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FEATURES OF THE COMPONENT COMPOSITION AND CALORIE CONTENT OF BREAST MILK IN OBESE MOTHERS

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Abstract. The article reviews the literature from 2013 to 2023, confirming changes in the composition of breast milk in obese women. It has been proven that in the breast milk of obese women, the content of lipids and the ratio of their fractions are changed, there are features in the composition of carbohydrate components (lactose and oligosaccharides of breast milk) in comparison with the breast milk of women with normal weight. There is also evidence of altered profiles of the hormones insulin, ghrelin, leptin and adiponectin, as well as microRNAs and immunological factors in the milk of obese mothers.

Key words: breast milk; obesity; BMI; composition of breast milk; breastfeeding; epigenetics; calorie content of breast milk; overweight; components of breast milk.

ОСОБЕННОСТИ КОМПОНЕНТНОГО СОСТАВА И КАЛОРИЙНОСТИ ГРУДНОГО МОЛОКА У МАТЕРЕЙ, СТРАДАЮЩИХ ОЖИРЕНИЕМ

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Резюме. В статье приведен обзор научных источников за период с 2013 по 2023 год, подтверждающий изменения состава грудного молока у женщин, страдающих ожирением. Доказано, что в грудном молоке женщин, страдающих ожирением, изменено содержание липидов и соотношение их фракций, имеются особенности состава углеводных компонентов (лактозы и олигосахаридов грудного молока) в сравнении с грудным молоком женщин, с нормальным весом. Имеются также данные об измененном профиле гормонов инсулина, грелина, лептина и адипонектина, а также микроРНК и иммунологических факторов в молоке матерей, страдающих ожирением.

Ключевые слова: грудное молоко; ожирение; ИМТ; состав грудного молока; грудное вскармливание; эпигенетика; калорийность грудного молока; избыточный вес; компоненты грудного молока.

INTRODUCTION

Breast milk (BM) is a physiological source of nutrients for a child in the first year of life. The composition of the BM is unique and optimally adapted to meet almost all the needs of an actively growing organism up to 6 months. Breastfeeding (BF) is associated with lower mortality in infants than formula feeding. The UN and UNICEF argue that up to 10 million under-five deaths worldwide can be prevented every year by exclusive breastfeeding during the first six months of life [1]. The BM is a source of commensal bacteria that prevent the addition of pathogenic flora and contribute to the colonization of the intestine by useful microorganisms. The World Health Organization (WHO) recommends only BF for the first six months and as supplementary feeding until age 2.

The function of the BM is not limited to energy, and there is evidence of its immune, protective, epigenetic, and metabolic regulatory actions. The scientific evidence shows that the BM is an evolutionary factor for the optimal development of not only a healthy but also a sick child because the composition of the BM is capable of dynamic change, adapting to the needs of the child in a given situation.

The epigenetic effects of the BM are now highly relevant for study. It is becoming apparent that maternal nutrition and lifestyles can have a direct life-long impact on the child; it's called health programming. It is known that the BF is known to reduce the risk of many non-communicable pathologies, including obesity [2]. This is very important given the adverse epidemiological situation of the disease.

The global prevalence of obesity nearly tripled between 1975 and 2016. In 2014, the number of overweight and obese pregnant women was 38.9 million and 14.6 million, respectively, worldwide [3]. The prevalence of overweight and obesity among children and adolescents increased from 4% in 1975 to 18% in 2016 [4]. WHO estimates that more than 1.9 billion adults aged 18 years and over are overweight, of whom more than 650 million are obese. If current trends continue, the majority of the adult global population will be overweight or obese by 2030 [5]. It has been proven that BF prevents rapid weight gain in the neonatal period and reduces the propensity to develop obesity in adults, as opposed to formula feeding [6]. The usefulness of the BM may vary depending on its composition [7, 8]. The pathological conditions in the mother may influ-

ence the composition of the BM, but not much research has been published on this topic. There is proof that a mother's obesity prior to becoming pregnant increases the child's chance of obesity by three times [9]. Studies on animals have shown that ingesting a lot of fat during breastfeeding has an impact on the offspring's long-term obesity [10, 11]. An interesting question is the impact of maternal obesity on the calorie content and composition of the BM. The objective of this work is to review the current literature on the subject.

