AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 2, Issue 6, 2024 ISSN (E): 2993-2149

Modern Ideas of Morphogenesis and Mammary Glands Function in Pregnancy and Lactation Dynamics

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Abstract: This article provides a brief overview of mammary gland structural and functional characteristics of a non-pregnant virgin mammal and occurring morphofunctional changes during the dynamics of pregnancy and lactation.

Keywords: mammary gland, mammogenesis, development, pregnance, lactation.

The mammary gland is a unique organ that has the ability to complete its full cycle of growth and development each time to fully provide the necessary nutrition and other substances to the emerging new offspring [1, 11, 44].

There is a significant number of works devoted to the morphological study of the mammary glands nowadays [38, 39, 40, 60]. It has been established that the functional activity of the mammary gland is supported by interrelated processes integration, such as mammogenesis - the growth and development of the gland; lactogenesis - the beginning of milk secretion after childbirth; lactopoiesis - maintenance of milk secretion.

Mammogenesis - the growth and development of the mammary gland takes a leading place in lobulo-alveolar structures development. This process begins in the fetus and later continues during puberty after a period of rest. However, final formation of the mammary gland processes only under the hormonal levels' influence during pregnancy [10, 23].

Having begun its development in the antenatal period, the mammary gland reaches morphological maturity during pregnancy, which is expressed by the growth and development of the lobulo-alveolar complex active form, making it capable of synthesizing specific milk components [3, 9]. Gland tissue lobulo-alveolar prelactation is regulated primarily by sex hormones (estrogen and progesterone), prolactin, and, especially, placental lactogen, which has a great influence on it. As per experimental studies' results mammogenic effect of hormones above is prepared and determined (to a certain extent) by growth hormone (GH), insulin, glucocorticoids and many other factors [1, 2].

Childbirth stops the function of the fetoplacental complex with its steroidogenesis. Placental lactogen disappearance from the circulation; estrogens and, especially, progesterone level decrease disinhibits prolactin secretory activity, which in turn leads to increased synthesis of milk components. Lactogenic factors also include prostaglandins, which stimulates lactogenic hormones release [5, 14, 15, 16, 20].

In the fetus during the early stages of pregnancy mammary glands are formed as epithelial cords running along the ventral wall of the body. Soon after this epithelial line segments proliferation leads to mammary buds' formation, localized depending on the final mammary glands' position [1].

After a relative period of rest during childhood, puberty begins a period of increased development of the gland, caused by an increase in the level of estrogen and progesterone. These hormones directly or indirectly stimulate ductal proliferation and deposition of periglandular adipose tissue [5, 31, 32, 53, 59].

According to most researchers, the transition from the infantile type of mammary gland of girls to the adult type occurs already 2-4 years after the start of regular menstruation, that is, by the age of 17-18 [9, 11, 15, 18]. Subsequently, enhanced development of the gland peaks only during pregnancy and lactation [5]. A similar relationship between the mammary gland development and after-puberty hormonal changes, during pregnancy and after childbirth, has also been noted in other species of mammals.

The mammary gland of sexually mature virgin rats mainly consists of ducts, groups - alveolar and terminal buds [7, 8]. Studies by other authors have shown that the terminal sections of the gland of nulliparous females are represented mainly by terminal and alveolar buds in almost all mammalian species [4, 6].

With the onset of pregnancy rapid growth of the glandular tree is observed, due to the intensive formation of alveoli. The alveoli of the mammary gland of mammals generally have a similar structure. They are formed by one layer of epithelial cells, an underlying layer of myoepithelial cells and a small amount of "light" cells located intraepithelially [9, 14].

The process of increased reproduction of glandular tissue is accompanied by the simultaneous development of connective tissue, as if continuing the growth that began during puberty [47, 49].

