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.

Keywords  Overweight, Human milk, Nutritional Composition, Systematic Review
Introduction

Human milk is a complex biological fluid containing adequate amounts of essential components for children’s health, growth, and development, such as nutrients, immunological and trophic factors, hormones, and essential bacteria for the modulation of the newborn’s intestinal microbiota. Breastfeeding provides economic and environmental advantages to the health of children, women, and society 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.

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

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

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.

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
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 615,16,19 and triglycerides17).

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.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type of study</th>
<th>Country</th>
<th>Sample n total and n by group</th>
<th>Follow-up losses</th>
<th>Age (years)</th>
<th>Ethnic groups</th>
<th>Anthropometric assessment indicators</th>
<th>Mean pregestational body mass index (Kg/m²)</th>
<th>Eligibility criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marín et al.15</td>
<td>2005</td>
<td>Cross-sectional</td>
<td>Argentina</td>
<td>46 21 eutrophic, 16 overweight, 9 obese</td>
<td>No losses</td>
<td>16-39</td>
<td>NI</td>
<td>Weight, height, BMI</td>
<td>NI</td>
<td>Women who gave birth to healthy full-term babies (38-42 weeks of gestational age)</td>
<td>NI</td>
</tr>
<tr>
<td>Storck Lindholm et al.19</td>
<td>2013</td>
<td>Cohort/ intervention</td>
<td>Sweden</td>
<td>82 41 eutrophic, 41 obese, of which 29 were part of the intervention group</td>
<td>No losses</td>
<td>Eutrophic: 32.07 ± 4.1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Obese without intervention: 30.5 ± 5.7&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Pregestational and gestational BMI (32 and 36 weeks)</td>
<td>Eutrophic: 22 ± 1.8&lt;sup&gt;1&lt;/sup&gt; Obese without intervention: 35 ± 3.8&lt;sup&gt;1&lt;/sup&gt; Obese with intervention: 36 ± 5.0&lt;sup&gt;1&lt;/sup&gt;</td>
<td>NI</td>
<td>Premature birth (&lt;37 weeks), multiple pregnancies and/or babies with major malformations</td>
</tr>
<tr>
<td>Mäkelä et al.16</td>
<td>2013</td>
<td>Cross-sectional</td>
<td>Finland</td>
<td>163 49 eutrophic, 51 overweight</td>
<td>No losses</td>
<td>Eutrophic: 29.7 (3.6)</td>
<td>Overweight: 31.0 (5.0)</td>
<td>Pregestational BMI</td>
<td>Eutrophic: 20.9 (2.1) Obese without intervention: 35 ± 3.8&lt;sup&gt;1&lt;/sup&gt; Obese with intervention: 36 ± 5.0&lt;sup&gt;1&lt;/sup&gt;</td>
<td>NI</td>
<td>NI</td>
</tr>
<tr>
<td>Linderborg et al.17</td>
<td>2014</td>
<td>Cross-sectional</td>
<td>Finland</td>
<td>40 Eutrophic with recommended food choices Eutrophic with non-recommended food choices Overweight with recommended food choices Overweight with non-recommended food choices</td>
<td>No losses</td>
<td>30.01 ± 3.96</td>
<td>NI</td>
<td>Pregestational BMI</td>
<td>Eutrophic with adequate food choices: 20.81 ± 1.69&lt;sup&gt;1&lt;/sup&gt; Eutrophic with inadequate food choices: 21.41 ± 2.31&lt;sup&gt;1&lt;/sup&gt; Overweight with adequate food choices: 29.79 ± 2.85&lt;sup&gt;1&lt;/sup&gt; Overweight with inadequate food choices: 31.22 ± 4.25&lt;sup&gt;1&lt;/sup&gt;</td>
<td>NI</td>
<td>NI</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
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<td>Country</td>
<td>Sample n total and n by group</td>
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</tbody>
</table>
| Fujimori et al.                | 2015 | Cross-sectional | Brazil  | 68 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.                 | 2016 | Cohort        | USA     | 42 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.                 | 2016 | Cross-sectional | France  | 100 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 |

*Table 1. Characteristics of selected studies on the impact of overweight on the nutritional composition of human milk, 2005-2017.*
### 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 |
|-----------------|-------------------|---------|-------------------------------|------------------|-------------|---------------|----------------|-------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Young et al.⁹   | 2017 Cohort       | USA     | 48 26 eutrophic, 22 overweight | No losses        | Eutrophic 30.8 ± 2.6¹ 30.3 ± 3.9¹ | NI            | Pregestational BMI                  | Eutrophic: 21.4 ± 2.0²  Obese: 30.4 ± 4.2¹ | 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 |

¹Mean data; ²Median data; NI = No information.
Table 2. Characteristics of the analyses, confounding factors, and main results found, 2005-2017.

