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Epidemiological Features of Diabetes in Kazakhstan in 2018-2021 (Population Study)

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Abstract

Background: During the COVID-19 pandemic, patients with diabetes are among the most vulnerable. Our purpose is to research the dynamics of morbidity, mortality, and survival of patients with diabetes in Kazakhstan before and during the current pandemic.

Methods: The indicators were calculated taking into account gender and nosological forms (E10-E14, according to ICD-10).The survival analysis was performed by the method of constructing survival tables and the Kaplan-Meier method. Based on methods, the official reporting data of 1,903,243 cases of diabetes and 20,605 deaths from diabetes were analyzed for the period 2018-2021.

Results: In Kazakhstan, during the COVID-19 pandemic, there has been an increase in the absolute frequency of all cases of diseases by 1.8 times (716,048 in 2021 against 396,990 in 2018) and newly detected by 2.0 times (from 38,396 to 75,027), also prevalence by 1.7 times (3743.9 in 2021 against 2142.2 in 2018) and incidence E10-E14 by 1.9 times (392.3 in 2021 against 207.2 in 2018). Mortality from E10-E14 in Kazakhstan increased during the pandemic by more than 1.5 times (34.1 per 100,000 in 2021 against 22.3 per 100,000 in 2018), and the average survival time at E10-E14 shifted (from 69.8 to 70.5 years) ($P = 0.001$).

Conclusion: To a greater extent, the increase in diseases and terminal outcomes occurred due to non-insulin-dependent type (E11) diabetes, mainly in the female population.

Keywords: COVID-19, Diabetes, E10-E14, Incidence, Prevalence, Mortality, Survival

Conflicts of Interest: *None declared*
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Introduction

The high rate of deaths due to coronavirus infection in patients with diabetes mellitus (DM) has become a serious challenge for the medical community in general and public health in particular.

DMmaydevelop at any age and peaks in people aged 65 years and older (1), but now type 2 diabetes, traditionally considered a disease of middle and older age, is increasingly being diagnosed in younger age groups (2).

According to IDF estimates, the prevalence of Diabetes Mellitus will increase from 537 million people worldwide in 2021 to 783 million by 2045 (3). According to the International Classification of Diseases (ICD-10), diabetes has several types. Forms of DM are classified according to the type of hypoglycemic therapy: (1) insulin-dependent type (E10) and (2) insulin-independent type (E11), (3) DM associated with malnutrition (E12), other (4) specified forms of DM (E13) and (5) unspecified form DM (E14) are also diagnosed.The division of diabetes into

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↑What is "already known" in this topic:
Scientific evidence shows an increase in the incidence of diabetes and a higher risk of death in the presence of coincident coronavirus infection.

→What this article adds:
The study confirmed the epidemiological trends in diabetes mellitus during the current pandemic. Health policy should develop a differentiated approach to patients of this group of nosologies.

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types 1 and 2 is due to pathogenetic mechanisms.Type 1 DM is the destruction of pancreatic β-cells, which leads to absolute insulin deficiency, while type 2 is associated with a progressive impairment of insulin secretion against the background of insulin resistance (4).

Type 2 diabetes and its associated complications account for 8.4% of deaths worldwide, the disease absorbs significant healthcare resources (5), and this situation is likely to worsen given the increasing prevalence of the disease (3).Despite modern methods of diagnosis, monitoring, and treatment, type 2 diabetes is associated with high mortality rates (6).

On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. This decision was based on the level of spread, the severity of the course, and untimely measures taken due to the lack of experience in providing medical care during the rapid spread of a little-known viral infection (7).

Because COVID-19 is a new disease, the theoretical foundations and practical applications are incomplete and under development.Many case-control studies have shown that in COVID-19 patients who had a history of diabetes mellitus, infectious pathology acquired a severe clinical course and was associated with high risks of death.However, most of these studies have small sample sizes, and the results obtained are heterogeneous and inconsistent. In addition, prevalence data of diabetes in COVID-19 patients also do not have a clear picture (8).