According to several authors [16], continuous proliferation occurs throughout pregnancy, as a result of which increase in the number of alveoli leads to a progressive increase in the size of the lobules. The maximum number of mitoses was observed in the first trimester of pregnancy, gradually decreasing in the second and third trimesters [17]. Similar dynamics of mammary gland cells' proliferative activity was observed in pregnant mice [17], rats [12, 13], pigs [22], and other mammalian species [22, 23, 26, 27]. Although mechanisms regulating cell proliferation have not been precisely established, pregnancy hormones' role in this process is obvious. Rat pregnancy, in particular, induces rapid glandular changes in both terminal and alveolar buds, differentiating alveolar groups into lobules [29, 30]. Data obtained by many authors indicate that gland cellular proliferation in rats continues throughout pregnancy and at the beginning of lactation [34, 35]. Same results were obtained for mice mammary gland [35]. However, some authors observed only one proliferative activity peak in the initial pregnancy period [38, 40].

When studying the mammary gland morphology in rats, it was noted that on the 5th day of pregnancy, minor morphological changes are observed in the terminal buds' transition form to alveoli and alveolar buds [38, 42, 52–58]. Pronounced lobules with formed alveoli and interalveolar ducts are revealed in the gland on the 10th day of pregnancy. Secretion determinate in the dilated cavities of the alveoli and ducts with the onset of lactation along with a large number of alveolar buds being noted with further transformation into alveoli during lactation [39].

Ultrastructural studies of the mammary gland have shown resting epithelial cells in a cylindrical or cuboidal shape containing several mitochondria, an underdeveloped Golgi complex and a small number of granular endoplasmic reticulum (GER) profiles.

Lactocytes' ultrastructural differentiation is noted after conception. Lipid droplets in acinar cells appear in the early period of pregnancy, nonetheless epithelial cell organelles' polarization has not been observed yet. Women mammary gland during the first three months of pregnancy contains lobules similar ones at rest [37]. Epithelial cells are in cylindrical and cuboid shape without pronounced organelles' polarization [39]. Myoepithelial cells are in the shape of a cone, elongated along the basement membrane. They form the outer layer of some epithelial cells and contact the basement membrane directly. According to electron microscopy scan alveoli lumen is narrowed at this stage and microvilli are observed on the apical part of the epithelial cells in most alveoli.

Further pregnancy is characterized by a gradual increase in the number of mitochondria and RER profiles, and the development of the Golgi complex. The latter becomes extensive and consists mainly of large and small bubbles. A certain structure polarization also takes place, expressed in the lipid droplets' distribution in the apical part of the cytoplasm with ZER profiles in the basal part at the same time. Increase in the number of cells containing protein granules and lipid droplets is observed during the prenatal period. The average diameter of lipid droplets in the apical part of lactocytes significantly increases and in some cases following can be observed: fusion with the plasma membrane and the release of contents into the lumen. A reduction in microvilli on the apical surface is observed in most epithelial cells [10, 21–27, 45, 58].

It is a clear polarization of the lactocytes subcellular organelles that is noted with the onset of lactation, namely, on the first day after birth. A well-developed ZER is located in the basal part in close proximity to the nucleus. An extensive Golgi complex is in the supranuclear zone, as well as fat and protein granules are accumulated in the apical part of the cytoplasm. Elongated microvilli number increases on the apical surface. In myoepithelioid cells contractile and trophic apparatus is noted to develop in the form of an increase in myofibrils and mitochondria number [45–52].

With further dynamics of lactation number of alveoli with an expanded lumen increases, which, according to some authors, indicates synthesis and secretion activation. Lumen secretory material in alveoli consists of numerous densely colored granules and lipid droplets of various sizes. Alveoli wall is formed by flattened lactocytes containing expanded RER profiles mainly in the basal cytoplasm part. Developed Golgi complex with numerous expanded vacuoles and secretory vesicles is located in the supranuclear zone [44].

Some authors based on morphological criteria identify several ultrastructural types of lactocytes during lactation, that can be determined by the phase of the secretory cycle [56–58].

Thus, sufficient information on mammary gland structural and functional rearrangements during various periods of ontogenesis in pregnancy and lactation dynamics has been collected to date. However, these works mainly focus on the state of glandular cells depending on secretory cycle phase.

