SCIENTIFIC OPINION

From Assoc. Prof. Dr. Rositsa Hristova Chamova, MD, PhD Department of Hygiene and Epidemiology Faculty of Public Health, Medical University – Varna

Subject: Dissertation work for obtaining the educational and scientific degree "Doctor" in the field of higher education 7. "Health and sport", professional field 7.1. "Medicine", scientific specialty "Hygiene (including occupational, communal, school, radiation, etc.)" of **Miglena Iordanova Marinova - Achkar, MD**, PhD student in full-time education at the Department of Hygiene and Epidemiology, Faculty of Public Health, Medical University of Varna

Topic of the dissertation: "The importance of breastfeeding for the health of children up to 3 years of age, born in families at high risk for allergy"

Scientific Supervisors: Prof. Rouzha Pancheva, MD, PhD

Assoc. Prof. Natalya Usheva, MD, PhD

According to Order \mathbb{N} P-109-191/ 15.03.2023 of the Rector of the Medical University - Varna I have been elected as a member of the Scientific Jury, and according to Protocol \mathbb{N} 1/ 27.03.2023 I have been appointed to prepare an scientific opinion on the procedure for acquiring of the educational and scientific degree "Doctor" with candidate Dr. Miglena Iordanova Marinova - Achkar, MD

- PhD student in full-time education at the Department of Hygiene and Epidemiology, Faculty of Public Health, Medical University of Varna.

Procedure details

Dr. Miglena Yordanova Marinova-Achkar has been enrolled as PhD student in full-time in the doctoral program "Hygiene (including occupational, communal, school, radiation, ect.)" in the field of higher education 7. "Healthcare and Sports", professional field 7.1. "Medicine", with the dissertation topic "Prevention of food allergy in infants in families with a history of atopy in Northeastern Bulgaria" and scientific supervisor - Prof. Dr. Rouzha Zlatanova Pancheva-Dimitrova, MD, PhD according to Order № P-109-44/01.02.2019 of the Deputy Rector of MU "Prof. Dr. Paraskev Stoyanov" - Varna Prof. Dr. Albena Kerekovska, MD, PhD.

Assoc. Prof. Dr. Nataliya Vasilevna Usheva, MD, PhD has been appointed as the second scientific supervisor according to Order № P-109-85/10.02.2020 of the Rector of the MU "Prof. Dr. Paraskev Stoyanov" – Varna.

The topic of the dissertation has been changed from "Prevention of food allergy in infants in families with pronounced atopy in North-Eastern Bulgaria" to "Importance of breastfeeding for the health of children up to 3 years of age from families with high risk for allergy"according to Order № P-109-86/10.02.2020 of the Rector of MU "Prof. Dr. Paraskev Stoyanov" - Varna and Order № P-109-500/29.11.2021 of Deputy. Rector "Career Development" Prof. Dr. Svetoslav Georgiev, MD, PhD.

Dr. Miglena Yordanova Marinova-Ashkar has successfully passed the doctoral minimum and foreign language exam.

Dr. Miglena Yordanova Marinova-Achkar was credited with the right to protection by Order № P-109-191/ 15.03.2023 of the Rector of Medical University - Varna.

All administrative documents on the procedure provided for in the Low for the Development of the Academic Staff of the Republic of Bulgaria, the Regulations for its implementation and the Regulations for the Development of the Academic Staff of the Medical University – Varna are presented.

Biographical data and the career development of the PhD student

Dr. Marinova-Achkar graduated from the First Language High School with English language teaching in Varna in 1982. In 1989, she obtained a Master's degree in Medicine from the Medical University of Varna. In 1999, she obtained a specialization in pediatric diseases at the Medical Academy in Sofia. From November 1998 to February 1999, she specialized in neonatology at the Ashkelon University Hospital at Ben Gurion University in Israel. In 2005, she obtained a qualification in Health Management from MU - Varna. In 2007, she obtained a medical specialization in Neonatology from MU - Pleven. In 2008, she underwent training in Public Health in Maternal and Child Health at the European School for Maternal, Infant and Neonatal Health - Burlo Garofolo Institute in Trieste, Italy. In 2005 and 2007, she completed internships in neonatology at the University Hospital at MU - Graz, Austria, and in 2010 - at the University Hospital at MU -Salzburg, Austria.

Dr. Marinova's work experience began in 1989 as a neonatologist in the Neonatology Department of St. Ivan Rilski Hospital in Razgrad, where she worked until February 2003. From 2003 to 2008, she worked as a neonatologist in the Newborns Sector of the Obstetrics Department of St. Anna Hospital -Varna. From 2008 to 2009, she served as Chief of the Newborns Sector of the Obstetrics Department of St. Anna Hospital - Varna. From 2009 to the present, she has been the Chief of the Neonatology Department at St. Anna Hospital - Varna. Dr. Marinova speaks English and Russian fluently. She has various professional and social skills, including communication, teamwork, organizational skills, and the ability to distribute functions and duties. She has good computer skills with Microsoft Office packages such as Word, Excel, and PowerPoint.

