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REVIEW

Overweight modifies the nutritional composition of human milk? A systematic review

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Abstract *This paper aims to identify the association between overweight and the nutritional composition of human milk. A systematic review was performed by searching on PubMed, Virtual Health Library (BVS), EMBASE, Web of Science, and SCOPUS databases, from May to June 2018, using keywords "Human Milk" AND "Overweight" OR "Obesity" OR "Body Mass Index". The bibliographic search returned 435 papers after the duplicates were removed. Of this total, 12 papers were selected for abstract reading, and nine works were incorporated into this systematic review. Eight papers showed that overweight increased the total concentration of lipids or glucose or macronutrient fractions, and only one study found no association between overweight and the nutritional composition of human milk. Most works selected evidenced that obesity changed the total concentration of lipids and their fractions. Thus, we recommend that women's weight and height be evaluated in the pregestational visit to identify and monitor nutritional deviations, contributing to weight adequacy before pregnancy and assisting in the production of milk with adequate nutritional composition.*

Key words *Overweight, Human milk, Nutritional Composition, Systematic Review*

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Introduction

Human milk is a complex biological fluid containing adequate amounts of essential components for children's health, growth, and development, such as nutrients[1], immunological and trophic factors[2,3], hormones[4,5], and essential bacteria for the modulation of the newborn's intestinal microbiota[6]. Breastfeeding provides economic and environmental advantages to the health of children, women, and society[7] in the short and long term.

Exclusive breastfeeding is recommended in the first six months of life as the only source of nutrients, followed by the introduction of food, however, still based on breastfeeding, which must be maintained for two years or more[8].

Several studies suggest that the nutritional composition of human milk can be modified by different factors such as maternal age[9], lifestyle, maternal food intake[10], lactation stage, type of delivery[11], and maternal disorders (arterial hypertension, and diabetes mellitus)[12,13].

Besides these factors, women's overweight has been considered a condition that can modify the nutritional composition of human milk[14]. However, there is still no consensus among the studies that aimed to evaluate this association[2,3].

Therefore, this systematic review aims to identify the association between overweight and the nutritional composition of human milk.

Methods

A systematic review of the literature was carried out, which consisted of searching for scientific papers that evaluated the association between overweight and the nutritional composition of human milk. The works were selected from PubMed, Virtual Health Library (BVS), EMBASE, Web of Science, and SCOPUS databases.

The search strategy employed descriptors "Human Milk" AND "Obesity" OR "Overweight" OR "Body Mass Index". The search for papers was carried out from May 18 to June 4, 2018, by two researchers independently. The reference lists of the selected papers were also examined to identify eligible publications.

All potentially eligible publications were selected for full-text reading. Data extraction and final classification for inclusion in the review were carried out independently, and results were compared. Any disagreement was resolved by consensus between the two reviewers.

The papers were considered on the following inclusion criteria: observational studies that assessed the association between overweight and the nutritional composition of human milk (carbohydrate or fat or protein or fractions of macronutrients or energy).

The publication period was not limited, and the language was not restricted. Studies with rats, different outcomes than those established for this review, which evaluated changes in the microbiota, hormonal composition, and papers with mothers of preterm babies or with any type of malformation were excluded.

The following was recorded in the data extraction table: year of publication, type of study, country of origin, sample size, losses, age of participants, ethnic groups, anthropometric assessment indicators, eligibility criteria, exclusion criteria, analyzed nutritional content, the method used to evaluate the nutritional composition of human milk, milk evaluation period, type of milk evaluated (colostrum, transitional, mature), confounding factors controlled in the analysis, and main results.

A checklist based on the Preferred Reporting Items for Systematic Reviews (PRISMA) guideline was used, which helps authors improve the reports of systematic reviews. The summary of the stages of the selection process of the papers in this systematic review is provided in the flowchart below (Figure 1).

Results

According to the established strategy, the bibliographic search returned 435 papers after excluding duplicates. Of this total, 12 works were selected for abstract reading. In the end, nine papers were selected for this systematic review. No works were added from the reference lists of the papers read.

Table 1 shows the main characteristics of the nine papers included in the ascending order of the study's publication period. While the publication period was not defined, the selected works were published from 2005 to 2017. Six studies were cross-sectional, and three were cohort. One was carried out in Asia, two in South America, four in Europe, and two in North America.

