

**Review**  
**by Prof. Dr. Valentina Christova Madjova, PhD**

Professor at the Department of General Medicine, Medical University - Varna

of the dissertation on the topic  
**"PARTICIPATION OF HUMORAL FACTORS OF INNATE IMMUNITY IN THE  
PATHOGENESIS OF ACTIVATED OSTEOARTHRITIS"**

**by Dr. Irina Ivanova Momcheva**  
correspondence doctoral student at the "Department of General Medicine"  
Faculty of Medicine at the Medical University - Varna  
and  
assistant in Propaedeutics of Internal Medicine and in Rheumatology  
at the Faculty of Medicine, University "Prof. Dr. Assen Zlatarov" - Burgas

**for awarding of the educational and scientific degree "DOCTOR"**

**1. General presentation of the procedure and the doctoral student**

According to the Order of the Rector of MU - Varna No. R-110-/26.02.2024, Protocol of FS No. 17/14.02.2024 and Protocol of the meeting of the Scientific jury, I was elected as its Chairman and reviewer of the scientific work of Dr. Irina Ivanova Momcheva.

The set of materials provided to me on paper / electronic media fully complies with the requirements of the Procedure for obtaining the educational and scientific degree "Doctor" according to the Regulations of MU - Varna.

I did not find any violations of the procedure for awarding the educational and scientific degree "Doctor".

**2. Brief biographical data for the doctoral student**

Dr. Irina Ivanova Momcheva completed her secondary education at the Trade High School in Burgas and higher education at the Medical University - Plovdiv (1993).

Her professional career as a doctor began in rural health care (village of Rosen, Burgas region) and passed through various levels of the healthcare system, which helped her in her practical work and in the development of her medical skills. She worked successively in the polyclinic in Sopot and as a therapist in the Admission Department at UMBAL Burgas.

Dr. Irina Momcheva has long been familiar with the problems of patients in general practice. An important moment in her biography is her work as a general practitioner in a group practice from 2000 to 2008, which is important for her development as a doctor with versatile knowledge and skills.

Dr. Irina Momcheva is a well-rounded doctor with broad competence in the field of internal medicine and rheumatology and has obtained 2 specialties: Internal Medicine (2002) and Rheumatology (2011).

From 2010 until the present moment, Dr. Irina Momcheva has been working as a rheumatologist in Burgas - UMHAT and Health Center "Nadezhda".

Dr. Irina Momcheva also holds a Master's degree in "Business Administration and Health Management" (2016), University "Prof. Dr. Assen Zlatarov" - Burgas.

Since 2021, Dr. Irina Momcheva has been an assistant professor at the Faculty of Medicine of the University "Prof. Dr. Assen Zlatarov" - Burgas and teaches students in 2 disciplines: Propaedeutics of Internal Medicine and Rheumatology.

**3. Relevance of the Topic and Appropriateness of the Objectives and Tasks**

Dr. Irina Ivanova Momcheva's dissertation deals with a very current and important practical problem for general practice because the problems caused by activated osteoarthritis often lead patients to visit a rheumatologist due to the recurring course of the disease.

An important factor that directs Dr. Irina Momcheva towards developing her dissertation is the fact that while osteoarthritis was previously classified as a non-inflammatory disease due to the absence of systemic inflammation and neutrophils in the synovial fluid, it is now believed that low-grade local inflammation is a key driver of the degenerative process.

Another important aspect is that, at this moment in Bulgaria, there has been no comprehensive study on these aspects related to arthrosis.

According to Dr. Irina Momcheva, the main hypothesis of the current study is to find evidence for the direct involvement of humoral factors of innate immunity in the pathogenesis of osteoarthritic disease by removing destructive and apoptotic products of the degenerative process from the joint space and in the process of maintaining low-grade inflammation in the arthritic joint.

I highly appreciate the relevance of the topic of Dr. Irina Momcheva's dissertation as very important for clinical practice in our country for several reasons: the increasing prevalence of osteoarthritis due to longer life expectancy, an increase in the elderly population; the chronically recurring course of the disease and the possibilities for changing treatment in connection with the discovery of new pathogenetic mechanisms and the development of new therapeutic methods.

