et al.* [37] reported that the overlap of breastfeeding and pregnancy caused increasing intake of supplements and reduced-fat stores in mother at first and second trimester, and the reduced-fat store disappeared at third trimester and postpartum. These findings are the evidences of overlapping of breastfeeding and pregnancy caused energetically stress, and maybe the increasing intake of supplements at two first trimester had closed the gap of energy deficit in mother.

In addition to the limitations mentioned earlier, the lack of analogous studied outcomes made it harder to prove a significant difference in some outcomes. We also could not acknowledge the trends of breastfeeding and possible outcomes through the years to prove if certain cultural and educational factors played a role. Methodological issues is another concern such as lacking of controlling for important confounders. Studies included in current systematic review were done at different places and time periods with large variation in age of participants and other special characteristics. Therefore, a sweeping conclusion, even though otherwise correct, may not entirely be attributable to the methodology employed. A much more in-depth analysis and rigor analysis may be needed.

CONCLUSION

The present studies showed that breastfeeding during pregnancy did not lead to the adverse outcomes in the mother and her fetus. For the benefices of both mother and her child, we suggest that the mother who had pregnancy during breastfeeding should keep feeding her child by breast milk if she wants and the adequate nutritional regime for these woman should be aware of.

SUPPLEMENTARY DATA

Supplementary data are available at *Journal of Tropical Pediatrics* online.

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AUTHORS' CONTRIBUTIONS

NTH was responsible for the idea and supervision. Screening and extraction were done by all authors under the supervision of NTH. Data analysis was done by HTNG, SG and GMT. LHNM, SG, GMT, HTNG, CS, NKQ, TNL and NTH contributed to the interpretation of the results. LHNM and HTNG took the lead in writing the manuscript. All authors contributed to the manuscript writing and gave approval of the final version.

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