ABSTRACT

of dissertation work of Kaidar Elmira Kaidarovna on the topic "Scientific justification of the effects of coronavirus infection on human health and medical care needs" for the academic degree of Doctor of Philosophy (PhD) on the specialty 8D10103 – «Public health»

Relevance of the study. On May 5, 2023, the World Health Organization (WHO, 2023) announced the end of the coronavirus pandemic. However, this did not eliminate concerns associated with COVID-19. Despite the announcement, new cases of coronavirus infection continue to be recorded worldwide, posing a serious public health problem. As of October 18, 2023, the cumulative number of registered COVID-19 cases worldwide exceeded 696 million (Worldometer Covid Tracker, 2023), indicating persistent uncertainty regarding the scale and long-term consequences of the disease.

According to the latest data, more than 700 million new cases of COVID-19 and 7 million deaths have been reported globally. In Kazakhstan, as of October 17, 2024, there were 1,411,831 confirmed cases and more than 13,848 deaths (Worldometer Covid Tracker, 2024). Nevertheless, COVID-19 incidence remained high in large cities of Kazakhstan such as Astana and Almaty (Statistical Bulletin of the Ministry of Health of the Republic of Kazakhstan, 2023).

Over time, it has become increasingly evident that individuals who have recovered from COVID-19 may experience prolonged consequences. Emerging data indicate that people who had COVID-19, especially in more severe forms, may face medium- and long-term health consequences, requiring appropriate medical attention (Saloner B., 2020; Arnold D., 2023).

In particular, pulmonary complications in hospitalized COVID-19 patients tend to persist for an average of 24 days after initial onset (Wang Y., 2020). Furthermore, evidence points to the development of cardiovascular diseases within 1–3 months after infection, and there are reports of irreversible kidney failure in individuals infected with COVID-19 (Puntmann V., 2020; Eiros R., 2023). Thrombotic complications such as deep vein thrombosis and pulmonary embolism are also recognized consequences (Cobos-Siles M., 2020). Acute kidney injury and renal failure have also been observed (Nugent J., 2021; Parpas A., 2021). Post-COVID complications may also include disorders of the digestive system (Ungaro R.C., 2021; Roth N.C., 2021; Durazo F.A., 2021). These manifestations may occur in the early stages of the disease or as long-term sequelae (Chen R., 2020; Martin T., 2020; Zhong P., 2020).

At the onset of the pandemic, the emergence and spread of the novel respiratory pathogen were accompanied by uncertainties regarding its key epidemiological and clinical characteristics, particularly its ability to spread among populations (Abdelmohsen M., 2020; Wu F., 2020; Zhou P., 2020). Globally, a significant number of studies were conducted on the acute phase of the disease. However, comprehensive studies assessing the long-term consequences of COVID-19 for public health remain limited (Chan L., 2024), as does information on the impact of disease severity on population health. Moreover, there is insufficient research in Kazakhstan on the development of complications after COVID-19.

The COVID-19 pandemic has become a global challenge for healthcare systems worldwide (WHO, 2024). The rapid spread of the virus, the increase in severe cases, and the need to adapt to new conditions led to substantial changes in the organization of medical care (Anderson M., 2020; Breitenbach M.C., 2021). Both the demand for medical services and for healthcare personnel played an important role in this adaptation (Dedeilia A., 2023). In a number of countries affected by large-scale COVID-19 waves, crisis response measures were undertaken to support health systems (Boccia S., 2020; Halm A., 2021). At the same time, in countries with limited resources, COVID-19-related mortality was high (Kuppalli K., 2021; Bigoni A., 2022).

Analyzing the demand for medical care and assessing the impact of COVID-19 on human health are complex tasks, as the severity of the disease was largely associated with the individual's pre-pandemic health status. Hospitalization, as reported in the literature, was more frequently required in patients with severe forms of the disease and was mainly related to sex, age, and the presence of comorbidities (Zhang H., 2022).