List of used literature:

1. Андреева Е.Н., Хамошина М.Б., Руднева О.Д. Пролактин и молочные железы: норма и патология // Гинекология. – 2012. – Т. 14. – № 1. – С. 12-16.
2. Бабаева А.Г. Регенерация и система иммуногенеза. -М.: Медицина, 1985. - 256 с.
3. Грачев И.И., Галанцев В.П. Физиология лактации сельскохозяйственных животных. - М.: Колос, 1974. - 279 с.
4. Душкин М. И. Макрофаг/пенистая клетка как атрибут воспаления: механизмы образования и функциональная роль // Биохимия. 2012. Т. 77. С. 419—432.
5. Зотов А.С. Щепотин И.Б. Костюченко Е.А. Роль пролактина в физиологии и патологии молочной железы // Вопросы онкологии. – 2007. – N 2. – С.131-139.
6. Зуфаров К. А., Гонтмахер В.М., Юлдашев А.Ю. Свойство почки расщеплять экзогенные белки при их всасывании из тонкой кишки в кровь «Открытие». Диплом № 332 // Открытия. Изобретения. - 1987, - № 48.
7. Зуфаров К. А., Тухтаев К. Р., Юлдашев А.Ю. Лейкоциты и клетки рыхлой соединительной ткани (ультраструктурно-функциональные аспекты). - Ташкент: Фан, 1979, - 192 с.

8. Зуфаров, К. А., Тухтаев, К. Р., & Хасанов, Б. Б. (2003). Количественные и ультраструктурные характеристики иммунокомпетентных клеток молочной железы в динамике беременности и лактации. Морфология, 124(4), 74-79.
9. Ивантер Э.В., Коросов А.В. Элементарная биометрия: учебное пособие. Петрозаводск: Изд-во ПетрГУ, 2010. 104 с.
10. Каримов, Х. Я., Тухтаев, К. Р., & Хасанов, Б. Б. (2008). Токсический гепатит и структурно-функциональные особенности молочной железы при беременности и лактации. Морфология, 133(2), 59-60.
11. Кешишян Е. С. Почему так важно для ребенка грудное вскармливание и как его сохранить? / Е.С. Кешишян // Медицинский совет. — № 12. — М.: Медицина, 2012. — С. 112–116.
12. Киселева Е.С., Мохова Ю.А. Грудное молоко и его компоненты: влияние на иммунитет ребенка. Педиатрия.2010;89(6):62-69.
13. Летягин В.П., Высоцкая И.В., Ким Е.А. Факторы риска развития рака молочной железы // Маммология. – 2006. – 4. – С.10-12.
14. Маммология: национальное руководство / под ред.В. П. Харченко, Н. И. Рожковой. М.: ГЭОТАР-Медиа, 2016.328 с.
15. Молочные железы и их заболевания у детей / А. Б. Окулов, Л. В. Адамян, Д. Н. Бровин [и др]. М.: МИА. – 2016. – 160 с.
16. Мустафин Ч. Н. Гормональная регуляция молочных желез и предменструальный синдром // Акушерство гинекология. – 2013. – №1. – С. 34-41.
17. Нетребенко О.К. Питание и развитие иммунитета у детей на разных видах вскармливания. Педиатрия. 2005;6:50-56.
18. Роль оптимизации потребления белка в укреплении здоровья детей /Лукушкина Е.Ф., Нетребенко О.К., Баскакова Е.Ю., Гуренко С.П. // Вопросы современной педиатрии. – 2013;12(1):99-102.
19. Самчук П.М., Розалиева Ю.Ю. Прогнозирование нарушения лактации по уровню гормонов плаценты после экстракорпорального оплодотворения // Международный научно-исследовательский журнал. – 2016. – № 9 (87). – Р. 79-84.
20. Сейдахметова З.Ш., Даниленко М.П. Цитологические изменения клеток молочной железы при гипогалактии // I Съезд физиологов Средней Азии и Казахстана: Тез.докл. - Душанбе, 1991. - С. 91.
21. Тухтаев, К. Р., Расулев, К. И., & Азизова, Ф. Х. (2008). Морфологические особенности лимфатических узлов крыс, рожденных в условиях токсического воздействия на организм матери. Морфология, 133(2), 139-140.
22. Хасанов, Б. Б. (2009). Структурно-функциональные особенности молочной железы в динамике беременности и лактации на фоне токсического гепатита. Врачебное дело, Киев" Здоров'я",(7-8), 94.
23. Хасанов, Б. Б. (2020). Субмикроскопическое строение иммунокомпетентных клеток молочной железы при беременности и лактации и их особенности при хроническом гепатите. Проблемы биологии и медицины. DOI, 10, 2181-5674.
24. Хасанов, Б. Б. (2022). Морфология молочной железы при беременности и лактации. Бухара. Типография ”Sadriddin Salim Buxoriy” при Бухарском государственном университете, 120.