#### **4. Familiarity with the Problem**

Dr. Irina Momcheva is very familiar with the subject matter she addresses in her dissertation. She began actively working in the field of rheumatology at the beginning of her specialization in 2008.

For the first time in Bulgaria, she started a serious study on the leading role of innate immunity in the pathogenesis of activated osteoarthritic disease using statistically significant quantitative indicators.

Her daily practical work is of great importance, as besides hospital patients with rheumatological problems, Dr. Irina Momcheva also consults outpatient patients, which enables her to monitor the course of their diseases and to intervene early and adequately when their condition worsens.

#### **5. Research Methodology**

The larger section of the dissertation represents a study in which Dr. Irina Momcheva actively participates as a researcher. The study includes patients with activated osteoarthritis (OA) of the knee joint in the absence of anamnestic, clinical, and laboratory data for another disease that could cause effusion, and the diagnosis of "gonarthrosis" is based on clinical and radiographic criteria of ACR (1991).

Dr. Irina Momcheva examined 156 patients in a wide age range (43 - 90 years) who meet the ACR criteria for OA of the knee joint. Women predominate (121), accounting for 71.07% of the total number of patients, while men are 35 (28.92%).

All participants in the study signed an informed consent form.

The scientific study was approved by the Ethics Committee of UMBAL Burgas AD (23.01.2019), and the clinical and instrumental methods used in it were performed in accordance with the requirements of Good Clinical Practice and compliance with the Helsinki Declaration on the rights of research subjects.

In her dissertation, Dr. Irina Momcheva uses the following methods:

**1) Clinical-laboratory methods** - detailed history taking and assessment of the objective condition of patients, including a full joint status. Material (blood and synovial fluid) was obtained through venipuncture and arthroscopy following a strict protocol. CRP, C3, and C4 fractions of complement and soluble and cell-bound fractions of CRP, C3, and C4 were examined in a certified clinical laboratory "Lina" - Burgas. The Cobas c501 analyzer (immunoturbidimetric analysis) with Roche reagents and calibration for C3, C4, CRP - c.f.a.c. Proteins was used, the method was standardized, and quality control was performed.

CRP was examined with an immunoturbidimetric test, enhanced with particles, where human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies.

After a comparative analysis of the synovial and plasma concentrations of CRP and C3 and C4, a correlation between the levels of humoral factors and the different radiographic stages according to Kellgren-Lewrence, as well as dependence on the patients' gender, was sought.

## **2) Instrumental methods:**

1/ conventional radiography to verify the radiographic stage according to the Kellgren-Lewrence scale in the supine position in "Schuss" position on an Agfa DX - D500 X-ray machine;

2/ ultrasound of the knee joint with a Chison Model Q9 ultrasound machine with a linear transducer D12L40L at a frequency range of 7-18 MHz for diagnosing the activity of gonarthrosis, confirming synovial effusion, and for assisted arthrocentesis.

## **3) Statistical methods:**

- Statistical data processing with IBM SPSS Statistics 20 software.

- Descriptive statistics: mean values, standard deviation, coefficient of variation, skewness, and kurtosis;

- Correlation analysis between the examined indicators: CRP, C3, C4 in blood serum and joint fluid A and B and correlation coefficients;

- Graphical analysis (scatter plot and other graphical models);

- Analysis of variance to establish a statistically significant difference in the examined indicators in different ages, gender, radiographic stage, etc.

- Testing the statistical hypothesis for dependent samples (Student's t-test).

The selected research methods allow for the comprehensive achievement of the set goal and obtaining an adequate answer to the tasks addressed in the dissertation.

## **6. Characteristics and Evaluation of the Dissertation**

Dr. Irina Momcheva's dissertation consists of 120 typewritten pages and is illustrated with 24 tables, 18 figures, and 6 histograms. The bibliography includes 237 titles, with 4 in Cyrillic and 233 in Latin script.

In the literature review, Dr. Irina Momcheva examines the problem of the chronic recurrent course of osteoarthritis, which increases every year. Due to the increasing life expectancy of patients, the proportion of geriatric patients with this disease and their disability also increases. This is a significant social and health problem affecting society globally and relevant for Bulgaria for the same reasons.

The main aim of Dr. Irina Momcheva's dissertation is to investigate the levels of certain humoral factors of innate immunity with the aim of establishing their clinical significance in patients with activated osteoarthritis.

