**ANNOTATION**

Of the dissertation work of doctoral student Dana Bekaryssova on the topic **«Articular syndrome in rheumatic diseases and reactive arthritis at the present stage: optimization of diagnosis, prevention and treatment (on the example of Turkestan region)»**, submitted for the degree of Doctor of Philosophy (PhD)

on speciality 8D10141 «Medicine»

**Relevance of the research topic.**

The relevance of this study is due to several factors reflecting current health problems. With the increasing incidence of musculoskeletal and connective tissue diseases worldwide, including the Republic of Kazakhstan, a deeper understanding of the causes and mechanisms of these diseases becomes necessary [Hartvigsen J, Hancock MJ, Kongsted A, et al. What low back pain is and why we need to pay attention. Lancet 2018; 391: 2356–67; Compilations of the Ministry of Health of the Republic of Kazakh stan (2011–2020) Health of the population of the Republic of Kazakhstan and the activities of healthcare organizations]. Particular attention should be paid to the increasing incidence among the young working-age population, which gives the problem additional social significance [Emilio B. Gonzalez, James S. Goodwin, Chapter 36 - Musculoskeletal disorders, Editor(s): Edmund H. Duthie, Paul R. Katz, Michael L. Malone, Practice of Geriatrics (Fourth Edition), W.B. Saunders, 2007, Pages 495-509, ISBN 9781416022619, https://doi.org/10.1016/B978-1-4160-2261-9.50039-2; Azabagic S, Spahic R, Pranjic N, Mulic M (2016) EPIDEMIOLOGY OF MUSCULOSKELETAL DISORDERS IN PRIMARY SCHOOL CHILDREN IN BOSNIA AND HERZEGOVINA. Mater Sociomed. 28(3):164-7. doi: 10.5455/msm.2016.28.164-167].

The global prevalence of arthritis is an important aspect that requires attention, as arthritis is the leading cause of disability in various countries, including the USA, Europe, Australia, Canada and Central Asian countries [DunlopD.D. et al. (2003) The costs of arthritis. Arthritis & Rheumatism. DOI: 10.1002/art.10913; Statistical compilation “Health of the population of the Republic of Tajikistan. 30 years of state independence”. https://www.stat.tj/en/news/publications/health-care-in-the-republic-of-tajikistan. Accessed 02 Feb 2023; National Statistical Committee of the Kyrgyz Republic (2023) Healthcare. Number of morbidity with acute and chronic diseases by main diseases groups. http://www.stat.kg/en/statistics/zdravoohranenie/. Accessed 02 Feb 2023]. An essential component of this study is examining the impact of the COVID-19 pandemic on morbidity and healthcare delivery patterns to rheumatic patients [Carbone T, Picerno V, Pafundi V, et al (2022) Impact of the COVID-19 Pandemic on the Appropriateness of Diagnostic Pathways of Autoimmune Rheumatic Diseases. J Rheumatol 49:219–224. https://doi.org/10.3899/jrheum.210611; Rebecca Grainger, Alfred H. J. Kim, Richard Conway, Jinoos Yazdany, and Philip C. Robinson. COVID-19 in people with rheumatic diseases: risks, outcomes, treatment considerations. Nat Rev Rheumatol. 2022; 18(4): 191–204. doi: 10.1038/s41584-022-00755-x]. The change in the traditional concept of reactive arthritis in the context of the COVID-19 pandemic needs to be emphasized, and there is a need to rethink approaches to the disease [Zeidler H, Hudson AP (2021) Reactive arthritis update: spot light on new and rare infectious agents implicated as patho gens. Curr Rheumatol Rep 23(7):53.https://doi.org/10.1007/s11926-021-01018-6].

**Aim of the study.**

To study clinical, sociodemographic characteristics of articular syndrome in rheumatic diseases and optimize tactics for diagnosing, treating, preventing reactive arthritis.

**Objectives of the study.**

1. To analyze and comparatively characterize morbidity of rheumatic and musculoskeletal diseases in Kazakhstan, particularly in the Turkestan region, in 2011-2020.