The causes of death can be associated with several factors, among which are: features of the state of the immune status and immune response to the effects of the virus in conditions of hyperglycemia, the presence of excess weight, and comorbidities.It should be noted that hypertension, coronary heart disease, and diabetes are significant risk factors for death among patients with COVID-19 (9).

There are studies confirming that long-term mortality from community-acquired pneumonia among patients with undiagnosed DM was higher than in patients without diabetes (10).

Some systematic reviews have data on mortality among hospitalized patients with comorbidity of COVID-19 and diabetes, ranging from 4% to 13% (11).

According to some scientific studies, the overall prevalence of DM in patients with COVID-19 was 9% (95% CI 6%-12%), with obvious heterogeneity. The prevalence of DM patients with moderate severity with 2019-nCoV was 7% (95% CI 4%-10%), while in severe 2019-nCoV patients, it was 17% (95% CI 13%-21%). The prevalence of DM in patients with severe 2019-nCoV was significantly higher than in patients with moderate 2019-nCoV (12).

According to Kazakhstan sources, the number of patients with diabetes doubles every 10 years (13).Despite an effective program of guaranteed volume of free medical care, it was not possible to control the prevalence of this disease and reduce the risks of complications.The coronavirus pandemic has divided the healthcare system of Kazakhstan into a “pre-pandemic” and “post-pandemic” period. Patients with diabetes were the most vulnerable group under the aggression of the virus, and the number of deaths and mortality rates tended to increase.

It should be noted that there is a lack of scientific data reflecting the real situation in Kazakhstan on the issue in question in the context of the current pandemic. The current situation that has affected the Healthcare of Kazakhstan has become an occasion for a detailed study of the specifics of the dynamics of morbidity, mortality, and survival in patients with diabetes in the Republic of Kazakhstan before and during the COVID-19 pandemic.

Methods

This article shows a retrospective study using descriptive and analytical statistics.The main sources of information are the official reporting data of the Ministry of Health on the number of diabetes cases (Form No. 15 “Report on the number of diseases registered in patients living in the service area of a medical organization and contingents of patients under dispensary observation”) and register data of the Ministry of Economy (“ Register of attached population") on cases of death from diabetes ("Register of death certificates") in the Republic of Kazakhstan for the period 2018-2021.

We study the frequency of cases of diabetes (including primary) and terminal cases from this pathology in the whole Republic, and also taking into account gender and type of diabetes (blocks E10-E14, according to ICD-10). The calculation of intensive and extensive indicators is carried out with a characteristic standard mean square error.Morbidity and mortality rates are calculated according to the generally accepted methodology (per 100,000 population). To calculate the medical and statistical indicators of demographic data uses, the Agency on Statistics of the Republic of Kazakhstan, in terms of population coverage (Table 1).

To perform the survival analysis, the method of constructing survival tables and the Kaplan-Meier methodswereused (mean and median survival time, the proportion of "survivors", and the survival function).The temporary variable is age (age survival). All deaths are uncensored data. Differences in survival were studied depending on the year of the declaration of death, by sex, by age (age groups with an interval of 10 years), taking into account the place of death (in a hospital, at home, elsewhere) and taking into account nosological forms (by blocks E10 - E14). Comparative analyzes are performed using the Wilcoxon (Gehan) test and the Log Rank, Breslow (Generalized Wilcoxon) and Tarone-Ware tests. The null hypothe-

Table 1. Population of the Republic of Kazakhstan (2019-2022)

Population Kazakhstan	Asof 01/01/2019	Asof 01/01/2020	Asof 01/01/2021	Asof 01/01/2022
Total	18 531 852	18 916 678	19 183 986	19 125 620
Men	8 913 012	9 112 651	9 250 976	9 288 350
Women	9 618 840	9 804 027	9 933 010	9 837 270

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sis is rejected (no difference) in favor of the alternative at $P < 0.05$.

Microsoft Excel programs and the IBM SPSS Statistics package served as a tool for the statistical processing of the obtained data.