Dr. Miglena Marinova has participated in numerous scientific conferences and seminars.

Structure and content of the dissertation work

The dissertation work developed by Dr. Miglena Marinova consists of 154 pages and is illustrated with 6 figures, 31 tables, and 11 appendices. A total of 306 literature sources are cited, 31 of which are in Cyrillic and 275 in Latin. The dissertation work is well-balanced and includes a literature review (54 pages), Objectives, Tasks, Materials and Methods (8 pages), Results (26 pages) and Discussion (11 pages), Conclusions (3 pages).

Relevance of the topic

Allergic diseases are among the most common diseases affecting up to 30% of children in our time. The observed trend in recent years towards an increase in the frequency of allergic diseases is associated with pollution of the environment by chemical substances, presence of food allergens, uncontrolled use of drugs, and changes in the way of life of the population. The main theories about the origin of allergic diseases are related to changes in diet along with general changes in the environment, which shape the type of immune response of the host towards an allergic reaction during a critical period of life. Preventive strategies are particularly important for children at high risk of developing allergies, such as

those with one or both parents who are allergic. The importance of allergies is related not only to their health effects, but also to the overall life of the individual. They have a strong impact on educational preparation, social skills, and professional realization, especially in children. Along with the health problems they bring to affected children, allergic diseases affect the quality of life of children and their families. They also cost significant economic expenses for the child's family and society. The first 1000 days, starting from conception and continuing until the beginning of the third year of postnatal life, are critical for ensuring the healthy development of the child and prevention of chronic diseases later in life.

The way of life and nutrition before and during pregnancy, lactation, infancy, and early childhood have been shown to have long-term effects on the later health status of children, including the risk of socially significant diseases such as diabetes, obesity, and cardiovascular diseases. It is assumed that the best opportunities for prevention are within the timeframe between conception and the first six months of life. Breastfeeding is considered the gold standard for infant feeding. The benefits of breastfeeding go beyond the properties and contents of breast milk. The question of the protective effect of breastfeeding can be examined from different aspects, including:

• how the duration of exclusive breastfeeding protects against atopic diseases;

• whether the duration of any breastfeeding affects their development;

• whether the lack of breastfeeding or not breastfeeding at all affects the development of atopies;

• whether the intensity of breastfeeding or feeding with infant formula affects atopies.

The literary review is purposeful, comprehensive, and well-structured. Abilities for critical evaluation, summarization, systematization, and interpretation of scientific literature are demonstrated.

The aim of the dissertation is clearly and precisely defined. The set of four tasks are well-formulated and correspond to the set aim.

The methodology is complex, described in detail, and corresponds to the set tasks. Appropriate research methods have been chosen for the purpose:

Documentary - in-depth analysis of various sources of information - scientific articles, publications, reports, messages, books, normative documents, and methodological guidelines related to the subject of the dissertation work;

Survey - survey research has been conducted to establish:

1. Demographic and socio-economic indicators of the parents - gender, age, education, harmful habits (smoking), place of residence (city/village), ethnic origin, family size, data on pets, types of allergies in the family;

2. Manner of conception, course of pregnancy, and delivery;

3. Demographic and anthropometric indicators of the child - gender, age, height, and body weight at birth, at 1 year of age, at 2-3 years of age;

4. Completion of a visual scale for evaluating data on atopic dermatitis (SCORAD) and a questionnaire for assessing potential expression of allergies (CoMiSS);

5. The child's feeding practices - periods of exclusive breastfeeding, overall duration of breastfeeding, mixed and replacement feeding;

6. The child's health status - frequency and duration of acute respiratory, digestive, excretory system, sensory organs, and other illnesses; manifestation of allergies;

7. Assessment of the child's developmental profile - through completion of a validated questionnaire, the Development Profile-3 (DP-3).

Clinical methods used include: medical history, physical examination, anthropometric measurements at birth, and at 2, 4, and 6 months, evaluation of any possible allergy in the child until the end of follow-up.

Statistical methods include:

Descriptive methods - frequency and variation analysis.

Hypothesis testing methods - parametric methods (Student's t-test for comparing the mean values of two independent samples), non-parametric methods (Pearson's chi-squared test, Kolmogorov-Smirnov test, Mann-Whitney test), logistic and linear regression analysis.

Graphical method.

The results and their discussion are the essence of the fifth and sixth chapters. Dr. Marinova divides her own research results into several main directions of study:

- 1. Socio-demographic characteristics of the participants in the study
- 2. Allergic manifestations
- 3. Predisposing factors for allergic manifestations
- 4. The influence of breastfeeding on the growth of children born into families with a history of allergies
- 5. The influence of breastfeeding on the incidence of acute illnesses in children with a family history of allergies
- 6. The influence of breastfeeding on the manifestation of allergies in children with a family history of allergies
- The influence of breastfeeding on the developmental profile of children with a family history of allergies.

