

# **S T A T E M E N T**

**for dissertation thesis of the procedure for obtaining an educational and scientific degree "DOCTOR"**

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**Dissertation Topic: "PAIN AS PART OF THE RHEUMATIC MANIFESTATIONS OF COVID-19 VIRAL INFECTION"**

The dissertation of Dr. Simona Bogdanova-Petrova deals with a topical problem in modern rheumatology - "Pain as part of the rheumatological manifestations of Covid-19 viral infection". In 2020, humanity was facing a severe health problem - the coronavirus pandemic caused by SARS-CoV-virus. The disease affects the respiratory system, musculoskeletal system, cardiovascular system, skin, urinary and nervous systems. In addition, haematological, gastroenterological and endocrine disorders have been reported. Tissue impairment also appeared to be immune-mediated, and joint and muscle pain was a frequent symptom. Unfortunately, health institutions worldwide have proved to be totally unprepared in the diagnosis and treatment of this infectious disease. Therefore, any scientific study in these patients would be essential for medical science and practice.

**The dissertation** of Dr. Bogdanova-Petrova is the result of a clinical study realized in the Clinic of Rheumatology at the University Hospital "St. Marina" after approval by the Research Ethics Committee at MU-Varna. It is written in 166 standard pages and illustrated with 55 tables, 21 figures and 9 graphs.

**The literature review** is based on data from 419 articles.

**Aim and objectives of the study.** The objective is very precisely and clearly defined. The tasks, 5 in total, specify the approaches to achieve the objective.

**Clinical material and methods of study.** A population of 364 patients was enrolled in the study - 234 with confirmed COVID-19 and new-onset musculoskeletal pain and a control group of 130 patients with chronic inflammatory joint disease pain on long-term anticytokine therapy.

The methods include: socio-demographic and clinical parameters; standard laboratory tests; instrumental tests - chest radiography or computed tomography; assessment of pain and emotions; and statistical processing, enabling the evaluation of the significance of the results.

**Results and discussion.** Almost all patients with COVID-19 have joint and or muscle pain. In COVID-19 patients, muscle pain is slightly worse than joint pain, and the opposite is true in patients with IBS. It is important that in COVID-19 pain is dependent on age, anxiety-depressive attitudes and gender. The severity of joint and muscle pain in COVID-19 did not correlate with the level of acute phase indicators and thrombotic biomarkers. In COVID-19 patients, these indicators accounted for only 4% of the variation in pain, compared with 8% in the control group. The severity of joint and muscle pain in COVID-19 can be used to define a group of patients in whom a specific therapeutic approach is needed. COVID-19 patients had more pronounced depressive symptoms and anxiety compared to patients in the control group. Depressive moods and anxiety increased with advancing age. In fact, this study reveals the frequency and variation of joint and muscle pain in this still insufficiently studied infectious disease.

**Conclusions.** The aim of the dissertation is accomplished. The 4 conclusions in total respond reasonably well to the objectives of the study.

**Contributions of the dissertation work.** Dr. Bogdanova-Petrova's research is original and validating. For the first time in our country were evaluated demographic characteristics, laboratory and clinical disease activity and psycho-emotional status of patients with Covid-19. It was evaluated the correlation of pain with inflammatory markers, thrombogenic biomarkers, and psycho-emotional state in hospitalized patients with COVID-19 and in patients with IJD. The author suggest an algorithm for defining a "risk group" of COVID-19 patients - polymorbid, elderly and with a severe disease presentation, in order to define a differential approach aiming to improve prognosis. It was confermed the relationship between inflammatory markers and disease manifestations. Age, gender and psycho-emotional variations in pain assessment are demonstrated.

**The summary of the dissertation** has a standard structure and summarizes the dissertation very accurately.

**Publications related to the dissertation.** Dr. Bogdanova-Petrova has published a total of 11 scientific publications related with her dissertation - 2

full-text publications in Rheumatology journal and 9 participations in scientific forums in Bulgaria and abroad.

**C O N C L U S I O N.** An intriguing scientific research paper addressing an actual and almost unknown problem in modern medical science and practice - "Pain as part of the rheumatic manifestations of COVID-19 viral infection". The literature review has academic value and illustrates relatively well the current level of knowledge on the treated problem. The aim of the thesis and the tasks for its realization are defined precisely and clearly. The clinical material is adequate to fulfill the defined aim and objectives. The research methods are modern and informative enough. Statistical analysis of the obtained results is optimal. The obtained results enrich the clinical knowledge related to the frequency, severity and nature of the musculoskeletal pain in COVID-19 patients. It is remarkable that inflammatory indicators, anxiety and depressive symptoms in patients of the main group were significantly higher than those in the control group. Furthermore, age, gender, anxiety and depressive disorders were relevant for pain assessment. Assessment of depressive and anxiety symptoms, assessment of joint and muscle pain, and age may form a subgroup of patients with COVID-19 who need specific psychological and psychiatric care. The mood disorder and the severity of pain complaints help to define a 'risk group' of patients - polymorbid, elderly, with a severe disease course, who should be referred to a specialist for further treatment. I believe that the aim of the dissertation has been fulfilled. The 4 conclusions in total fulfill the set objectives.

A total of 11 scientific reports have been published in reference to the dissertation. This means that Dr. Bogdanova-Petrova's research is already well popularized among the rheumatological society.

The dissertation work of Dr. Bogdanova-Petrova is contributive and confirmatory. It fulfills the requirements for educational and scientific degree "DOCTOR". Therefore, I will vote for it positively and recommend the other members of the scientific jury to do the same.

25.04.2023, Varna

Statement from .....

(Prof.dr. Nikolay Penkov)