<table>
<thead>
<tr>
<th>Author</th>
<th>Nutritional content analyzed</th>
<th>Method used to assess the composition of human milk</th>
<th>Milk evaluation period</th>
<th>Moment of evaluation of human milk (colostrum, transitional, mature)</th>
<th>Confounding factors controlled in the analysis</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marín et al.15</td>
<td>Lipid (fatty acids) and protein</td>
<td>Total lipids: Folch Fatty acids: gas chromatography Protein: Lowry et al.</td>
<td>1 and 3 months</td>
<td>Mature¹</td>
<td>NI</td>
<td>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.</td>
</tr>
<tr>
<td>Storck Lindholm et al.¹⁹</td>
<td>Lipid (fatty acids)</td>
<td>Fatty acids: gas and liquid chromatography</td>
<td>3 days, 10 days, 1 month and 2 months</td>
<td>Colostrum¹, Transitional² and Mature³ (posterior)</td>
<td>NI</td>
<td>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. 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.</td>
</tr>
<tr>
<td>Mäkelä et al.¹⁶</td>
<td>Lipid (fatty acids)</td>
<td>Fatty acids: gas chromatography</td>
<td>3 months</td>
<td>Mature³</td>
<td>Maternal diet</td>
<td>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.</td>
</tr>
<tr>
<td>Linderborg et al.¹⁷</td>
<td>Lipid (fatty acids and triglycerides)</td>
<td>Fatty acids: gas chromatography</td>
<td>3 months</td>
<td>Mature³</td>
<td>NI</td>
<td>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.</td>
</tr>
<tr>
<td>Fujimori et al.²</td>
<td>Lipid (cholesterol, triglycerides), glucose and protein</td>
<td>Total lipids: Enzymatic colorimetric method Glucose: Enzymatic system Protein: Biuret colorimetric method</td>
<td>48-72 hours postpartum</td>
<td>Colostrum¹</td>
<td>Maternal age, gestational age at delivery, smoking, high blood pressure, pre-gestational body mass index, pre-gestational diabetes and gestational diabetes</td>
<td>Increased calories, fat, and glucose were found in the colostrum of obese women. Protein concentration was similar between groups.</td>
</tr>
</tbody>
</table>

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

<table>
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<tr>
<th>Author</th>
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<th>Confounding factors controlled in the analysis</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panagos et al.</td>
<td>Lipids, lactose, protein</td>
<td>Total lipids, lactose and protein: Julie Z7 Automatic MilkoScope equipment by ultrasound technique Fatty acids: modified Folch method, followed by saponification and methylation</td>
<td>2 months</td>
<td>Mature&lt;sup&gt;3&lt;/sup&gt;</td>
<td>NI</td>
<td>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.</td>
</tr>
<tr>
<td>De Luca et al.</td>
<td>Protein (amino acids)</td>
<td>Free amino acids: ultra-performance liquid chromatography and tandem mass spectrometry</td>
<td>1 month</td>
<td>Mature&lt;sup&gt;3&lt;/sup&gt;</td>
<td>NI</td>
<td>The amount of branched-chain amino acids was 20% higher in the mature milk of obese puerperae and 30% concerning tyrosine.</td>
</tr>
<tr>
<td>Young et al.</td>
<td>Lipids, lactose, protein, calorie</td>
<td>Lipid: creatamoticrit; Lactose: enzymatic digestion Protein: modified version of the Bradford method</td>
<td>2 weeks, 1,2,3,4 months</td>
<td>Transição&lt;sup&gt;2&lt;/sup&gt; e Maduro&lt;sup&gt;2&lt;/sup&gt; (Anterior e posterior)</td>
<td>NI</td>
<td>There was no association between pregestational BMI and the concentration of lipids, lactose, and protein.</td>
</tr>
<tr>
<td>Hahn et al.</td>
<td>Lipids, protein, lactose, calorie</td>
<td>MIRIS</td>
<td>4 weeks</td>
<td>Mature&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Maternal age</td>
<td>The interaction between maternal age and BMI modified milk macronutrients in different ways, according to the different subgroups.</td>
</tr>
</tbody>
</table>

*Colostrum: Up to 5 days after delivery; 2Transitional: 6 to 15 days after delivery; 3Mature: > 15 days after delivery. NI = Not Informed.*
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\textsuperscript{22} and gestational\textsuperscript{23} periods due to the several negative consequences of this condition to the mother-child dyad\textsuperscript{23}.

Some studies have evaluated the possible impact of overweight on the nutritional composition of human milk\textsuperscript{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.\textsuperscript{15}, Mäkelä et al.\textsuperscript{16}, Linderborg et al.\textsuperscript{17}, and Storck Lindholm et al.\textsuperscript{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.\textsuperscript{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\textsuperscript{16,17,19}.

Unlike the studies mentioned above, the studies conducted by Fujimori et al.\textsuperscript{2} and Young et al.\textsuperscript{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.\textsuperscript{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.\textsuperscript{1} 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\textsuperscript{24}.

In a cross-sectional study with 80 puerperae, Hahn et al.\textsuperscript{20} analyzed the concentration of lipids in mature milk using Miris, a piece of equipment already validated for the analysis of human milk\textsuperscript{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.\textsuperscript{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.\textsuperscript{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\textsuperscript{2,20}. However, Fujimori et al.\textsuperscript{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\textsuperscript{3,18,20}.

Regarding human milk protein, it was observed that women’s overweight did not change the amount of this macronutrient\textsuperscript{3,18,20}. However, results are different when amino acids are evaluated. De Luca et al.\textsuperscript{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 babies28.

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 stages29, this index is knowingly not suitable for quantifying body fat1. Thus, it is vital to assess body composition30 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 status12,13. 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 milk31,32, 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 losses46,21, 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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