The results of this study will play an important role in shaping decisions regarding COVID-19 containment, as well as in understanding the health consequences of COVID-19 in recovered patients and their need for medical care in the post-COVID period. The data may also contribute to planning further actions to combat the virus in the event of future outbreaks, both in Kazakhstan and globally, and may serve as a foundation for developing preventive measures aimed at reducing post-COVID complications.

Purpose of the study is to assess the impact of COVID-19 on public health and the healthcare system in Kazakhstan in order to develop scientifically grounded measures to minimize the consequences of the pandemic.

Research objectives:

1. To analyze the dynamics of public health indicators in Kazakhstan during the COVID-19 pandemic and to assess the performance of the healthcare system.

2. To study and determine the epidemiological characteristics of COVID-19 among individuals with confirmed and probable diagnoses, as well as the level of prevalence considering comorbidities and complications.

3. To assess the quality of life of patients one year after recovering from coronavirus infection.

4. To study and determine the impact of COVID-19 severity on the development of health consequences in patients.

5. To develop methodological recommendations for organizing medical and social assistance for patients with post-COVID complications at the level of primary healthcare.

Research Materials: Official statistical data on morbidity and mortality, global ranking databases (Web of Science, Scopus, PubMed), confirmed COVID-19 case databases of the Ministry of Health of the Republic of Kazakhstan (MOH RK), healthcare information systems (ERHP - Electronic Register of Hospitalized Patients, UPS - Unified Payment System).

Research Methods: Epidemiological analysis, comprehensive quantitative analysis (quasi-experimental) (ITSA), statistical modeling (AAPC), indicator analysis,

prospective cohort study, quantitative analytical cross-sectional study, statistical methods.

Research Object: Public health indicators of Kazakhstan (morbidity, mortality, healthcare system indicators: hospitalization, bed occupancy, bed availability, medical staff availability, etc.). Patients – confirmed COVID-19 cases with positive PCR test results, probable COVID-19 cases with negative PCR test results; Contacts – close contacts living in the same household with COVID-19 cases; Data from healthcare information systems regarding the health status of patients included in the study (ERHP, UPS).

1. Review of the literature. International databases MEDLINE (PubMed), Web of Science, Scopus, ScienceDirect, and Elsevier have published the studied data. The search was carried out using the following keywords: "COVID-19" AND "clinical characteristics", "epidemiology of COVID-19" OR "epidemiology of coronavirus disease", "risk factors of COVID-19" AND "comorbidities", "close contacts of COVID-19" AND "basic reproductive number of COVID-19" OR "transmission" OR "secondary attack rate", "COVID-19" AND "quality of life", "long COVID-19" OR "post-COVID-19 symptoms" OR "complications of COVID-19" OR "effect of COVID-19" "impact of COVID-19" AND "health".

2. Analysis of public health indicators in Kazakhstan during the COVID-19 pandemic and assessment of the healthcare system of the Republic of Kazakhstan from 2018 to 2023. The study used Interrupted Time Series Analysis (ITSA) for the period 2018 – Q2 2024 for morbidity and monthly data from 2018 to August 2024 for mortality to evaluate morbidity and mortality dynamics, examined healthcare system load including bed occupancy, bed and staff availability, and access to medical services during the pandemic and post-pandemic periods. Average Annual Percent Change (AAPC) was calculated with confidence intervals and p-values for annual changes.

3. A prospective study of confirmed and probable COVID-19 cases, including 487 participants: 172 patients (122 confirmed and 50 probable COVID-19 cases of varying severity) and 315 close contacts residing in the same household as the cases in Astana. The study followed the WHO protocol: "Investigation of confirmed and probable SARS-CoV-2 cases and their close contacts in Kazakhstan." Participant enrollment occurred from November 26, 2020, to February 15, 2021. All participants were tested by PCR and ELISA upon inclusion and again 14-21 days later.

Primary cases were selected from the confirmed COVID-19 case database of the MOH RK, and close contact data were reported by the patients themselves.