Results

We analyze the frequency of E10-E14 diseases among the Kazakhstan population (including by sex) in the period 2018-2020 (Table 2). To compare diabetes trends, we divide the data into two periods: 2018-2019 (before the COVID-19 pandemic) and 2019-2021 (current pandemic period).

It has been established that in the period of 2018-2019, a downward trend is characteristic of both the absolute frequency of cases (the rate of decrease is 0.5%) of diseases and the prevalence rate (the rate of decrease is 2.5%) E10-E14. Along with this, the number of primary cases of diseases and the incidence rate E10-E14 increased in the period 2018-2019 (growth rate of 21% and 18.6%, respectively).It should be noted that in 2018-2019, the prevalence rate and incidence rate for E10-E14 in the female population significantly exceeded those in the male population, on average 1.6 and 1.4 times, respectively. It should also be noted that in the general Kazakhstan population (including men and women) non-insulin-dependent type (E11) diabetes is the most common.

In the period 2020-2021, there was an increase in the absolute frequency of cases of E10-E14 diseases.The absolute increase in diseases in 2020 was due to E10 and E11, and in 2021 due to all types of diabetes (including unspecified types of diabetes).Noteworthy is the recorded level of E10-E14 diseases in 2021.The growth rate in 2021 compared to 2020 was 81.2%. The prevalence rate in 2020 (the first year of the pandemic) decreased slightly. However, in 2021 (the second year of the pandemic), it increased by 1.7-1.8 times compared to 2018-2019.The growth rate of primary cases and the incidence of E10-E14 in 2020-2021 were90.2% and 90.8%, respectively.It

Table 2. The incidence of diseases and the incidence rate of diabetes in the Republic of Kazakhstan (2018-2021)

Categories ICD-10	Beforethe COVID-19 pandemic				Period of the current pandemic			
	2018		2019		2020		2021	
	abs. number	per 100,000	abs. number	per 100,000	abs. Number	per 100,000	abs. number	per 100,000
Totaldiseases	396990	2142.2	394919	2087.7	395286	2060.5	716048	3743.9
E10	31195	168.3	25564	135.1	27227	141.9	41042	214.6
E11	363728	1962.7	367604	1943.3	367226	1914.2	671356	3510.2
E12-E14	2067	11.2	1751	9.3	833	4.3	3650	19.1
Men	142066	1593.9	145216	1593.6	142372	1539.0	255858	2754.6
E10	15172	170.2	12819	140.7	13612	147.1	19938	214.7
E11	126146	1415.3	131641	1444.6	128418	1388.2	234462	2524.3
E12-E14	748	8.4	756	8.3	342	3.7	1458	15.7
Women	254924	2650.3	249703	2546.9	252914	2546.2	460190	4678.0
E10	16023	166.6	12745	130.0	13615	137.1	21104	214.5
E11	237582	2470.0	235963	2406.8	238808	2404.2	436894	4441.2
E12-E14	1319	13.7	995	10.1	491	4.9	2192	22.3
Primary causes	38396	207.2	46476	245.7	39447	205.6	75027	392.3
E10	1706	9.2	2112	11.2	2140	11.2	3208	16.8
E11	36624	197.6	43945	232.3	37097	193.4	71151	372.0
E12-E14	66	0.4	419	2.2	210	1.1	668	3.5
Men	15344	172.2	18720	205.4	16442	177.7	30217	325.3
E10	957	10.7	1090	12.0	1109	12.0	1611	17.3
E11	14377	161.3	17486	191.9	15259	164.9	28364	305.4
E12-E14	10	0.1	144	1.6	74	0.8	242	2.6
Women	23052	239.7	27756	283.1	23005	231.6	44810	455.5
E10	749	7.8	1022	10.4	1031	10.4	1597	16.2
E11	22247	231.3	26459	269.9	21838	219.9	42787	434.9
E12-E14	56	0.6	275	2.8	136	1.4	426	4.3

