

**REVIEW**  
**From**  
**PROF. VESSELKA DULEVA, MD, PhD**  
**Head of Department Food and Nutrition**  
**National Center of Public Health and Analysis**

**REGARDING:** dissertation work of Dr. Miglena Yordanova Marinova-Ashkar "Importance of breastfeeding for the health of children up to 3 years of age from families at high risk for allergy" for the awarding of a scientific and educational degree "doctor" by field of higher education 7. Health care and sports, professional direction 7.1. Medicine by scientific specialty - "Hygiene (incl. labor, communal, school, radiation, etc.)", at Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

By order No. P-109-191/ 15.03.2023 of the Rector, of the Medical University - Varna, I have been appointed to prepare a review under the procedure for acquiring the SED "doctor" in the doctoral program "Hygiene (incl. labor, communal, school, radiation, etc.)", professional direction 7.1. Medicine, field of higher education 7. Health care and sports, with candidate Dr. Miglena Yordanova Marinova-Ashkar.

Dr. Miglena Yordanova Marinova-Ashkar is a doctoral student, regular form of education, enrolled by order No. P-109 -44/02/01/2019.

In 1989, Dr. Miglena Yordanova Marinova - Ashkar graduated from the Medical University of Varna with a Master's degree, after which from 1989 to 2003 she worked as a neonatologist in the Department of Neonatology, "St. Iv. Rilski" - city of Razgrad. From 2003 to 2008, she was a neonatologist - Department "Newborns" of the Maternity Department, MBAL "St. Anna-AD" - Varna, after which in the period 2008 2009 she was the Head of the Department "Newborns" of the Maternity Department, and from 2009 to the present Dr. Marinova-Ashkar is the Head of the Department of Neonatology, "St. Anna-AD" Medical Center - Varna.

Dr. Marinova - Ashkar since 1999 has a specialty in pediatric diseases, MA - Sofia, and since 2007 has a specialty in neonatology, acquired from the Medical University - Pleven. Since 2005, he has a qualification in health management from the Medical University - Varna. Dr. Marinova-Ashkar specialized in neonatology at leading university hospitals - University Hospital of MU - Salzburg, Austria (2010), University Hospital of MU - Graz, Austria (2007

and 2005), University Hospital - Ashkelon at MU "Ben Gurion", Israel (1999). She completed public health training in Maternal and Child Health - Trieste, Italy in 2008.

Dr. Marinova-Ashkar is a member of BLS, the Bulgarian Neonatological Association (a member of the World Newborn Association), ESPGHAN and BULSPGHAN

Dr. Marinova-Ashkar speaks English and Russian.

The topic of the dissertation submitted for review "Importance of breastfeeding for the health of children up to 3 years of age from families at high risk for allergy" is relevant and practically relevant.

In recent decades, the frequency of allergic diseases has increased significantly, covering up to 20% of the world's population, and 60% of allergies appear already in the first year of life. Many studies prove that atopic dermatitis and food allergy usually debut in infancy and early childhood and gradually progress to allergic asthma and allergic rhinitis in preschool and school age in some children. Worldwide, the incidence of atopic dermatitis ranges from 0.2% to 24.6%, and its prevalence in the first 2 years of life is 21.5%. Children with a family history of allergies are at higher health risk not only for other allergic diseases, but also for somatic and psychosomatic diseases. Along with the health problems they bring to affected children, allergic diseases affect the quality of life of children and their families. Preventive strategies are especially important for children at high risk of developing allergies - when one or both parents are allergic. Various factors during breastfeeding, which complexly modulate children's health, can influence its health effects on the growing child's organism. Exclusive breastfeeding in the first 4-6 months of a child's life, a period of metabolic and immune programming, provides short- and long-term benefits for children's health and intellectual development, and is thought to reduce the risk of food allergies, especially to cow's milk protein. Publications from recent years, as well as the opinion of the European Academy of Allergy and Clinical Immunology do not support the avoidance of allergenic foods as a strategy for the prevention of allergies during pregnancy, lactation and during the feeding period. Mother's breast milk provides protection to the child according to its specific microbiological environment and its own immune capacity and thus compensates for the insufficient immune response in the most vulnerable period of the development of the child's immune system. Breast milk contains substances that support not only passive immunity, but also stimulate the child's own immune system. The role of breastfeeding on the development of the immune system and the manifestation of food allergy remains an area for future research, due to the different results, depending on the heterogeneity of the studies, as well as the complexity of the development of food allergy. The subject of research and

discussion are questions related to but also stimulating the child's own immune system. The role of breastfeeding on the development of the immune system and the manifestation of food allergy remains an area for future research, due to the different results, depending on the heterogeneity of the studies, as well as the complexity of the development of food allergy. The subject of research and discussion are questions related to but also stimulating the child's own immune system. The role of breastfeeding on the development of the immune system and the manifestation of food allergy remains an area for future research, due to the different results, depending on the heterogeneity of the studies, as well as the complexity of the development of food allergy. The subject of research and discussion are questions related to the protective effect of breastfeeding in terms of prevention of atopic diseases.