25. Хасанов, Б. Б. (2022). Экстрагенитальная патология и функциональные особенности процесса лактации. Астана медициналық журналы, (S1), 155-160.
26. Хасанов, Б. Б. (2024). Она сути цитокин ва гормонларининг (пролактин) янги туғилган чақалоқнинг иммун ҳужайралари функцияларига таъсири. Пробл. биол. и медиц, №2, (152), 364-370.
27. Хасанов, Б. Б. (2024). Сут безларининг иммунологик функциялари сут бези секретларидаги иммуноглобулинлар ва антитаналар. Scientific Journal of Applied and Medical Sciences, 3(4), 198-214.
28. Хасанов, Б. Б. (2024). Сут безларининг иммунологик функциялари пасив иммунитет ҳосил бўлишида сут безининг ўрни. Scientific Journal of Applied and Medical Sciences, 3(4), 186-197.
29. Хрущев Н.Г., Суетина И.А., Мичурина Т.В. Морфофизиологические особенности развития и инволюции структур молочных желез мышинных радиационных химер // Онтогенез. - 1981. -Т. 12, № 3. - С. 283-288.
30. Чумаченко П.А., Шлыков И.П. Молочная железа: морфометрический анализ. - Воронеж: Изд-во ВГУ, 1991. - 160 с.
31. Breast milk composition and infant nutrient intakes during the first 12 months of life / Grote V.; Verduci E.; Scaglioni S.; Vecchi F.; Contarini G.; Giovannini M.; Koletzko B.; Agostoni C. // Eur. J. Clin. Nutr. – 2016. – №70. – P. 250–256.
32. Breast pump use amongst mothers of healthy term infants in Melbourne, Australia: A prospective cohort study / Johns H.M.; Amir L.H.; McLachlan H.L.; Forster D.A. // Midwifery. – 2016. – 33. – P. 82–89.
33. Burtkhanovich, K. B. (2022). Extragenital Pathology and Immunocompetent Cells Relations of Lactating Breast Gland and Offspring Jejunum. American Journal of Internal Medicine, 10(2), 28-33.
34. Elfstrand L: Immunoglobulins, growth factors and growth hormone in bovine colostrum and the effects of processing. Int Dairy J 2002, 12:879–887.
35. Estrogen therapy and coronary-artery calcifi cation / Manson J.E. [et al.] // N. Endl. J. Med. — 2007. — Vol. 356. — P. 2591-2602.
36. Estrogen, progesterone, and vascular reactivity: potential cellular mechanisms / White M. et al. // Endocrine Rev. – 2005. – Vol.16. - P.739-751.
37. Estrogens, progestogens, normal breast cell proliferation, and breast cancer risk / Pike M.C. et al. // Epidemiol. Rev. – 1993. – Vol.15, N1. - P.17-35.
38. Fan Y, Chong YS, Choolani MA, Cregan MD, Chan JKY. Unravelling the mystery of stem/progenitor cells in human breast milk. PLoS One. 2010;5:e14421.
39. Fateyeva Ye. M., Kovalenko N. P. Perinatal psychology as a new direction of studies in system supporting breast feeding. Questions of children’s dietology. 2005; 3 (6): 52–57.
40. Function of milk polymorphonuclear neutrophil leukocytes in bovine mammary glands infected with Corynebacterium bovis / Blagitz M.G.* Souza F.N., Santos B.P., Batista C.F. and others. // Journal of Dairy Science. Volume 96, Issue 6, June 2013, Pages 3750-3757. https://doi.org/10.3168/jds.2012-6370
41. Gallego, M. I., Binart, N., Robinson, G. W., Okagaki, R., Coschigano, K. T., Perry, J., Kopchick, J .J., Oka, T., Kelly, P. A., and Hennighausen, L. (2001). Prolactin, growth hormone, and epidermal growth factor activate Stats in different compartments of mammary tissue and exert different and overlapping developmental effects. Develop Biol 229(1), 163–75.