GENERAL INFORMATION ON THE COMPOSITION OF BREAST MILK

The human BM is a complex biological fluid containing a large number of components: macronutrients, hormones, biologically active molecules, stem cells, and microbial communities. Each of them is potentially responsible for a specific and synergistic impact on child health and the growth and development of organs and systems [12]. Lactose is the main carbohydrate in the human BM. Also, BM oligosaccharides (BMO) are important components of the BM. There are three main categories of BMOs: fucosylated neutral BMOs (35–50%), unfucosylated neutral BMOs (42–55%), and sialylated acidic BMOs (12–14%). The primary source of energy is lipids, which are found in milk as an emulsion.

Triacylglycerides make up approximately 98% of the lipid fraction; 2% are phospholipids, monoacylglycerides, diacylglycerides, and free fatty acids. The human BM contains more than 400 different proteins, which can be divided into three main groups: casein, whey, and mucin proteins. The age of the child has a gradual effect on the protein ratio, which varies. Breast milk also contains non-protein nitrogen, which is up to 25% of the total nitrogen present in milk. In addition, the human BM contains the trace elements that the infant needs, except for vitamins K and D [13].

IMPACT OF MATHER'S OBESITY ON THE COMPONENTS OF MUTHER'S MILK

Summarizes the literature on the qualities of the component composition and calorie content of breast milk produced by obese moms in table 1.

Features of macronutrient content. The relationship between female obesity and changes in the composition and calorie content of the BM has been studied by many researchers. G.E. Leghi et al. did a large meta-analysis of the macronu-

trients found in the BM of normal-weight (NW) and overweight or obese women (OV/OW). They looked at colostrum, transitional milk, and mature milk. There was no difference in the concentration of fat in colostrum between OV/OW and NW. Also, in transient milk, the fat concentration was lower in OV/OW compared to NW. In mature milk, the fat concentration was higher in OV/OW than in NW. There was no discernible change in the protein concentration of the colostrum, transition, or mature BM between OV/OW and NW. The lactose concentration in colostrum was higher in OV/OW and NW. Nonetheless, there was no discernible variation in the lactose concentration between the transitional and mature BM samples [14]. The meta-analysis by A.I. Daniel et al. showed a positive relationship between the maternal body mass index (BMI) and the fat content of the BM. There is no discernible correlation between the mother's BMI and the amount of protein, lactose, or energy in milk [15]. Research findings about the lipid profile of the BM show that the milk of obese mothers has a higher ratio of ω -6 fatty acids (ω -6/ ω -3 PUFA), a decrease in monounsaturated fatty acids (MUFA) and ω -3 in polyunsaturated fatty acids (PUFA), and an increase in saturated fatty acids (SFA) [16]. Based on a systematic review of most studies, it was found that moms who were overweight had higher levels of ω -6 PUFA and lower levels of ω -3 PUFA in their breast milk than eutrophic women [17, 18]. In the study by L. Ellsworth and others, there was no significant relationship between the ratio of ω -3 and ω -6 long-chain polyunsaturated fatty acids (LC-PUFA) in milk and the weight of the mother. But the content of palmitic, digomo-gamma-linolenic, and adrenal acids in milk was statistically significantly higher. The content of oleic and conjugated linoleic acids is lower in the OV/OW group. The same study did not reveal a significant difference in macronutrient content between groups of mothers [19]. PGE2 and LTE4 levels are not significantly different in groups NW and OV/OW [20]. Compared to women with NW, colostrum with OV/OW had higher levels of fat, glucose, and sIgA content, as well as more calories. There was no difference in the amounts of complement components C3 and C4, IgG, and IgM. [21]. The study by J.L. Saben et al. found that the BMI of nursing mothers was negatively correlated with the concentration of N-Neoserum radioactivity, disialyllacto-N-hexaose, fucosyllacto-N-hexaose, and total acid BMOs and positively correlated with the lacto-N-Neo-

tetrazoma, 3-fucosyllactose, 3-Sialillactose, and 6-Sialillactose concentrations [22].

Features of the content of biologically active compounds. Information on the hormone concentration in the body's BM, OV/OW, and NW varies. T.T. Guler and colleagues claim. In the BM group OV/OW, the grelin level before feeding was significantly higher than that of NW. In the BM group NW, after feeding, adiponectin levels were higher than those of OV/OW. There was no significant difference between the leptin and IGF-1 levels between the two groups [23].