Inclusion criteria: voluntary participation and signed informed consent; for cases - positive PCR test; for contacts - negative PCR test and absence of symptoms at inclusion; for probable COVID-19 cases - presence of symptoms, CT or X-ray confirmation of pneumonia, negative PCR test. Participant age: 0 to 90 years.

Exclusion criteria: voluntary withdrawal by the participant or legal representatives/guardians; failure to provide follow-up PCR and ELISA tests.

Epidemiological data were collected via interviews during hospitalization, home visits, or telephone for those in self-isolation. Data included age, gender, ethnicity, occupation, household size, contact date, comorbidities, symptoms and onset, travel history. WHO-developed questionnaires were used (Appendices A and B).

Additionally, 5 ml blood samples were collected for ELISA testing between days 1-7 and again on days 14-21 post-inclusion. IgM and IgG antibody levels were measured. ELISA was not used for case categorization but served as a diagnostic confirmation. Nasopharyngeal swabs were repeated 14-21 days post-inclusion to assess infection or virus persistence using PCR.

4. In April 2022, 1.5 years after the inclusion of the first case, a quality-of-life assessment was conducted using the SF-36 survey, which includes 36 questions and 8 scales: Physical Functioning (PF), Role Physical Functioning (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). Scores range from 0 to 100, with 100 indicating optimal health. Data analysis was done using MS Excel and SPSS version 23, including mean, standard deviation, and percentage calculations. Validity and reliability of the SF-36 were tested.

Inclusion criteria: participants who consented in the first stage of the study. Exclusion criteria: voluntary withdrawal, deceased participants, or those difficult

to follow due to rehospitalization for complications.

5. A prospective analysis (March 1, 2021 - October 12, 2022) assessed COVID-19 severity impact on post-COVID complications requiring medical care. Data sources included ERIP and UPS. A new Excel database was developed including medical services provided, new diagnoses, treatment outcomes, and complications in hospitalized patients. Associations between complications and gender, age, comorbidities, level of care at inclusion (PHC, hospital), and readmissions were analyzed.

Participants were divided into two cohorts: 118 hospitalized patients and 364 outpatients with mild/asymptomatic COVID-19. Correlations were assessed using chisquare test and logistic regression. Propensity Score was calculated considering gender, age, and comorbidities (obesity, diabetes, cardiovascular and chronic lung diseases) to estimate hospitalization probability. Bonferroni correction (p=0.004) was applied. Odds Ratios (OR) were used to compare diagnoses among hospitalized versus mild cases. Analysis was performed in SPSS v23.

Scientific novelty of the study

For the first time in Kazakhstan, a comprehensive study of the consequences of COVID-19 has been conducted, including the analysis of epidemiological indicators, the quality of life of patients, the impact of COVID-19 severity on subsequent health, and the development of recommendations for primary healthcare.

1. A comprehensive analysis of the impact of the COVID-19 pandemic on key health indicators of the population of Kazakhstan was carried out, which made it possible to identify changes in the structure of morbidity and mortality, as well as to determine the main epidemiological trends related to the pandemic and its consequences.

2. The epidemiological characteristics of COVID-19 and its prevalence among individuals with confirmed and probable diagnoses were identified, taking into account comorbidities and complications.

3. The quality of life of patients one year after recovering from coronavirus infection was assessed, which made it possible to identify key issues related to post-COVID recovery, including functional and social limitations.

4. The impact of COVID-19 severity on the health consequences of patients was studied and determined, enabling clarification of patient needs in the post-pandemic period.

5. Methodological recommendations were developed for the organization of medical and social assistance for patients who have recovered from COVID-19 at the level of primary healthcare, aimed at improving the quality of medical services.

Research Subject: Epidemiological and organizational impacts of COVID-19 on public health and the healthcare system in Kazakhstan.

Practical significance

Results can inform healthcare resource planning, epidemic response strategies, bed allocation, rehabilitation development, and disease monitoring at regional and national levels. Applicable in training public health professionals. Results support follow-up of severe COVID-19 patients, improved surveillance, care algorithms, and strategies to enhance patient quality of life.