Regarding the anthropometric assessment of women, only one study measured weight and height to calculate body mass index (BMI), two studies used self-reported data, and six did not inform the method used to calculate BMI. Six

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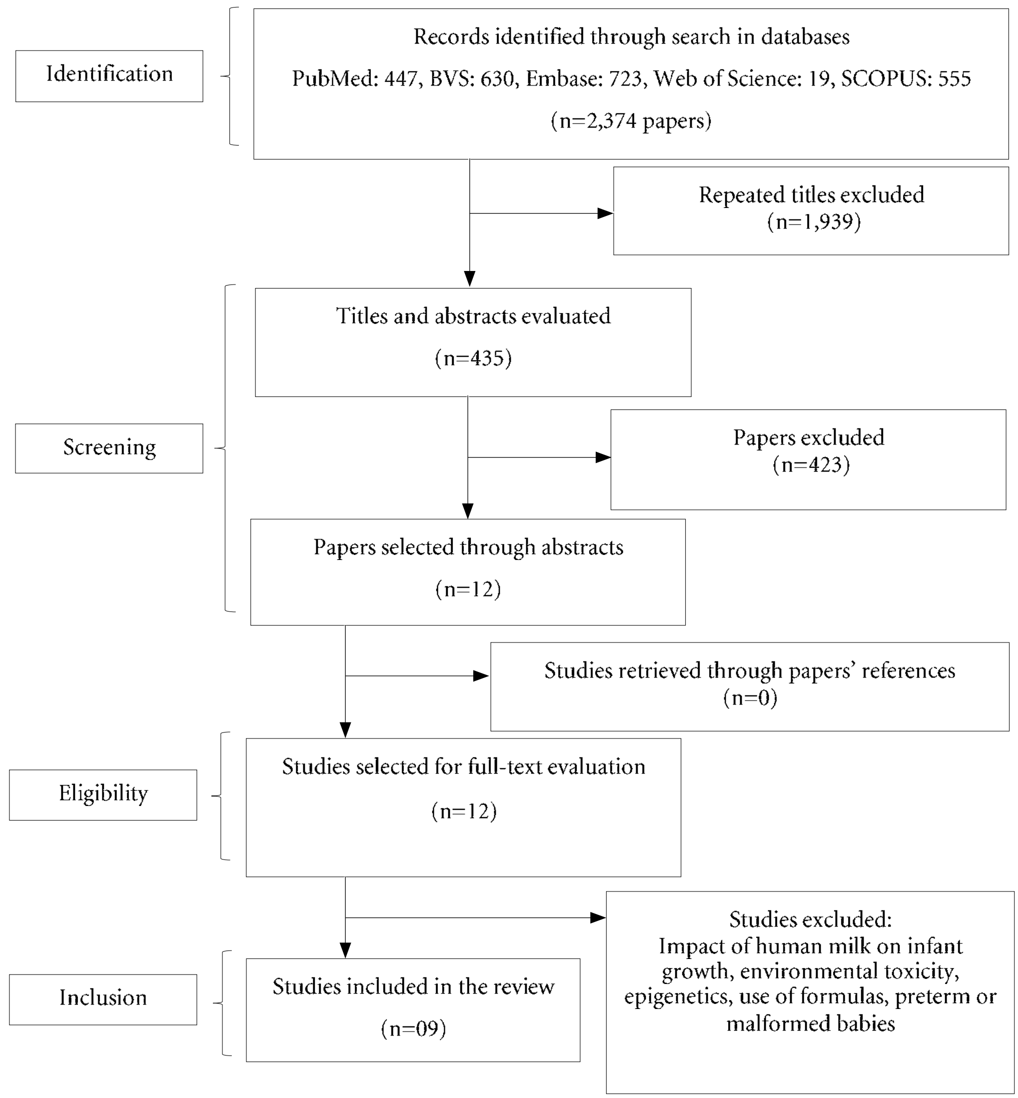

Figure 1. Flowchart of the selection process for studies included in the systematic review of overweight and changes in the nutritional composition of human milk.

studies assessed BMI in the pregestational period, and the others did not specify when the anthropometric assessment was performed.