In another study, the concentration of leptine in foremilk was correlated with the mother's BMI at 7 days and 3 months after delivery. Within three months of birth, there was a positive correlation between the mother's BMI and the BM's insulin. Grelin and BM resistine were not correlated with the mother's BMI [24]. According to the A. de Luca study, leptine content in OV/OW milk was higher than in NW milk, but macronutrient concentrations were the same [25]. There was no association found between BMI and adiponectin in the study by D. Chan et al., although there was a positive correlation between the mother's BMI and insulin and leptin [26]. Bioactive substances make up the BM, stem cells, and antibodies — particularly secretory immunoglobulins (sIgA and sIgG), including microRNAs — have drawn increasing attention in recent years. MicroRNA is a small, non-coding RNA molecule with a length of 18–25 nucleotides involved in transcription and posttranscriptional regulation of gene expression via RNA interference. The BM is one of the most miRNA-rich biological fluids, identifying about 1,400 species of miRNA. The study by K.B. Shah et al. found that the amount of miR-148a and miR-30b in the BM of women with OV/OW was 30% and 42% less than that of the NW group, respectively [27]. The following data on variations in leukocyte subsets in colostrum are intriguing for further research: In comparison to the control group, OV/OW has dramatically decreased the B-lymphocyte proportion in colostrum, and CD16+ blood monocytes have enhanced CD16 expression [28]. The concentration of lactoferrin in colostrum mothers with BMIs >30 kg/m² is noticeably higher than in mothers with normal BMIs [29]. There is proof that other non-specific protective variables have changed. It is known that a baby who is exclusively breastfed for the first year of their life may obtain up to 20% of the required daily allowance of vitamin D from the BM [30]. The way that the

Table 1. Features of the component composition and calorie content of breast milk in obese mothers (summary data)

Таблица 1. Особенности компонентного состава и калорийности грудного молока у матерей, страдающих ожирением (сводные данные)

Автор, год / Author, year	Тип исследования / Type of study	Популяция / Sample characteristic	Исследуемые показатели / Nutritional content analyzed	Результаты / Results
Mäkelä et al., 2013 [34]	Кросс-секционное / Cross-sectional	100 женщин, 49 НВ, 51 ОЖ / 100 women 49 NW, 51 OB	Уровень и состав жирных кислот / Fatty acid levels and composition	В молоке женщин с ИВ/ОЖ содержалось значительно больше НЖК и меньше ω -3 ПНЖК по сравнению с молоком женщин с нормальной массой тела. Соотношение ПНЖК и НЖК было ниже, а соотношение ω -6/ ω -3 выше у ИВ/ОЖ / Overweight women had significantly more saturated fatty acids and lower omega 3 when compared to normal weight mothers. 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
Fujimori et al., 2015 [21]	Когортное / A cohort study	68 женщин, 25 НВ, 24 ИВ, 19 ОЖ / 68 women 25 NW, 24 OW, 19 OB	Общий уровень липидов, глюкоза, белок / Total lipid levels, glucose levels, protein levels	В молозиве женщин с ИВ/ОЖ была повышена калорийность, содержание жиров и глюкозы. Содержание белков не отличалось / Calories, fat and glucose content were increased in the colostrum of overweight and obese women. Protein concentration was similar between groups
Daniel et al., 2021 [15]	Метаанализ / Meta-analysis	66 исследований, 4764 женщины / 66 studies 4764 women	Калорийность, содержание липидов, белков / Calories, lipid content, protein content	Имелась устойчивая положительная связь между ИМТ матери и содержанием жира в грудном молоке. Не было обнаружено ассоциаций между ИМТ матери и общим содержанием белка или энергии в грудном молоке / There was a consistent positive association between maternal BMI and breast milk fat content: No associations were found between maternal BMI and total protein or energy content of breast milk
Saben et al., 2020 [39]	Когортное / A cohort study	172 женщины / 172 women	Концентрация 115 известных и 240 ранее неизвестных метаболитов ГМ / Concentrations of 115 known and 240 previously unknown BM metabolites	Содержание 111 метаболитов было связано с ИМТ матери. Молоко матерей, страдающих ожирением, было обогащено моносахаридами и сахарными спиртами. Часть метаболитов, различающихся в зависимости от массы тела матери, были предикторами более высокой степени накопления жировой ткани у младенцев в течение первых шести месяцев жизни / The content of 111 metabolites was related to maternal BMI. The milk of obese mothers was enriched in monosaccharides and sugar alcohols. Some of the metabolites differing according to maternal weight were predictors of a higher degree of adipose tissue accumulation in infants during the first 6 months of life