Table 3. The incidence of deaths and the mortality rate from diabetes in the Republic of Kazakhstan (2018-2021)

Categories ICD-10	Beforethe COVID-19 pandemic				Period of the current pandemic			
	2018		2019		2020		2021	
	abs. number	per 100,000	abs. number	per 100,000	abs. number	per 100,000	abs. number	per 100,000
Total	4130	22.3	4219	22.3	5731	29.9	6525	34.1
E10	592	3.2	525	2.8	716	3.7	845	4.4
E11	3461	18.7	3637	19.2	4921	25.7	5619	29.4
E12-E14	77	0.4	57	0.3	94	0.5	61	0.3
Men	1453	16.3	1499	16.4	2167	23.4	2371	25.5
E10	243	2.7	229	2.5	312	3.4	302	3.3
E11	1172	13.1	1245	13.7	1818	19.7	2043	22.0
E12-E14	38	0.4	25	0.3	37	0.4	26	0.3
Women	2677	27.8	2720	27.7	3564	35.9	4154	42.2
E10	349	3.6	296	3.0	404	4.1	543	5.5
E11	2289	23.8	2392	24.4	3103	31.2	3576	36.4
E12-E14	39	0.4	32	0.3	57	0.6	35	0.4

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should be noted that the DM prevalence (including newly diagnosed) in the female population is significantly higher than in the male population, on average of 1.4 times.

Also, we analyze the frequency of deaths from E10-E14 diseases among the Kazakhstan population (including by sex) for two periods: 2018-2019 and 2020-2021 (Table 3).

Based on the results of the analysis, it is found that for the Kazakhstan population in the period 2018-2019, the number of deaths from diabetes increased slightly, and stable dynamics of the mortality rateweretypical.The growth rate of deaths from E10-E14 was 2.2%.

In 2020-2021 the number of E10-E14 deaths have been increasing in Kazakhstan.The intensity of the increase in deaths from E10-E14 and the mortality rate was 13.9% and 14.1%, respectively.At the same time, in the female population, the frequency of E10-E14 deaths is on average 1.4 times higher compared to the male population.

At the final stage of the study, we perform an analysis of survival at E10-E14 among the Kazakhstan population (including by gender) for 2018-2021, taking into account the time of occurrence / course of the pandemic.We calculate average survival rates (Table 4) and the probability of

Table 4. Average and median survival in diabetes mellitus in the Republic of Kazakhstan (2018-2021), in years

Categories ICD-10	Beforethe COVID-19 pandemic				Period of the current pandemic			
	2018		2019		2020		2021	
	Average	Median	Average	Median	Average	Median	Average	Median
Total	70.5	71.0	70.1	71.0	69.7	70.0	69.8	71.0
E10	65.2	67.0	61.9	65.0	62.2	65.0	63.8	67.0
E11	71.5	72.0	71.4	72.0	70.8	71.0	70.8	71.0
E12-E14	63.1	68.0	62.9	66.0	65.0	68.0	67.3	68.0
Men	67.1	68.0	66.6	68.0	66.8	68.0	67.2	68.0
E10	61.0	63.0	56.5	60.0	59.5	62.0	60.1	63.0
E11	68.7	69.0	68.5	69.0	68.2	68.0	68.2	69.0
E12-E14	56.3	64.0	61.0	63.0	60.7	65.0	68.4	70.0
Women	72.3	74.0	72.0	73.0	71.4	72.0	71.3	72.0
E10	68.1	71.0	66.0	69.0	64.3	68.0	65.8	69.0
E11	73.0	74.0	72.9	73.0	72.4	73.0	72.2	72.0
E12-E14	69.8	70.0	64.4	68.0	67.8	69.0	66.5	66.0

Table 5. Indicators of the proportion of deaths and survival function in diabetes in the Republic of Kazakhstan (2018-2021)