To achieve this, she has formulated several main tasks to correspond to the hypothesis and the aim of the dissertation work, namely:

1. Analysis of scientific literature regarding the involvement of humoral factors of innate immunity in the inflammatory process and the development of a model of low-grade local inflammation in OA.

2. Selection of patients with activated gonarthrosis according to ACR criteria (1991) and the absence of another disease that could cause effusion.

3. Verification of the radiographic stage according to the Kellgren-Lewrence scale.

4. Use of ultrasonography to demonstrate synovial effusion and for controlled arthrocentesis.

5. Examination of the indicators of humoral immunity CRP, C3, and C4 complement fractions in blood plasma and synovial fluid.

6. Comparative analysis of their levels in both body fluids and search for a correlation dependence according to the radiographic stages of gonarthrosis by Kellgren-Lewrence and the gender of the patients.

From her study, the doctoral student formulates 5 main conclusions. All of them correspond to the set goal and the specified tasks.

## **7. Contribution and Significance of the Development for Science and Practice**

In her study, Dr. Irina Momcheva, for the first time in Bulgaria, quantitatively and statistically proves the leading role of innate immunity in the pathogenesis of activated osteoarthritic disease. Additionally, she establishes with statistical significance the correlation between elevated levels of CRP, C3, and C4 in synovial fluid and the activation of arthritic disease.

The obtained results confirm and support the concept of pathways initiating and maintaining synovial inflammation in this cohort of patients, which she summarizes in a proposed pathogenetic model of low-grade inflammation in OA.

An interesting and important conclusion by Dr. Irina Momcheva is that a stronger correlation is found between elevated clinical indicators and radiographic changes in the knee joint in the early stages of the disease when the activity of repair processes is more pronounced.

I fully accept the conclusions made and the contributions indicated by the doctoral student.

#### **8. Evaluation of Publications Related to the Dissertation Work**

The doctoral student has provided the necessary number of publications and communications related to the dissertation work. The attached list meets the requirements for obtaining a Ph.D. degree.

#### **9. Personal Involvement of the Doctoral Student**

The conducted dissertation research, the formulated contributions, and the obtained results are entirely the merit of Dr. Irina Momcheva and are supported by her academic supervisor - Assoc. Prof. Dr. Zhenya Ruseva, MD.

#### **10. Abstract**

The abstract is fully sufficient in content and quality to present the main results achieved in the dissertation. It meets the requirements of the Regulations of the Medical University - Varna.

#### **11. Critical Remarks and Recommendations**

I have no critical remarks or recommendations regarding the conducted research and the materials provided to me.

#### **12. Personal Impressions**

I have known Dr. Irina Momcheva since the competition for enrollment in a part-time doctoral program. I was her first academic supervisor up to a certain stage of her dissertation work, and I have excellent impressions of her as an intelligent and knowledgeable physician, as well as a very precise doctoral student in the preparation and execution of her scientific project.

The dissertation work and the abstract proposed for evaluation stand out for their accuracy, precision, consistency, and depth of the formulated goals, tasks, conclusions, and contributions.

#### **Conclusion**

Overall, I evaluate Dr. Irina Momcheva's dissertation as timely and valuable as a scientific work with practical significance given the continuously increasing number of patients with osteoarthritis and the need to expand the therapeutic approach to them.

The dissertation work contains important scientific and practical results and meets all the requirements of the ZRASRB, its Regulations for Implementation, and those of the Medical University - Varna.

The materials presented and the dissertation results fully meet the specific requirements of the Medical University - Varna.

The dissertation work demonstrates in-depth theoretical knowledge and professional skills of the doctoral student in the scientific specialty "general medicine" and demonstrates her qualities and abilities for independent scientific research.

As a reviewer, I confidently give my positive assessment of the conducted research, dissertation work, abstract, achieved results, and contributions, and I propose to the respected scientific jury to award the educational and scientific degree of 'Doctor' to Dr. Irina Ivanova Momcheva in the scientific specialty "general medicine."

21.03.2024  
City of Varna

Reviewer: Prof. Dr. Valentina Madjova, PhD  
Professor in the Department of General Medicine

Заличено на основание чл. 5,  
§1, б. „В“ от Регламент (ЕС)  
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