Ending of the table 1 / Окончание табл. 1

Автор, год / Author, year	Тип исследо- вания / Type of study	Популяция / Sample characteristic	Исследуемые показатели / Nu- tritional content analyzed	Результаты / Results
Leghi G. E. et al., 2020 [14]	Метаанализ / Meta-analysis	9 исследований, 872 женщины / 9 studies 872 women	Концентрация липидов, белков, лактозы в молозиве, переходном и зрелом ГМ / Con- centration of lipids, proteins, and lactose in colostrum, transi- tional and mature BM	Не было выявлено различий в концентрации жиров в молозиве между ИВ/ОЖ и НВ. В переходном молоке концентрация жира была ниже у ИВ/ОЖ по сравнению с НВ. В зрелом молоке концентрация жира была выше у ИВ/ОЖ по сравнению с НВ. Различий в концентрации белка в ГМ между ИВ/ОЖ и НВ не было обнаружено в молозиве, переходном и зрелом ГМ. Концентрация лактозы в молозиве была выше у ИВ/ОЖ по сравнению с НВ. Не было обнаружено различий в концентрации лактозы в переходном и зрелом молоке / There were no differences in fat concentration in the colostrum between overweight/obese (OW/OB) and normal weight (NW) women. In transitional milk, fat concentration was lower in OW/OB compared to NW. In mature milk, the fat concentration was higher in OW/OB compared to NW. No differences in protein concentration in breast milk (BM) between OW/OB and NW were found in colostrum, transitional and mature BM. The concentration of lactose in the colostrum was higher in the OW/OB compared to the NW. No differences were found in lactose concentration in transitional and mature milk
Bardanzellu F. et al., 2021 [33]	Метаанализ / Meta-analysis	15 исследо- ваний / 15 studies	Производные нуклеотидов, 5-метилтио- аденозин, сахарные спирты, ацилкарнитин и аминокислоты, полиамины, моно- и олигосахариды, липиды / Nucleo- tide derivatives, 5- methylthio- adenosine, sugar alcohols, acylcar- nitine and amino acids, polyamines, mono- and oligo- saccharides, lipids	В молоке матерей с ИВ/ОЖ по сравнению с молоком женщин с НВ уровень ПНЖК был значительно снижен, отмечено повышение уровня НЖК и/или снижение уровня МНЖК или изменение соотношения МНЖК/НЖК или ПНЖК/НЖК. Содержание метаболитов углеводного обмена было повышено по результатам большинства исследований. Обнаружено повышенное содержание шикимовой кислоты, лейцина, изолейцина, валина, глутамина, аспарагина, орнитина, тирозина, АМФ, аденина, мочевиной кислоты, сахарных спиртов. Обнаружено снижение уровня кинуреновой кислоты, цАМФ, общего уровня полиаминов, спермидина, утресина / ω -3 PUFAs were significantly reduced in the milk of mothers with OW/OB compared to NW, there was an increase in SFAs and/or a decrease in MUFAs or a change in the ratio of MUFAs/SFAs or PUFAs/SFAs. The content of carbohydrate metabolites was elevated in most studies. Shikimic acid, leucine, isoleucine, valine, glutamine, asparagine, ornithine, tyrosine, AMP, adenine, uric acid, and sugar alcohols were elevated. A decrease in kynurenine acid, cAMP, total polyamines, spermidine, putrescine was found

vitamin D concentration of women with BM obesity varies is not well studied. However, research indicates that mothers with NW had higher serum concentrations of 25(OH)D than obese women do. In babies born to mothers with OV/OW, the serum concentration of 25(OH)D was reliably lower than in infants with NW [31].

Metaboloma Features. Metabolomics is regarded by many as the most promising technique for examining variations in the composition of BM in women with different diseases, including obesity. There are several expert groups working on this right now. Metabolom is a complete set of low molecular metabolites — metabolites, hormones, and other signaling molecules — and secondary metabolites. As per the research conducted by E. Isganaitis and colleagues, The breast milk of the OV/OW and NW groups differed in terms of metabolite content one month after delivery; 3 out of 10 metabolites were human milk oligosaccharides and 4 out of 10 were nucleotide derivatives. There was a positive correlation found between the BMI of the mother and the accumulation of fat in the infants. A composition study of 20 milk metabolites had different contents six months after delivery. At 1 and 6 months, the mother's BMI was favorably correlated with the 1.5-anhydrocytol content of human milk, which had not before been reported in milk [32].