Age(years)	Beforethe COVID-19 pandemic				Period of the current pandemic			
	2018		2019		2020		2021	
	Proportionof-deaths	Survivalfunc-tion	Proportionof-deaths	Survivalfunc-tion	Proportionof-deaths	Survivalfunc-tion	Proportionof-deaths	Survivalfunc-tion
				Total				
0-10	0	1	0	1	0	1	0	1
10-20	0	1	0	1	0	1	0	1
20-30	0	0.99	0	0.99	0	0.99	0.01	0.99
30-40	0.01	0.98	0.01	0.98	0.01	0.98	0.01	0.98
40-50	0.03	0.96	0.03	0.95	0.03	0.95	0.03	0.96
50-60	0.11	0.85	0.11	0.84	0.12	0.83	0.11	0.85
60-70	0.34	0.56	0.34	0.55	0.36	0.54	0.36	0.55
70-80	0.59	0.23	0.57	0.24	0.58	0.23	0.61	0.21
80-90	0.91	0.02	0.93	0.02	0.93	0.02	0.92	0.02
90-100	1	0	1	0	0.99	0	1	0
100+	-	-	-	-	1	0	-	-
				Men				
0-10	0	1	0	1	0	1	0	1
10-20	0	1	0	1	0	1	0	1
20-30	0.01	0.99	0.01	0.99	0	0.99	0.01	0.99
30-40	0.02	0.97	0.03	0.97	0.01	0.98	0.01	0.98
40-50	0.04	0.93	0.05	0.92	0.05	0.93	0.04	0.94
50-60	0.17	0.77	0.17	0.76	0.18	0.77	0.14	0.8
60-70	0.42	0.45	0.43	0.43	0.45	0.43	0.44	0.44
70-80	0.7	0.13	0.66	0.15	0.66	0.14	0.7	0.13
80-90	0.95	0.01	0.96	0.01	0.93	0.01	0.93	0.01
90-100	1	0	1	0	1	0	1	0
				Women				
0-10	0	1	0	1	0	1	0	1
10-20	0	1	0	1	0	1	0	1
20-30	0	1	0	0.99	0	0.99	0	0.99
30-40	0.01	0.99	0.01	0.99	0.01	0.99	0.01	0.99
40-50	0.02	0.97	0.02	0.97	0.02	0.96	0.02	0.97
50-60	0.09	0.89	0.08	0.89	0.09	0.87	0.09	0.89
60-70	0.3	0.62	0.3	0.62	0.31	0.6	0.32	0.6
70-80	0.55	0.28	0.53	0.29	0.54	0.28	0.57	0.26
80-90	0.9	0.03	0.93	0.02	0.93	0.02	0.92	0.02
90-100	1	0	1	0	0.99	0	1	0
100 +	-	-	-	-	1	0	-	-

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survival for E10-E14 (Table 5).

It was found that the average and median survival time for E10-E14 before the COVID-19 pandemic was 70.5 and 71.0 (in 2018) and 70.1 and 71.0 years (in 2019), respectively. Duringthe current pandemic, these figures were 69.7 and 70.0 (2020) and 69.8 and 71.0 years (2021), respectively. This survival bias is statistically significant: the Wilcoxon (Gehan) test shows $P = 0.001$.

In the dynamics, the average survival rates for E10-E14 in the female population changed significantly (Wilcoxon test (Gehan), $P = 0.001$).In the male population, changes in average survival rates for E10-E14 are statistically insignificant (Wilcoxon (Gehan) test, $P = 0.413$). It should be noted that the average survival rates are significantly higher in the female population than in the male population (year-adjusted Log Rank test (Mantel-Cox) - $P \leq 0.001$, Breslow test (GeneralizedWilcoxon) $-P \leq 0.001$ and Tarone-Ware test $-P \leq 0.001$).

