Review

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On the basis of an order № P-109-135/05.04.2024 to the Rector of Medical University "Prof. Dr. Paraskev Stoyanov", Varna

Subject: Defense of a dissertation on the topic „Organization and results of a Programme for early detection and follow-up of children born small for their gestational age" of Tanya Lyubomirova Zlateva, MD - doctoral student in full-time training under the Doctoral Program „Pediatrics" to the Department of Pediatrics, Faculty of Medicine, Medical University Varna in connection with a procedure for acquiring Educational degree "PhD" professional direction 7 „Healthcare and sports" 7.1 „Medicine"

At the first meeting of the Scientific Jury on 17.04.2024, I was appointed to prepare a review

Biographical data about the student

Tanya Lyubomirova Zlateva, MD graduated in medicine at Medical University "Prof. Dr. Paraskev Stoyanov" - Varna in 2017. In the same year, she started working in the Pediatric Emergency Department of UMHAT "St. Marina" - Varna, and since the beginning of 2019 she has started her specialization in Pediatrics at the Pediatrics' Intensive Care Unit of the First Pediatric Clinic in the same hospital. At the same time, by order № P-109-75/01.02.2019 of the Rector of Medical University - Varna, she was enrolled as a doctoral student in full-time training in the doctoral program „Pediatrics" at the department of the same name of the Faculty of Medicine, Medical University of Varna. At the moment, after a successful competition, she is an assistant in the same department.

Zlateva MD has been actively participating in seminars, trainings and congresses since she was a student. She gains experience as a member of project development teams in the Pediatrics, Social Medicine and Health Management departments.

She is a member of the Bulgarian Pediatric Association and the Bulgarian Association of Neonatology, the European Society of Pediatric Endocrinology – ESPE. She speaks English.

Normal fetal growth is determined by the genetically determined growth potential, which is influenced by many factors: maternal, placental, fetal, genetic, environmental

factors. Some of them cause a small risk of intrauterine retardation in the growth of the fetus, while in others the frequency of births of small for their gestational age /SGA/ newborns is much higher. The last group of children does not reach the optimally expected birth weight.

Globally, researchers of this problem find a different relative share of SGA newbornscompared to total births – 11% in developed countries to 53% in underdeveloped countries. For Bulgaria, the limited number of studies to date do not give an idea of the real prevalence of SGA children – there is a lack of national statistics, register and data from their follow-up given the early /in the neonatal period/ and late /childhood to adult age/ complications arising in them. A systematic complex approach is needed, applied by interdisciplinary teams - OB/Gyn specialists, neonatologists, pediatric endocrinologists, general practitioners, etc. to solve the problem and reduce its negative consequences.

In this sense, the topic of the dissertation work is current and dissertatable.

The present scientific work consists of 180 standard pages comprising 16 appendices. **Its structure meets the requirements for a dissertation** and is presented as follows:

- Content and abbreviations used - 3 pages.
- Introduction - 1 page.
- Literature overview - 30 pages.
- Purpose and tasks - 2 pages.
- Material and methods - 13 pages.
- Results - 51 pages.
- Discussion - 28 pages.
- Conclusions - 2 pages.
- Deductions - 1 page.
- Contributions - 1 page.
- Scientific publications related to the dissertation work – 2 pages.
- Annexes - 15 pages.
- Bibliography - 23 pages.

Literature review

In the literature review, the data related to the definition of the term SGA newborn are presented in a historical aspect. It can be seen that this group of children is the subject of

multidirectional studies by numerous researchers. Real steps to identify children in this direction are the Fenton curves from 2003, corrected in 2013, the consensuses for diagnosis, treatment and follow-up of SGA children from 2007 and 2023.

The dissertation dwells on the differences between newborns with intrauterine hypotrophy and SGA, the varying world data on the prevalence of births of the latter and those for the country. In this subsection, Zlateva presents a summary of some of the reasons for the lack of valid statistics at the moment for those born in Bulgaria.

The text of the review related to the role of maternal and fetal risk factors for the birth of an SGA child, divided into medical and social is interesting. The importance of infections during pregnancy, assisted reproduction, some chromosomal aberrations and the most common in this group of genetic syndromes, the timely diagnosis of which is relevant for their later development, are emphasized.

The author discusses the early and late complications of SGA births. The former concern neonatologists and the latter can manifest themselves in different age periods and be the subject of research by pediatricians, general practitioners, therapists, etc. This further outlines the interdisciplinary nature of the problem. It is for this reason that the development of scientific and applied research to build working measures and sustainable strategies in health care, valid for our country, are relevant and necessary.

I accept the presented after the end of the review under the title "Prerequisites" as part of its summary motivating the dissertation to develop the present dissertation.

The literary review is well structured, the data from the bibliography are skillfully and concisely presented, which shows theoretical and practical knowledge of the problem, the ability to systematize knowledge and information from the dissertation.

The purpose of the study is clearly formulated and **8 tasks are indicated** for its implementation, which detail the guidelines of the study.

They must be derived from the section "Materials and methods" and presented before it.

The numbering of some of the tasks diverges from the sequence in the text and their exact spelling in the "Results" section.

Material and methods:

The exposition in this part of the dissertation begins with a description of the methods applied in the study and to them are indicated data that concern subsection „Materials" – 4.4. „Participants and Criteria for inclusion and exclusion of participants in the first and second years of the study". The criteria are well formulated.