Table 2 presents the main characteristics of milk, controlled confounding factors, and main results. As for the type of human milk analyzed (colostrum, mature, or transitional), one study looked only at colostrum, six analyzed only mature milk, and two evaluated different lactation stages. There was no standard method for evaluating the composition of macronutrients. A standard method was only used for analyzing fatty acids.

Regarding the confounding factors controlled in the analysis, three papers made adjustments to the analyses.

Concerning the association between overweight and the nutritional content of human milk, of the nine selected papers, five found that women's overweight altered the concentration of lipid fractions (reduced amount of omega 3[16-19], and increased amount of omega 6[15,16,19] and triglycerides[17]).

Table 1. Characteristics of selected studies on the impact of overweight on the nutritional composition of human milk, 2005-2017.

Author	Year	Type of study	Country	Sample n total and n by group	Follow-up losses	Age (years)	Ethnic groups	Anthropometric assessment indicators	Mean pregestational body mass index (Kg/m²)	Eligibility criteria	Exclusion criteria
Marín et al.[15]	2005	Cross-sectional	Argentina	46 21 eutrophic, 16 overweight, 9 obese	No losses	16-39	NI	Weight, height, BMI	NI	Women who gave birth to healthy full-term babies (38-42 weeks of gestational age)	NI
Storck Lindholm et al.[19]	2013	Cohort/ intervention	Sweden	82 41 eutrophic, 41 obese, of which 29 were part of the intervention group	No losses	Eutrophic: 32.07 ± 4.1[1] Obese without intervention: 30.5 ± 5.7[1] Obese with intervention: 32.17 ± 3.7[1]	NI	Pregestational and gestational BMI (32 and 36 weeks)	Eutrophic: 22 ± 1.8[1] Obese without intervention: 35 ± 3.8[1] Obese with intervention: 36 ± 5.0[1]	NI	Premature birth (<37 weeks), multiple pregnancies and/or babies with major malformations
Mäkelä et al.[16]	2013	Cross-sectional	Finland	163 49 eutrophic, 51 overweight	No losses	Eutrophic: 29.7 (3.6) [1] Overweight: 31.0 (5.0) [1]	NI	Pregestational BMI	Eutrophic: 20.9 (2.1) [1] Overweight: 29.7 (3.3) [1]	NI	NI
Linderborg et al.[17]	2014	Cross-sectional	Finland	40 Eutrophic with recommended food choices Eutrophic with non-recommended food choices Overweight with recommended food choices Overweight with non-recommended food choices	No losses	30.01 ± 3.96[1]	NI	Pregestational BMI	Eutrophic with adequate food choices: 20.81 ± 1.69[1] Eutrophic with inadequate food choices: 21.41 ± 2.31[1] Overweight with adequate food choices: 29.79 ± 2.85[1] Overweight with inadequate food choices: 31.22 ± 4.25[1]	NI	NI

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Author	Year	Type of study	Country	Sample n total and n by group	Follow-up losses	Age (years)	Ethnic groups	Anthropometric assessment indicators	Mean pregestational body mass index (Kg/m²)	Eligibility criteria	Exclusion criteria
Fujimori et al.[2]	2015	Cross-sectional	Brazil	68 25 eutrophic, 24 overweight, 19 obese	No losses	Eutrophic: 25.0 (18-37) [2] Overweight: 24.1 (18-37) [2] Obese: 26.8 (21-38)[2]	NI	Pregestational BMI	Eutrophic: 21.4 (18.4 – 24.4) [2] Overweight: 26.6 (25.2 – 28.6) [2] Obese: 34.7 (30.1 – 47.9) [2]	Women with breasts without fissures on nipples or mastitis; who were exclusively breastfeeding their babies	Multiple pregnancies, fetal malformation and births before the 37th gestational week
Panagos et al.[18]	2016	Cohort	USA	42 21 eutrophic, 21 obese	No losses to evaluate the nutritional composition of milk	Eutrophic: 31 ± 3.7[1] Obese: 30 ± 5.7[1]	Multiethnic (Hispanic, Caucasian, African American, and Asian)	Weight, height and pregestational BMI	Eutrophic: 22 (1.9) [1] Obese: 35 (4.0) [1]	Recruited at the Tufts Medical Center. Visits between 34 and 40 weeks of gestational age. Women who planned to offer breast milk as the main form of nutrition for their babies and were willing to provide a sample of human milk on a study visit between 4 and 10 weeks postpartum	Childbirth before 35 weeks of gestational age, multiple pregnancy, tobacco use, intrauterine growth restriction, fetal abnormalities, stillbirth.
De Luca et al.[4]	2016	Cross-sectional	France	100 50 eutrophic, 50 obese	No losses	Eutrophic 30.1 ± 4.2[1] Obese 30.2 ± 4.7[1]	NI	Weight, height and BMI	Eutrophic: 21.6 ± 1.4[1] Obese: 34.3 ± 3.9[1]	Continuous breastfeeding up to 1 month	Pre-existing chronic or gestational disease, smoking during pregnancy, twin pregnancy, prematurity, low birth weight or hospitalization in the neonatal period