F. Bardanzellu and co-author conducted one of the largest studies on the metabolomics of BM [33] by conducting a meta-analysis of numerous publications and considering the characteristics of the composition of BM in overweight or obese women. In general, a significant increase in the ratio of ω -6/ ω -3 was observed in the colostrum, transition, and mature milk of mothers with OV/OW. In all but one of the studies included in the analysis, the level of ω -3 PUFA was significantly reduced in the group of mothers with OV/OW. A few studies [34–37] also reported changes in the ratios of MUFA/SFA or PUFA/SFA, as well as a rise or decrease in the level of SFA. In most studies, women with OV/OW have been promoted based on the content of carbohydrate metabolites such as mannose, d-xylose (in the form of its main derivative, xylolactone), ribose (the essential component of DNA, RNA, acetyl coenzyme A, and ATP), lycose, glucose-6-phosphate, and 1,5-angydrucitol (1,5-AGH) in the BM.

It is also intriguing that the BM women with OV/OW had elevated shikimic acid. In a study in

vitro [38], shikimic acid was discovered to diminish lipid buildup in hepatocellular carcinoma cells and adipocytes. This metabolite displayed anti-inflammatory and antioxidant characteristics in animal models. In the examination of amino acid composition in the BM, numerous amino acids (leucine, isoleucine, valine, glutamine, asparagine, ornithine, and tyrosine) were shown to be different in the NW and OV/OW groups [32, 39]. In the study by A. de Luca et al., there is evidence that the mature milk of obese women includes 20% more branched-chain amino acids and 30% more tyrosine than that of eutrophic women [40]. Notably, increasing branched-chain amino acids can change insulin production and insulin sensitivity, which can lead to obesity in children and adolescents [41]. 6 months after delivery, the amount of kynurenic acid is lowered by around 30% in the group of mothers with OV/OW [32]. This acid is generated as a result of tryptophan catabolism, and tryptophan-kynurenine metabolic pathway disruption is considered to promote obesity [42]. Among the purine derivatives in the BM of women with OV/OW at the 1st month of breastfeeding, a rise in adenosine monophosphate and its catabolite adenine and a decrease in cyclic adenosine monophosphate [32] were found. Saben et al. identified an increase in uric acid in breast-milk women with obesity at 6 months of breastfeeding [39]. Increased purine exchange can promote weight gain long after birth. At the same time, it enhances glucose tolerance and insulin sensitivity during obesity, as well as lowers cardiovascular risk [33]. Polyamines of putressin and spermidine (and total polyamine levels) have been reduced in the BM of women with OV/OW, according to the study by Ali et al. [43]. Some research on mouse obesity models [44, 45] demonstrates that higher levels of polyamines in white adipose tissue, liver, and skeletal muscles boost energy consumption, resisting obesity. They are essential in the early stages of adipocyte differentiation in adipocyte tissue because they alter the expression levels of transcription factors involved in the regulation of adipogenesis at the preadipocyte level [46]. These findings suggest that the long-term effects of the BM's decreased polyamine levels may include adverse effects on body weight gain. The amount of erythrol, arabitrol, rabitrol, and glycerine sugar alcohols in the BM of moms with OV/OW has increased. Hootman et al. [47] consider erythrol to be one of the possible indicators of obesity. There is one case-control study

that demonstrates a connection between maternal obesity and elevated arabitol in infants [48].

CONCLUSION

The changed composition of the BM may be a factor potentially affecting a child born to a mother with obesity. 48 research that assessed the distinctions in breast milk between women who are overweight or obese and those who are of normal weight, either directly or indirectly, were analyzed. There are differences in the macronutrient content, micronutrients, metabolites, and biologically active substances in the breast milk of obese women. These data serve as the foundation for further thorough research because single experimental investigations have not yet provided a good understanding of the mechanisms behind the consequences of these alterations on children's health. A thorough examination of the metabolic traits of children born to obese mothers is necessary to determine the causal linkages between alterations in the composition of breast milk and the corresponding advantages or risks. Investigating how obese moms' diets and lifestyle changes affect the makeup of their breast milk could be one pathway for future research.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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