Separately, it is necessary to say about the indicators of the rate of deaths (the probability that an event will occur in the studied age interval) and cumulative survival (the probability of surviving or not receiving a fatal outcome)

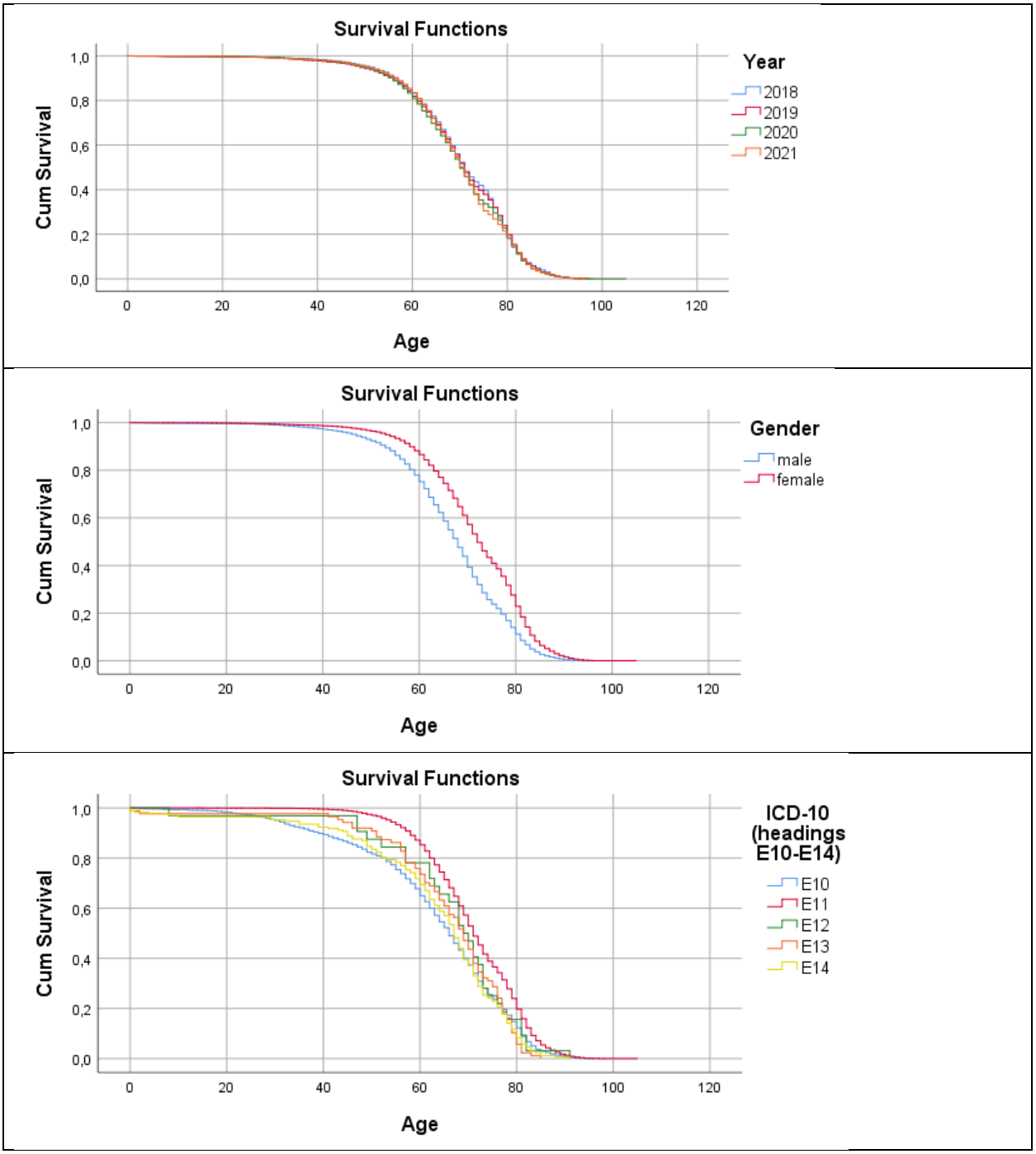

Figure 1. Kaplan-Meier survival curves at E10-E14 for the period 2018-2021 in the Republic of Kazakhstan

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at E10-E14 in the Republic of Kazakhstan in 2018-2021 (Table 5).