The dissertation "Importance of breastfeeding for the health of children up to 3 years of age from families at high risk for allergy" contains 159 pages, divided into separate parts: introduction (1 p.), literature review (50 p.), aim, tasks, hypotheses (1 p.), materials and methods (7 p.), results (26 p.) discussion (11 p. .), conclusions (3 pages), contributions (1 page), publications on the topic (1 page), appendices (26 pages), bibliography (20 pages).

The material is illustrated with 6 figures, 31 tables and 11 appendices. The literature reference contains 306 literary sources, of which 31 are in Cyrillic and 275 are in Latin.

There are 4 publications related to the dissertation work, 2 of which are in English. 7 participations in scientific forums are presented, of which 3 in foreign scientific forums.

The dissertation on Dr. Marinova – Ashkaris competently and comprehensively written. Demonstrates good knowledge and mastery of the methods and procedures related to the present study.

The structure of the work is in the format of a dissertation work.

The literature review is included in 2 sections with 7 subsections and 12 parts: Epidemiology and importance of atopy in childhood; Economic losses from atopy in childhood; Factors increasing the risk of atopy (Genetic family, Environmental factors, Hygiene theory); Preventive practices in atopic families (Nutrition during pregnancy, Breastfeeding, Hydrolyzed milks, Feeding practices, Probiotics, Vitamin D, Omega-3 fatty acids, Acute infections, Food diversity); Risks of comorbidity in children from atopic families and in atopic children; Growth in children at risk of developing atopy and with atopy, Importance of breastfeeding for growth.

International literary sources predominate, national publications in the field are also presented, a review of the literary sources was also made in a retrospective aspect, with a sufficient number of publications from recent years also included. The literature review shows

a good command of the problem and the scientific literature by Dr. Marinova-Ashkar, the problems in the field are presented comprehensively and competently argues the choice of the methods used in the scientific development of the dissertation.

The main goal of the dissertation is adequately defined - to study the influence of breastfeeding on the growth, development and health of children of early childhood (including physical and neuropsychological development, acute morbidity, manifestation of allergies) from families with evidence of atopy .

The formulated 4 tasks make it possible to achieve the set goal.

The fulfillment of the tasks of the dissertation development allow: To assess the influence of breastfeeding on the growth of children born in families with a history of allergy; To measure the relationship between breastfeeding and acute morbidity in children with a family history of allergy; To track the manifestations of allergy and their relationship with milk feeding in the studied group of children; To evaluate the neuropsychological development of children born in families with a history of allergy, as well as the influence of breastfeeding on it, while controlling for the factors maternal smoking, number of family members, number of brothers/sisters.

The formulated working hypotheses (that in children born in families with a high risk of atopy, breastfeeding favorably affects the indicators of physical and neuropsychological development in the first years of life; and that the frequency of acute diseases and the appearance of atopic conditions in infancy age is lower in breast-fed children) find confirmation in the developed dissertation work.

To achieve the goals of the dissertation, a wide range of methods was used: Documentary method - a targeted, thematically oriented analysis of more than 300 publications available in PubMed, SCOPUS and Science Direct, etc.; Survey method - direct individual surveys, including data on demographic and socio-economic indicators of parents, method of conception, course of pregnancy and delivery; demographic and anthropometric indicators of the child; Atopic Dermatitis Data Rating Scale (SCORAD) and Potential Allergy Score Questionnaire (CoMiSS); child's eating practices; health condition of the child; manifestation of allergies; assessment of the child's neuropsychological development; Clinical methods; Anthropometric measurements; Statistical methods - descriptive methods, frequency analysis of qualitative variables, variance analysis of quantitative variables; Hypothesis testing methods – parametric and non-parametric methods, logistic regression analysis. The statistical analysis of the data was performed using the software package SPSS 25.0, Jamovi 2.2.2., Graphical method

The scientific study is a prospective cohort among children with a family history of allergy, conducted in the period 2017-2021. The object of the scientific study are: 156 women giving birth out of 1210 invited to the "St. Anna - AD" - Varna, and those who completed the research protocol were 120 children born from families with a high risk of allergy (54 girls and 66 boys). Participants were included in the study after obtaining written informed consent from their parents or guardians. Adequate criteria were developed for including or excluding children during their selection at the beginning of the study.

The study was approved by the REC (Research Ethics Committee) of the MU "Prof. Dr. P.Stoyanov" - Varna.