The presentation of the results of the conducted studies follows the set tasks.

The **conclusions** drawn are correctly formulated. They meet the set goals and objectives and logically follow the results and statistical analysis.

I approve **contributions** that are divided into:

A. Contributions of original character

For the first time in our country it is being studied:

1. The influence of breastfeeding on the health (growth, acute morbidity, manifestation of allergies) of children with a family history of allergy in early childhood - up to 3 years;

2. ND of the children from the mentioned sample and the influence on it of the way of feeding and of some epigenetic factors;

3. The influence of the type of milk feeding on growth, acute morbidity, manifestation of allergies and ND of children at risk of allergy;

4. The influence of the duration of breastfeeding on the pointed out indicators in children with family history of allergy.

B. Contributions of a confirmatory nature

The study confirmed that:

1. Children with a family history for allergy fed by IF, especially those with standard IF, have more rapid growth rate;

2. Breastfed babies get sick rarely and are less often hospitalized due to diseases of the respiratory and digestive systems as well as having a shorter hospital stay than those fed by IF;

3. Children with pronounced AD have a slower growth rate than those without AD;

4. Those with FA (in our study – only boys) suffer from acute gastroenteritis more often and for a longer period of time;

5. The manifestation of allergies is more common in boys than in girl;

6. Allergies occur most often in children fed by standard IF;

7. Children with FA suffer more often from acute illnesses and are hospitalized more often;

8. Most allergies occur in children breastfed for less than 6 months;

9. Children of smoking mothers have lower ND indicators;

10. Children (in our case only boys) who have siblings have higher ND indicators, as well as the fact that the use of IF compared to breast milk is a statistically significant factor on the general ND of boys;

11. Duration of breastfeeding does not affect ND;

12. The number of family members affects children's ND

The dissertation work is written in good language, precise in terms of terminology. Technically, the dissertation is designed according to the requirements, and the bibliography is comprehensive.

The abstract of thesis faithfully reproduces the content of the dissertation. It is prepared in a volume of 64 standard pages and is composed of 11 parts that accurately represent the structure and content, contributions and participations and publications of the dissertation work.

In connection with the dissertation work, the doctoral student presented 4 publications in the journals "Medinfo", "Medical News", "Varna Medical Forum", "Frontiers in Nutrition".

Seven participations in scientific forums are indicated:

1. Marinova M. Feeding disorders in newborn with kernicterus - AHP ESPGHAN Summer School, Worcester College, Oxford, UK, 11-14.09.2019

2. Marinova M, N. Usheva, S. Eyubova, R. Pancheva. Factors influencing early childhood neuropsychological development in children from families at high risk for allergies. Fifth multifaceted conference on child development -Plovdiv, 02-04.04.2021

3. Marinova M, N. Usheva, S. Eyubova, R. Pancheva.. Atopic predisposition and developmental profile of children in early childhood in Bulgaria. 8th International conference on Nutrition and growth, 26-28.08.2021

4. Marinova M, N. Usheva, R. Pancheva, A. Toneva, S. Kuneva. Early childhood food allergy in families with atopy in Bulgaria, UEGW, 10.2021

5. Marinova M, R. Pancheva, N. Usheva, S. Eyubova. Neurodevelopment of children from atopic families in the early childhood in Bulgaria, 4-th International Pediamediterranea Conference, Istanbul, 11-13.05.2022

6. R. Chamova, M. Marinova, R. Pancheva, S. Popova, E. Karaglani, A. Toneva. Frequency of different forms of allergies among families at high risk for atopy in Varna. XV National Congress of the Bulgarian Pediatric Association – 23-26.09.2021

7. A. Toneva, M. Marinova, R. Pancheva, E. Karaglani, N. Usheva, L. Rangelova, R. Chamova. Influence of some risk factors related to the growth of children from atopic families during the first 1000 days. XV National Congress of the Bulgarian Pediatric Association - 23-26.09.2021

In conclusion, the dissertation fully covers the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria. The work is presented in a complete and well-formed form.

In the dissertation work of Dr. Miglena Marinova her own experience from the study of a significant problem of modern society is presented. The comprehensive and consistent analysis performed provides opportunities to develop innovative approaches to improve and promote public health. I find the topic developed by the autor extremely relevant and timely. The content of the dissertation is legitimately and thoroughly developed, well illustrated and presented in good professional language.

The mentioned merits of the disertation give me a reason for positive assessment and to convincingly propose the award of to Dr. Miglena Marinova-Achkar educational and scientific degree "Doctor" in the field of higher education 7. "Health and sport", professional field 7.1. "Medicine", in the scientific specialty "Hygiene (including occupational, communal, school, radiation, etc.)".

08.05.2023

Scientific jury member:

Varna

/Assoc. Prof. Dr. Rositsa Hristova Chamova, MD, PhD/