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Author	Year	Type of study	Country	Sample n total and n by group	Follow-up losses	Age (years)	Ethnic groups	Anthropometric assessment indicators	Mean pregestational body mass index (Kg/m²)	Eligibility criteria	Exclusion criteria
Young et al.[3]	2017	Cohort	USA	48 26 eutrophic, 22 overweight	No losses	Eutrophic 30.8 ± 2.6[1] Obese 30.3 ± 3.9[1]	NI	Pregestational BMI	Eutrophic: 21.4 ± 2.0[1] Obese: 30.4 ± 4.2[1]	Maternal age 21 to 36 years, with pregestational BMI from 17.0 to 39.9 kg / m², single fetus, planning to breastfeed exclusively for at least four months, healthy, delivery at the study hospital	Women with chronic medical conditions requiring treatment, such as cardiopulmonary, rheumatological or kidney disease or pre-existing diabetes, gestational diabetes, pre-eclampsia or premature birth
Hahn et al.[20]	2017	Cross-sectional	South Korea	80 20 eutrophic among 20 years, 20 eutrophic among 30 years, 20 Overweight among 20 years and 20 Overweight among 30 years	NI	Eutrophic > 20 and < 30 Obese > 30	NI	BMI	NI	Mothers who exclusively breastfed, gave birth to a healthy baby, without any breast diseases including inflammatory diseases, started to breastfeed from the first day of delivery and children with normal weight at birth, head circumference and birth height	Mothers with a disease including gestational diabetes mellitus and hypertensive diseases

[1]Mean data; [2]Median data; NI = No information.

Table 2. Characteristics of the analyses, confounding factors, and main results found, 2005-2017.

Author	Nutritional content analyzed	Method used to assess the composition of human milk	Milk evaluation period	Moment of evaluation of human milk (colostrum, transitional, mature)	Confounding factors controlled in the analysis	Main results
Marín et al.[15]	Lipid (fatty acids) and protein	Total lipids: Folch Fatty acids: gas chromatography Protein: Lowry et al.	1 and 3 months	Mature[3]	NI	The human milk protein was not modified by the woman's nutritional status. There was a higher concentration of total lipids, linoleic acid, polyunsaturated fatty acids (omega 6) among obese puerperae.
Storck Lindholm et al.[19]	Lipid (fatty acids)	Fatty acids: gas and liquid chromatography	3 days, 10 days, 1 month and 2 months	Colostrum[1], Transitional[2] and Mature[3] (posterior)	NI	The concentrations of omega 6 in human milk were higher in eutrophic women on the third day after birth, and omega 3 was lower in obese women without intervention. The proportion of omega 6/omega 3 was higher in the milk of obese women without intervention compared to the other two groups. Obese mothers with dietary monitoring had concentrations of polyunsaturated fatty acids close to those of eutrophic ones.
Mäkelä et al.[16]	Lipid (fatty acids)	Fatty acids: gas chromatography	3 months	Mature[3]	Maternal diet	Overweight women had significantly more saturated fatty acids and lower omega 3 when compared to eutrophic mothers. Moreover, the proportion of unsaturated and saturated fatty acids was significantly lower, and the proportion of omega 6 to omega 3 was higher in overweight women.
Linderborg et al.[17]	Lipid (fatty acids and triglycerides)	Fatty acids: gas chromatography	3 months	Mature[3]	NI	Eutrophic puerperae with recommended dietary choices had more linoleic acid and less diacylglycerol fragments in milk compared to eutrophic puerperae with non-recommended food choices.
Fujimori et al.[2]	Lipid (cholesterol, triglycerides), glucose and protein	Total lipids: Enzymatic colorimetric method Glucose: Enzymatic system Protein: Biuret colorimetric method	48-72 hours postpartum	Colostrum[1]	Maternal age, gestational age at delivery, smoking, high blood pressure, pre-gestational body mass index, pre-gestational diabetes and gestational diabetes	Increased calories, fat, and glucose were found in the colostrum of obese women. Protein concentration was similar between groups.