The results of research and surveys are original in nature, correspond to the tasks set, presented and illustrated appropriately. The dissertation covers all aspects and algorithms for assessing the development and health of children in early childhood (including physical and neuropsychological development, acute morbidity, manifestation of allergies) and is an in-depth analysis of information about children from families with data on atopy .

The results and discussions are presented thoroughly and in accordance with the tasks, which facilitates their systematization and perception.

Four main conclusions are formulated, corresponding to the set tasks and the main goal. Each of the conclusions logically follows from the obtained results. The conclusions are formulated depending on the gender of the children. The influence of breastfeeding on growth in the first years of life of children born to families with a history of allergy was evaluated, confirming the facts - Breastfed children have a healthier growth rate; The type of milk that the child took during the breastfeeding period had borderline statistical significance for some of the anthropometric indicators. It was found that children without atopic dermatitis had a faster rate of growth in height and weight at 2 years than those with atopic dermatitis at statistical significance of the results, which were presented depending on the gender of the children. Conclusions are also drawn regarding the acute morbidity in children - boys with food allergy suffer more often from acute infections, respiratory infections, gastroenteritis and are hospitalized more often, while exclusively breastfed boys suffer less frequently and for a shorter duration of diseases. Girls with food allergy suffer from acute bronchiolitis and acute laryngitis significantly more often and for longer. It has been established that the duration of breastfeeding is important for the number of hospitalizations due to diseases of the respiratory system. The type of milk that children receive has an effect on the number of hospitalizations for digestive system diseases - breastfed girls are less often hospitalized for digestive system diseases. When analyzing the manifestations of allergy and their relationship with milk

feeding in the studied group of children, it was found that the manifestation of allergies is more common in males than in females; most often allergies appear in children fed with standard infant milk. The duration of breastfeeding is a statistically significant factor for the appearance of allergic rhinoconjunctivitis within the studied period. According to the type of feeding, more allergies occur in children on replacement/mixed feeding than in breastfed children. With regard to children's neuropsychological development, it is found that the number of other children and family members matters for boys and girls, and in larger families, children have better development, and the duration of breastfeeding does not affect the assessment.

Contributions are formed in two aspects - Contributions of an original nature and Contributions of a confirmatory nature.

#### *Contributions of original character*

The original contributions of the dissertation work are related to the fact that for the first time in Bulgaria an assessment was made and the following were investigated: the influence of breastfeeding on the health of children with a family history of allergy in early childhood - up to 3 years; the neuropsychological development of children and the influence on it of the way of feeding and some epigenetic factors, as well as the influence of the type of milk feeding on growth, acute morbidity, the manifestation of allergies and the neuropsychological development of children at risk for allergy.

#### *Contributions of a confirmatory nature*

Also valuable are the contributions of a confirmatory nature, with which the dissertation confirms literature data that: children with a family history of allergy, fed with infant milk, have a faster growth rate; breastfed children get sick less often, are hospitalized less often and have shorter hospitalizations due to diseases of the respiratory and digestive systems than those fed with infant formula; Children with severe atopic dermatitis have a slower growth rate than those without atopic dermatitis; People with food allergy suffer from acute gastroenteritis more often and for a longer period of time; In men, the appearance of allergies is more common than in women; Allergies are most common in children fed standard infant formula; Children with food allergy suffer more often from acute illnesses and are hospitalized more often; Most allergies occur in children breastfed for less than 6 months; Children of smoking mothers have lower indicators of neuropsychological development; Boys who have a brother/sister have higher indicators of neuropsychological development; the use of infant formula versus breast milk was a statistically significant factor on the general

neuropsychological development of boys; The number of family members affects children's neuropsychological development.

**In conclusion:** The topic of the dissertation is current, scientifically based and dissertable. The main goal and tasks are formulated clearly and in accordance with the topic. The results are of an original nature and of certain practical applicability. The presented material contains scientific information, results of own research and analysis, which are adequately interpreted. Dr. Miglena Yordanova Marinova-Ashkar's mastery of applied methods and knowledge of scientific literature is evident. The contributions are of an original and confirmatory nature and enable practical solutions in the feeding of children up to 3 years of age from families with a high risk of allergy.

Based on the above, I express a positive assessment of the thesis submitted for review "Importance of breastfeeding for the health of children up to 3 years of age from families with a high risk of allergy". I firmly believe that the scientific jury can positively evaluate the development and support the awarding of a scientific and educational degree "doctor" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine by scientific specialty - "Hygiene (incl. occupational, communal, school, radiation, etc.)" of Dr. Miglena Yordanova Marinova-Ashkar at Medical University "Prof. Dr. Paraskev Stoyanov", city of Varna.

15.05.2023

Prof. Veselka Duleva, MD, PhD:.....