42. Gherghiceanu, M., & Popescu, L. M. (2005). Interstitial Cajal-like cells (ICLC) in human resting mammary gland stroma. Transmission electron microscope (TEM) identification. Journal of cellular and molecular medicine, 9(4), 893-910.
43. Hassiotou F, Hepworth AR, Metzger P, et al. Maternal and infant infections stimulate a rapid leukocyte response in breastmilk. Clin Transl Immunology. 2013;2:e3.
44. Hourly Breast Expression to Estimate the Rate of Synthesis of Milk and Fat / Kent J.C., Gardner H., Lai C.T., Hartmann P.E., Murray K., Rea A., Geddes D.T. // Nutrients. – 2018 – Aug 22;10(9). pii: E1144. doi: 10.3390/nu10091144.
45. Hurley W.L. Immunoglobulins of the mammary secretions. In: Fox P.F., McSweeney P.L.H., editors. Advanced Dairy Chemistry: Proteins.3rd. Kluwer Academic/Plenum Publishers; New York, NY, USA: 2003.
46. Khasanov, B. B. (2020). Experimental chronic toxic hepatitis and hematological features in the dynamics of mother's and the offspring lactation. European Journal of Molecular & Clinical Medicine, 7(09), 1367-1373.
47. Khasanov, B. B. Experimental chronic toxic hepatitis and hematological features in the dynamics of mother’s and the offspring lactation. European Journal of Molecular & Clinical Medicine, 7(09), 2020.
48. Khasanov, B. B. (2021). Offspring jejunum structural and functional development during breastfeeding against the background of mother’s chronic toxic hepatitis. Europe's Journal of Psychology, 17(3), 330-335.
49. Khasanov, B. B. (2021). Structural and functional features of immunocompetent breast cells glands during pregnancy and lactation in chronic hepatitis. Psychology and Education, 58(2), 8038-8045.
50. Khasanov, B. B., & Azimova, S. B. (2023). Extragenital pathology of the mother and morphological features of the development of the thymus in the period of early postnatal ontogenesis. European Chemical Bulletin, 12(8), 8322-8331.
51. Khasanov, B. B., Ilyasov, A. S., & Sultanova, D. B. (2023). Extragenital pathology of the mother and morphological features of the development of the spleen in the period of early postnatal ontogenesis. European Chemical Bulletin, 12(8), 8332-8341.
52. Khasanov, B. B. (2020). The influence of chronic toxic hepatitis on lactation processes. Morphology. 157(2-3), 226.
53. Khasanov, B. B. (2009). Structural and functional features of the mammary gland in pregnancy and lactations on the background of toxic hepatitis. Likars' ka sprava, (7-8), 94-97.
54. Masso-Welch, P. A., Darcy, K. M., Stangle-Castor, N. C., and Ip, M. M. (2000). A developmental atlas of rat mammary gland histology. J Mamm Gland Biol Neoplasia 5(2), 165–85.
55. McCarty K.S. Proliferative stimuli in the normal breast: Estrogens or progestins? // Hum. Pathol. - 1989. -Vol. 20, N 12. - P. 1137-1138.
56. Mehta R, Petrova A: Biologically active breast milk proteins in association with very preterm delivery and stage of lactation. J Perinatol 2010, 31:58–62.
57. Ruan,W., Monaco, M. E., and Kleinberg, D. L. (2005). Progesterone stimulates mammary gland ductal morphogenesis by synergizing with and enhancing insulin-like growth factor-I action. Endocrinology 146(3), 1170–8.
58. Sara McNally & Finian Martin. Molecular regulators of pubertal mammary gland development // Annals of Medicine, 43:3, 212-234, DOI:10.3109/07853890.2011.554425