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Table 2. Characteristics of the analyses, confounding factors, and main results found, 2005-2017.

Author	Nutritional content analyzed	Method used to assess the composition of human milk	Milk evaluation period	Moment of evaluation of human milk (colostrum, transitional, mature)	Confounding factors controlled in the analysis	Main results
Panagos et al.[18]	Lipids, lactose, protein	Total lipids, lactose and protein: Julie Z7 Automatic MilkoScope equipment by ultrasound technique Fatty acids: modified Folch method, followed by saponification and methylation	2 months	Mature[3]	NI	The mature milk of obese mothers had a lower amount of omega 3. However, there was no association between pre-gestational BMI, caloric density and macronutrients in human milk.
De Luca et al.[4]	Protein (amino acids)	Free amino acids: ultra-performance liquid chromatography and tandem mass spectrometry	1 month	Mature[3]	NI	The amount of branched-chain amino acids was 20% higher in the mature milk of obese puerperae and 30% concerning tyrosine.
Young et al.[3]	Lipids, lactose, protein, calorie	Lipid: creamatocrit; Lactose: enzymatic digestion Protein: modified version of the Bradford method	2 weeks, 1,2,3,4 months	Transição[2] e Maduro[3] (Anterior e posterior)	NI	There was no association between pregestational BMI and the concentration of lipids, lactose, and protein.
Hahn et al.[20]	Lipids, protein, lactose, calorie	MIRIS	4 weeks	Mature[3]	Maternal age	The interaction between maternal age and BMI modified milk macronutrients in different ways, according to the different subgroups.

[1]Colostrum: Up to 5 days after delivery; 2Transitional: 6 to 15 days after delivery;3Mature: > 15 days after delivery. NI = Not Informed.

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Besides the alteration caused by overweight in the lipid fractions, an increase in total fat content was observed in three studies[2,15,20]. As for the protein fraction, only one study found an increase of around 20% in the concentration of branched-chain amino acids in the milk of obese women[21]. Regarding the carbohydrate content, one study observed 2.5 times higher concentration of glucose in the colostrum of obese women compared to eutrophic women[2]. Only one study showed no significant association between human milk macronutrients and women's body composition[3].

Discussion

Overweight is a global problem in both developed and developing countries. This issue must be addressed at all stages of life, particularly in women in the reproductive[22] and gestational[23] periods due to the several negative consequences of this condition to the mother-child dyad[23].

Some studies have evaluated the possible impact of overweight on the nutritional composition of human milk[2,20]. However, their results diverge mainly regarding the nutritional content evaluated, the methods to assess the nutritional composition of milk, the type of milk analyzed (colostrum, transitional, and mature), and the control of confounding factors in the analysis.

Regarding lipids, similar results were observed regarding the association between the women's overweight and fatty acids based on gas chromatography in the studies conducted by Marin et al.[15], Mäkelä et al.[16], Linderborg et al.[17], and Storck Lindholm et al.[19]. These studies observed an increased proportion of omega 6 compared to omega 3 and reduced omega 3 in overweight women's human milk. Panagos et al.[18] carried out a cohort study to assess newborns' body composition and a cross-sectional analysis to obtain the nutritional composition of human milk of 42 women at two months of the child's life. The authors did not identify any difference in the amount of saturated, monounsaturated, and polyunsaturated fatty acids of the omega 6 type in the mature milk of obese women using the modified Folch method. However, this paper's result was similar to the others cited concerning the lower content of omega 3 in the mature milk of these women. These findings corroborate several studies that have already demonstrated that being overweight generates an inflammatory state marked by an increased amount of omega 6 and a reduced amount of omega 3[16,17,19].