Theoretical significance of the study

Findings expand understanding of health and quality of life in post-COVID patients. Useful for developing modern approaches to medical and social care for post-COVID complications, and can be used in academic lectures and case-based learning.

Research Base: State Enterprise "City Polyclinic No. 4", Clinical Laboratory of Nur-Sultan (Astana), City Multidisciplinary Hospital No. 2 of Nur-Sultan (Astana).

Main provisions submitted for the defense of the dissertation

1. The COVID-19 pandemic had a significant impact on the health of the population of Kazakhstan, which necessitates the study of its long-term consequences and the development of measures to minimize them.

2. Among close contacts living in the same household with an infected individual, 98% tested positive for COVID-19. However, it cannot be definitively concluded that secondary cases were infected within the household from the primary case, as transmission may have occurred in other public settings such as workplaces or crowded locations.

3. The impact of the consequences of a past COVID-19 infection on individuals' health status and quality of life is reliably substantiated. Individuals who have recovered from COVID-19, regardless of gender and age, assess their overall health as below satisfactory after the illness.

4. It was found that the severity of COVID-19 has a direct effect on the development of subsequent diseases, which necessitates the implementation of mechanisms for early detection and long-term monitoring of patients during the post-pandemic period.

5. Scientifically grounded methodological recommendations have been developed for organizing medical and social assistance at the primary healthcare level for patients who have recovered from COVID-19. These include the advancement of multidisciplinary approaches for follow-up of patients who had severe forms of infection, the implementation of proactive prevention models (such as early detection of post-COVID complications), psychological support, and remote patient monitoring, all of which aim to improve the healthcare system's resilience and adaptability to the longterm effects of the pandemic.

Approbation of the dissertation

The dissertation work's primary provisions are discussed during:

1. International Conference – The 8th International Conference on Public Health 2022 (ICOPH 2022) "The impact of COVID-19 on public health, the economy and the public sector: solving the problems of the present and shaping the future" (Malaysia, July 28-29, 2022);

2. International Scientific Conference – Modern scientific technology (Sweden, October 13-14, 2022);

3. V International Conference, "World science priorities" (Vienna, Austria, 10-11.08.2023).

Personal contribution of the candidate of Ph.D.

At the PHC level in the Republic of Kazakhstan, she independently gathered information, carried out a sociological survey of study participants, and contributed to the creation of recommendations to stop health decline and enhance the quality of life for patients who have complications from coronavirus infection.

She conducted the statistical processing, analysis, and generalization of the collected data on her own. She also gathered literature on the dissertation topic. Participation in scientific conferences on the dissertation's subject and publishing in scholarly journals attest to the author's contribution to the study.

Implementation into practice

The results of the dissertation work have been put into practice in the following organizations:

1. "City polyclinic No. 8" of the Public Health Department of the Akimat of Astana (act of implementation on methodological recommendations dated 04/18/2023);

2. "Dostyk PHC Center" of the Public Health Department of the Akimat of Astana (act of implementation on methodological recommendations dated 04/17/2023);

3. "City polyclinic No. 6" of the Department of Public Health of the Akimat of Almaty (act of implementation on methodological recommendations dated 04/20/2023);

4. "City polyclinic No. 1" of the Department of Public Health of the Akimat of the Kyzylorda region (act of implementation on methodological recommendations dated 04/20/2023);

5. "City polyclinic No. 3" of the Department of Public Health of the Akimat of the Kyzylorda region (act of implementation on methodological recommendations dated 04/20/2023);

6. The Yessil District Hospital of the Department of health of the Akmola region (act of the implementation on methodological guidelines dated 04/21/2023);

7. The Atbasar Multidisciplinary Interdistrict Hospital of the Department of Health of the Akmola region (act of the implementation on methodological guidelines dated 04/17/2023).