There is a lack of information on the number of children covered in the two stages, as well as their characteristics - gender, birth weight, gestational age, distribution by the country's regions, etc. One part of this data appears in section "Results".

The methods used in conducting the study are described in detail – survey, organizational - incl. technical assurance, clinical methods - with a developed algorithm for re-evaluation and follow-up of SGA children by a pediatric endocrinologist after 2 years of age.

The scientific–applied nature of the Pilot Programme has been assessed by analyzing the influence of favoring and barrier factors at its beginning and end.

The statistical methods that guarantee the reliability of the results are listed.

Results:

Based on the analysis of the literature, the dissertation points out that in our country studies on SGA children are limited to a small number of publications that consider various aspects of the problem.

Task two presents data on the number of births in the neonatal units participating in the Programme for 2020 by region, with the relative share of premature babies compared to all newborns 25 343 children being 12.7%. The results for the material security of the units in determining the weight and height of the newborns, the methods for determining the gestational age, as well as the criteria for full-term and premature babies for their categorization as SGAare evaluated.

The results obtained in the first two tasks highlight the lack of a unified approach when evaluating this group of newborns immediately after birth and the need to develop the Programme and with this goal.

Tasks 3 and 4 reveal the large volume of preliminary and during the research organizational and research activity, referring to the expected barrier and facilitators for the implementation of the Programme, as well as the results of the first 6 months of its implementation. The data from the analysis confirm again the role and responsibility of neonatologists for the early detection of children with deviations in intrauterine growth.

In continuation, the conducted survey on the degree of application of the pilot Programme /task 5/ reveals the additional participation of parents, institutions, general practitioners, etc. for the success of the work in this direction.

In the following two tasks, Zlateva MD thoroughly and in detail presents the data on the frequency of SGA children by region and month based on the information submitted by the neonatal structures, establishing significant differences between them – from 1.4% to 10.34%. They can be associated with a certain seasonality of the births of SGA children, but partly testify to the inconsistency of work in the primary units under the first stage of the Programme.

The dissertation also presents the characteristics of 409 SGA children by gender, average weight, height and head circumference of full-term and premature infants, but this is not included in the formulation of the tasks.

Results of the second /endocrinological/ stage of the Programme, which has not yet been completed, are also described. I hope that by the end of it they will not be significantly changed.

The created algorithm for detecting and tracking SGA children in four steps specifies the activities of medical specialists. Further details are also reflected in annex 1 and they are useful for practice.

Discussion:

The discussion of the results of the assigned tasks is presented in a separate section, which inevitably leads to a certain repetition of some of the same in their interpretation, although Zlateva tried to avoid it to a large extent.

Here she compares her data with those from the bibliography, critically and objectively presenting explanations about the discrepancies between the situation in Bulgaria and foreign results, as well as the possible reasons for this.

Literature sources that are not directly related to the topic of the dissertation work are cited in the text /188 and 189, 237/.

Based on the results of the conducted research, **8 conclusions** are outlined, respectively, of the assigned tasks. They are well formulated and outline the state of the problem being developed in our country at the current stage.

I accept the contributions of the dissertation work /7 issues/, defined as scientific and applied. It is necessary to emphasize again the original nature and significance of the scientific development.

The bibliography includes 238 literary sources – 11 in Cyrillic and 227 in Latin. 66.4% of all publications are from the last 10 years, of which 71% - from the last 5 years – the bibliography is modern.

The usual formation of the bibliographic reference to a dissertation is an alphabetical arrangement of the authors in Cyrillic and Latin. The dissertant has listed the literature

sources used in the order of their citation, which is a requirement when publishing studies in some foreign specialized scientific journals.

I do not consider it appropriate that the literature review and bibliography include self-citation /№ 136 and №164/ of publications that are part of the dissertation work.

The results of the presented scientific study are **illustrated with 29 figures, 11 tables and 16 annexes**, which are clear and easy to perceive.

Full-text publications /3 issues in Bulgarian scientific journals/ and **participation in scientific forums** /4 issues – 2 of which international / related to the dissertation meet the requirements.

The abstract is well formed and presents the dissertation in a synthesized form. The latter is written in grammatically and stylistically sound language.

Conclusion: Tanya Lyubomirova Zlateva, MD is a promising young scientist. Regardless of the difficulties, with her inherent persistence and persistence, she managed to summarize the data from the study in a dissertation work that has not only scientific and applied significance, but also contains elements of a methodological nature.

I am convinced that Dr. Zlateva will continue the research on the discussed problem, given its medical and social significance.

The scientific work meets the requirements for structure and content. It is the personal work of the dissertation. The remarks made do not diminish its value.

My overall assessment of the dissertation on the topic „Organization and results of a program for early detection and coverage of children born small for their gestational age" by Tanya Lyubomirova Zlateva is positive. The author's report shows compliance and fulfillment of the minimum national requirements for educational degree "PhD" according to ZRASRB and RDAS of Medical University Varna.

I confidently propose to the Honorable Members of the Scientific Jury to award educational degree "PhD" to Tanya Lyubomirova Zlateva, MD – full-time doctoral student in Doctoral Program „Pediatrics" at the Department of Pediatrics in Medical University -Varna.

02. 05. 2024

Prof. Maya Krasteva-Vilmosh, MD, PhD