2. To present clinical and sociodemographic characteristics of articular syndrome in rheumatic diseases in the Turkestan region from 2019 to 2021.

3. To examine the effect of COVID-19 on the development of arthritis in case

studies, including those in the Turkestan region.

4. To survey knowledge and views of health professionals on diagnosis, prevention, and treatment of reactive arthritis using self-administered online questionnaire.

5. To develop recommendations for timely diagnosis, treatment, and prevention of reactive arthritis.

**Research methods.**

-Information-analytical study (study of annual statistical compilations of the MH RK from 2011 to 2020);

-Retrospective monocentric study (study of data of 370 patients);

-Clinical case series study (study of clinical cases of reactive arthritis in world practice);

-Cross-sectional study (creation, dissemination and interpretation of the questionnaire).

-Statistical methods (the SPSS software package version 26.0 (IBM) was used for statistical and mathematical data processing).

**Object of study.**

      The object of the study is reactive arthritis and articular syndrome in patients with rheumatic diseases.

**Scientific novelty.**

1. The study examined the impact of the COVID-19 pandemic on the development of reactive arthritis.
2. Clinical and socio-demographic characteristics of rheumatic diseases with joint syndrome in the Turkestan region from 2019 - to 2021 were presented.
3. Using a survey among rheumatologists and generalists from several countries, Kazakhstan, Turkey, Morocco, India, and Croatia, valuable data on managing patients with reactive arthritis during the COVID-19 pandemic was obtained.
4. An information sheet with recommendations for timely detection, treatment and prevention of patients with reactive arthritis has been developed.

**Practical significance of the results.**

1. Based on the newly obtained knowledge was an "Information sheet on timely detection, treatment and prevention of patients with reactive arthritis at the outpatient level", which was introduced for use in the clinical work of the polyclinic of "Regional Clinical Hospital" of Turkestan region, Shymkent city (Act of implementation, 2023), in the educational and methodical work of the department "GP-2" of JSC "South Kazakhstan Medical Academy" (Act of implementation, 2023), as well as in the educational and clinical work of LLP "Student Polyclinic", Shymkent city (Act of implementation, 2023).
2. According to the Scopus database, scientific articles with the results of this study were cited in 30 scientific papers at the international level.

**Positions put forward for defence.**

1. The total incidence of diseases of the musculoskeletal system and connective tissue increased 1.5 times in Kazakhstan in 2011-2020.

2. Delayed diagnosis of rheumatic diseases was longer during the onset of the COVID-19 pandemic, particularly in 2020, reaching 3-6 months, compared to a duration of no more than two months in 2019 and 2021.

3. COVID-19 can be associated with reactive arthritis, with post-COVID-19 reactive arthritis distinctive of its classic clinical form.

**Results.**

The results were presented in a series of articles:

1. "Revisiting articular syndrome in the peri-pandemic COVID-19 era" (Rheumatology International, Germany; Q2 according to Journal Citation Reports (Clarivate Analytics); first author, corresponding author);
2. Scientific publication "Reactive arthritis before and after the onset of the COVID-19 pandemic" (Clinical Rheumatology, UK; Q3 according to Journal Citation Reports (Clarivate Analytics); first author);
3. "Trends in the incidence of musculoskeletal diseases in Kazakhstan in 2011-2020: an information-analytical study" ("Rheumatology International", Germany; Q2 according to Journal Citation Reports (Clarivate Analytics); corresponding author, second author);
4. "Structure, demography, and medico-social characteristics of articular syndrome in rheumatic diseases: a retrospective monocentric analysis of 2019-2021 data" ("Rheumatology International", Germany; Q2 according to Journal Citation Reports (Clarivate Analytics); first author, corresponding author);
5. "Reactive arthritis following COVID-19: clinical case presentation and literature review" ("Rheumatology International," Germany; Q2 according to Journal Citation Reports (Clarivate Analytics); first author, corresponding author);
6. "Knowledge and Perceptions of Reactive Arthritis Diagnosis and Management Among Healthcare Workers During the COVID-19 Pandemic: Online Survey" (Journal of Korean Medical Science, Republic of Korea; Q2 according to Journal Citation Reports (Clarivate Analytics); first author).