Publications

According the dissertation's subject seven (seven) scientific papers has been published, including:

- 1 (one) journal article indexed in the Scopus database "The impact of COVID-19 severity on health in Kazakhstan: a prospective cohort study" Journal of Clinical Epidemiology and Global Health;

- 3 (three) - in publications recommended by the Committee for Quality Assurance in Education and Science of the Ministry of Higher Education and Science of the Republic of Kazakhstan (1) "Review of the main clinical and epidemiological characteristics of COVID-19", Science and Healthcare, Peer-reviewed Medical Scientific and Practical Journal 6 (Volume 23), 2021. 2) "Assessment of quality of life through a year after COVID-19 cases using the SF-36 questionnaire", Journal of Clinical Medicine of Kazakhstan 19(6):13-17, 2022. 3) the frequency of occurrence of primary confirmed and probable causes of COVID-19 (using the example of Astana), Journal of Health Development 4 (49), 2022);

- 3 (three) abstracts at the International Scientific and practical forum (1) "Clinical and epidemiological characteristics of COVID-19 in Kazakhstan", 8th International Conference on Public Health 2022 (ICOPH 2022), "The impact of COVID-19 on public health, the economy and the public sector: solving current and shaping the future" (Malaysia, July 28-29, 2022) – nomination "**Best poster presentation''**, "Grammy" – the best space report. 2) "Assessment of health status after COVID-19 using the SF-36 questionnaire", Modern Scientific Technologies (Sweden, October 13-14, 2022); 3) "Using ARIMA and SARIMA models to predict new COVID-19 cases in Kazakhstan", V International Scientific Conference "Priorities of World Science" (Vienna, Austria, 10-11.08.2023)).

- 2 (two) methodological recommendations (Guidelines for the organization of medical and social care for patients with post-covid syndrome at the primary health care level in Russian and Kazakh languages) (Minutes of the meeting of the Scientific and Technical Council of the Scientific Research Institute of Balneology and Medical Rehabilitation of the Ministry of Health of the Republic of Kazakhstan, Protocol No. 2 dated 06/28/2023.);

- 4 (four) author's certificates (1) "Investigation of confirmed and probable SARS-COV-2 cases and contacts in the Republic of Kazakhstan" No. 28229 dated 08/10/2022; 2) "Guidelines for the organization of medical and social care for patients with postcovid syndrome at the primary health care level" No. 35856 dated 05/16/2023; 3) "Behavioral aspects of COVID-19 in Kazakhstan. Monitoring awareness, risk perception, models of preventive behavior and confidence levels to support the response to the outbreak of the pandemic" No. 37151 dated 06/14/2023); "Guidelines for the organization of medical and social care for patients with postcovid syndrome at the primary health care levels to support the response to the outbreak of the pandemic" No. 37151 dated 06/14/2023); "Guidelines for the organization of medical and social care for patients with postcovid syndrome at the primary health care level in Kazakh language" No. 52316 dated 12/06/2024.

Findings

The study's findings led to the following deductions being made.

1. COVID-19 significantly increased overall mortality in Kazakhstan in 2020-2021, followed by gradual decline. Mortality rose by 3,2 per 1 000 population post-June 2020 intervention (p < 0,001), then declined by 0,09 monthly (p < 0,001). Statistically significant increases occurred in circulatory (0,74/1000, p<0,001), respiratory (0,556/1000, p=0,001), infectious (0,083/1000, p=0,006), and digestive diseases (0,112/1000, p=0,001). Overall morbidity remained stable (p > 0,05) but spiked 37% in

Q4 2020, then declined 3,72% annually (p < 0,01). Increases were noted in endocrine system diseases (+5,41%/year, p<0,001) and musculoskeletal diseases (+1,98%/year, p<0,01), with mental health disorders steadily rising (3,06%/year, p=0,085). Peak demand occurred in 2021 (416 000 COVID-19 hospitalizations, 42 600 ICU admissions). Rehabilitation needs surged by 105% annually in 2020–2021 but sharply declined by 2023. Chronic shortages were identified in psychiatric/endocrinology beds and specialists (2018–2023).