Unlike the studies mentioned above, the studies conducted by Fujimori et al.[2] and Young et al.[3] did not observe statistically significant differences in the concentration of lipids in the milk of overweight women compared to eutrophic women. The study by Fujimori et al.[2] differed from the others concerning the type of lipids evaluated (triglycerides), the method used to evaluate the composition of human milk (enzymatic colorimetric), and the type of milk (colostrum). On the other hand, the cohort conducted by Young et al.[3] analyzed the concentration of fat in the transitional and mature milk using the creamatocrit. However, there was no complete milk extraction during the collection, which consequently may have interfered with the fat concentration, as there is a difference in the number of lipids in anterior and posterior milk[24].

In a cross-sectional study with 80 puerperae, Hahn et al.[20] analyzed the concentration of lipids in mature milk using Miris, a piece of equipment already validated for the analysis of human milk[25]. The authors observed that maternal age and nutritional status changed the composition of lipids in human milk. The authors affirm that overweight women aged 30 years had a higher lipid concentration than eutrophic women of the same age, but did not explain their findings. Argov-Argaman et al.[26] aimed to assess whether maternal age was associated with changes in fatty acid concentrations in human milk. The authors observed that the lipid content was higher among women over 37 years of age. Lubetzky et al.[27] observed that the lipid concentration in transitional milk is higher in women over 35 years of age. However, both highlighted that the mechanism and biological plausibility for such findings are unknown.

Lactose was the most discussed disaccharide among studies, possibly because it is the most significant glycosidic fraction in human milk[3,20]. However, Fujimori et al.[2] was the only study that assessed the concentration of glucose in colostrum. The authors observed that the amount of this monosaccharide was higher among obese puerperae. However, the authors did not elucidate the findings. The other studies did not observe differences in the number of carbohydrates in the human milk of overweight women[3,18,20].

Regarding human milk protein, it was observed that women's overweight did not change the amount of this macronutrient[3,18,20]. However, results are different when amino acids are evaluated. De Luca et al.[21] observed that the mature milk of obese women contained 20% more branched-chain amino acids and 30% more tyrosine than eutrophic human milk. Noteworthy is that the increased amount of branched-chain amino acids can modify insulin secretion and sensitivity, resulting in adverse outcomes for women and babies[28].

Concerning the anthropometric assessment of women to perform the nutritional diagnosis, most of the selected papers used pregestational weight and height to calculate BMI. While this measure is used to carry out the nutritional diagnosis in all life stages[29], this index is knowingly not suitable for quantifying body fat[5]. Thus, it is vital to assess body composition[30] and calculate BMI to diagnose the nutritional status.

Regarding the control of potential confounding variables, except for the study conducted by Fujimori et al.[2], Mäkelä et al.[16], and Hahn et al.[20], the other selected studies did not focus on the control of potential factors associated with the nutritional composition of human milk. This data must be taken into account since this outcome can be modified by other factors besides women's nutritional status[12,13]. Exemplifying the effect of tobacco use and food consumption on the nutritional profile of human milk, Mäkelä et al.[16] observed that smoking decreased omega 3 and increased omega 6 in human milk. Concerning food consumption, only two evaluated the influence of this variable on the lipid quantity in human milk. Noteworthy is that the puerperal diet is pointed out by several studies as a factor associated with changes in lipid concentrations and the profile of long-chain polyunsaturated fatty acids in human milk[31,32], confirming the need to adjust these and other essential variables in the analyses.

Regarding follow-up losses, only two papers selected for this systematic review reported sample losses[16,21], and the cohort conducted by Marin et al.[15] did not inform the number of losses. Thus, the association estimates may be compromised by follow-up losses or by not having controlled critical confounding factors.

Even if estimates of the selected studies are compromised, pregestational nutritional surveillance is still paramount, preferably in the preconception visit, so that women start the pregnancy with adequate weight, favoring, among other several aspects, the production of milk with an adequate nutritional profile.

Collaborations

All authors made substantial contributions to the study's conception and design, obtaining, analyzing, and interpreting the data, elaborating the paper, and approved the final version of the manuscript.

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