As part of the fifth objective, an "Information sheet for physicians on the management of patients with reactive arthritis at the outpatient level", was developed, for which 3 acts of implementation and a copyright license were obtained in the Republic of Kazakhstan.

**Conclusions.**

1. An information-analytical study has shown that during the studied ten-year period, throughout Kazakhstan, there was an increase in the incidence of diseases of the musculoskeletal system and connective tissue, especially among people aged above 18 years. The general incidence in Kazakhstan increased by 1.4 times, and the primary incidence of the country's entire population increased by 1.5 times.

2. A study conducted in the Turkestan region of Kazakhstan (n=370) revealed that rheumatoid arthritis (49%) predominates among rheumatic diseases accompanied by articular syndrome, especially among women (53%). A retrospective monocentric study revealed a significant delay in diagnosing several rheumatic diseases, averaging 31.4 months. The delayed diagnosis was particularly noted during the onset of the COVID-19 pandemic in 2020 (3 to 6 months), compared to less than two months in 2019 and 2021.

3. While examining a series of clinical cases, the association between COVID-19 and subsequent development of articular syndrome in 10 to 48 days was reported. Clinical features of the articular syndrome were characterized by considerable heterogeneity, ranging from joint pain and swelling to more complex symptoms such as conjunctivitis and circular balanitis. Analysis of a series of clinical cases showed that the coronavirus infection can be viewed as a trigger of inflammatory arthritis.

4. A cross-sectional survey of health professionals revealed that more than half of the respondents knew about the definition of ReA and its origin. The study revealed that nearly half of the respondents believed that the triad of conjunctivitis, urethritis, and asymmetric oligoarthritis was the classic clinical picture of ReA. Over one-third reported dermatitis in addition to the classic triad. Among the tests used to examine the patients, C-reactive protein was the most commonly used (68,4%), followed by the Chlamydia trachomatis test (62,2%), and joint ultrasound (61,1%). NSAIDs were the most commonly used for the treatment (83.9%).

5. An information sheet on managing patients with reactive arthritis (COVID-19 is considered a trigger for ReA) was developed. The recommendations developed in the information sheet consider the current clinical protocol and include additions on diagnosis, differential diagnosis, prevention and treatment of reactive arthritis at the outpatient level.

**Approbation of the research results.**

Materials of the scientific research were presented at the conferences: 75th International Scientific and Practical Conference of medical students and young scientists "Modern medicine and pharmaceutics: new approaches and topical research", Samarkand city, Republic of Uzbekistan (May 18, 2021); International Scientific and Practical Conference "Science and Youth: New Challenges and Solutions", Almaty, Kazakhstan (April 22, 2022); IX International Scientific Conference of Young Scientists and Students "Prospects of Development of Biology, Medicine and Pharmacy", Shymkent, Kazakhstan (December 8-9, 2022); II-International Scientific and Practical Conference "Innovative Technologies in Healthcare: New Opportunities for Internal Medicine", city of Samarkand, Republic of Uzbekistan (April 7-8, 2023) and International Congress "Global Health" dedicated to the 25th anniversary of the founding of the Kazakhstan Medical University "HSPH" and the signing of the Agreement between the WHO Regional Office for Europe and the Ministry of Health of the Republic of Kazakhstan, Almaty, Kazakhstan (September 23, 2022). The results of the research were presented at a travel-grant competition. As a result, a travel-grant was received to participate in a seminar organized by EULAR and EMEUNET, held in Berlin on October 21-22, 2023.

**Personal contribution of the doctoral student.**

The author of the dissertation work conducted a literature review of modern databases on the problem of articular syndrome in rheumatic diseases and reactive arthritis. Based on the identified problem, the goals and objectives of the scientific study were formed, and the study's design, object and subjects were selected. The author also collected information about the object of research, analyzed the obtained results and formed appropriate conclusions. The author of the dissertation work participated in creating, piloting and disseminating an international online questionnaire for health professionals. In collaboration with other authors, several publications on the dissertation research topic were written and published.