2. 98% of close contacts tested positive by PCR or ELISA. COVID-19 serial interval averaged 4,02 days (SD 2,52), 4,43 for PCR-positive and 3,21 for PCR-negative cases. Reproductive number Rt was 1,43 [95% CI=1,27-1,59] for confirmed and 0,96 [95% CI=0,70-1,22] for probable cases, highlighting diagnostic accuracy and control measures like vaccination, testing, and isolation. Misclassification risk exists due to lack of viral genetic studies.

3. Mental health, pain, physical/social functioning, vitality, and general health scores inversely correlated with age. Men reported better post-COVID health than women (p<0,05). Mental health scores were similarly low for both sexes. Mean HRQoL score was $45,89\pm10,37$, below average and lower than in other countries, possibly due to sample specifics and COVID-19 effects.

4. Severe COVID-19 led to higher medical care needs for respiratory diseases (OR=2,37, 95% CI 1,35-4,16, p=0,003), eye diseases (OR=5,60, 95% CI 1,96-15,98, p=0,001), infectious diseases (OR=6,61, 95% CI 1,84-23,75, p=0,004). Hospitalization was more frequent among severe cases (OR=3,49, 95% CI 1,78-6,84, p<0,001), confirming the need for long-term monitoring and support of post-COVID patients. These complications may be part of the post-COVID-19 syndrome.

5. The developed methodological recommendations will enable the most effective organization of medical care for patients in the post-COVID period, with an emphasis on the early detection of post-COVID complications, extended follow-up, and ensuring access to medical services and psychological support for patients who have experienced a severe form of coronavirus infection.

Practical recommendations

The results and conclusions of this study are applicable for healthcare managers as well as general practitioners and are recommended for use in planning medical care and improving the early detection of complications associated with coronavirus infection.

1. It is necessary to develop and implement a unified database for recording conditions related to previous COVID-19 infections, including post-COVID complications. This will enhance data monitoring and analysis.

2. Develop and implement incentive mechanisms for healthcare workers for accurate diagnosis coding, particularly regarding complications following COVID-19.

3. Introduce screening programs for the early detection of post-COVID complications.

4. Improve educational programs for healthcare personnel and the general population to raise awareness about post-COVID complications and their prevention.

5. Include training on the management of patients with long-term consequences of COVID-19 in the educational curricula of physicians and mid-level

healthcare workers.

6. Consider ensuring access to qualified psychological support, especially for patients with mental health disorders following COVID-19.

7. Conduct monitoring of the adequacy of psychiatric bed capacity, including the development of alternative forms of care: opening mental health offices and centers with ensured access for the population. Increase the number of psychiatrists, psychotherapists, and medical psychologists.

8. Evaluate the adequacy of bed capacity in endocrinology and gastroenterology. Study the effectiveness of outpatient care as an alternative to hospitalization. Restore bed availability to the minimum standard (0.3 per 1,000 population). Reconsider the organization of endocrinological and gastroenterological services, and explore the development of specialized departments for "borderline" clinical profiles. Introduce modern treatment protocols.

9. Strengthen vulnerable healthcare areas (endocrinology, gastroenterology, psychiatry, rehabilitation) by training medical personnel in these fields, and consider the growth of chronic diseases when planning infrastructure development across regions.

10. When developing rehabilitation programs, gender differences should be considered, as women may require more intensive support after recovering from COVID-19.

Structure and Volume of the Dissertation: The dissertation is presented on 125 pages (excluding appendices) and includes the following sections: introduction, literature review, materials and methods, research results and discussion, ways to strengthen the healthcare system in the post-pandemic period, conclusion, and practical recommendations. The manuscript includes 24 tables, 24 figures, and 7 appendices. The reference list consists of 188 sources, of which 90% (170) are in English and 10% (18) in Russian and Kazakh.