The following results of the analysis are noteworthy. During the pandemic, in comparison with previous years, the proportion of E10-E14 deaths in the age intervals "20-30 years" and "50-60 years" increased by 1%, in the interval "60-70 years" got bigger by 2% and in the interval "70-80 years" raised by 1-4%.

An assessment of cumulative survival at E10-E14 was carried out.In general, this indicator is characterized by the following fluctuations: 1) in the age interval “up to 60 years old” survival increased by 1-2% in 2020 compared to 2018-2019, 2) in the age interval “up to 70 years old” survival increased by 1-2% in 2020 compared to 2018-2019, 3) in the age range “up to 80 years old” survival decreased by 1% in 2020 and by 3% in 2021 compared to 2019.

Figure 1 shows the Kaplan-Meier survival curves at E10-E14 for the period 2018-2021 and in the Republic as a whole, as well as survival curves for diabetes, taking into account gender and ICD-10 categories.

Discussion

There is no doubt that diabetes morbidity and mortality is a serious problem for healthcare systems around the world (including in Kazakhstan), especially during this pandemic.

The main issue answered by the results of this study is the features of the dynamics of morbidity, mortality, and survival in Kazakhstan patients with diabetes before and during the COVID-19 pandemic.

According to the results of the study, in Kazakhstan during the COVID-19 pandemic (mainly in 2021), there is an increase in the absolute frequency of all cases of diseases (by 1.8 times) and newly detected (by 2.0 times), as well as the prevalence rate (by 1.7 times) and incidence (1.9 times) for E10-E14. In our opinion, the fact of the increase in diabetes is due to additional screening diagnostics (including the determination of glucose levels), which werecarried out during the current pandemic in order to identify risk groups for SARS-CoV-2 infection.In turn, the increased level of medical aid appeal ability of the population to healthcare organizations during the pandemic contributed to greater coverage of the population in terms of diagnosing diabetes.

It was found that during the pandemic, E10-E14 mortality increased by more than 1.5 times in Kazakhstan.This is due to the fact that diabetes patients are at high risk for complications and mortality from coronavirus infection. Moreover, the most vulnerable is the female population, where we observe a higher frequency of terminal outcomes, with an increase of about 1500 cases in 2021 compared to 2018. Also, in our opinion, the increase in deaths E10-E14 (especially non-insulin dependent diabetes) may be associated with inaccuracies / errors in the statistical registration of deaths from COVID-19, since DM is one of the most common comorbid pathologies in patients with COVID-19. Additional studies are needed to test this hypothesis.

We studied the average survival rates, which indicate a statistically significant (at the level of $P \leq 0.001$) shift in survival in the Kazakhstan population from E10-E14 during the COVID-19 pandemic.Differences in E10-E14 survival by sex are significant: the median survival time in the female population (73-74 years in 2018-2019 and 72 years in 2020-2021) is significantly higher compared to the male population (68 years in 2018-2021).It should also be noted that the longest survival time is typical for E11, and the shortest for E10 and E12-14.

During the pandemic, the indicator of the proportion of E10-E14 dead shifted: in the age intervals of “20-30 years old” and “50-60 years old” the probability of death grew up by 1%, in the interval of “60-70 years old” it increased by 2% and in the interval "70-80 years" raised by 1-4%.

It has been established that during the pandemic, the E10-E14 cumulative survival rate of the Kazakhstan population has also changed.The cumulative survival rate increased by 1-2% in the age group "up to 70 years" and the survival rate decreased by 1-3% in the age "up to 80 years".The probability of surviving less than 90% is typical for the age interval "over 50 years", and the fifty percent threshold of cumulative survival of the Kazakhstan population with E10-E14 is reached by the age of 60-70 years.

Summing up the above, it is necessary to note the possibilities of applying the results of this study and some of its weaknesses.We hope that our results of the study will be able to have a certain impact on the formation of health care policy in terms of planning the volume of care for patients with diabetes, as well as in terms of organizing differentiated activities for this contingent. The “weak” point in this study is the limitations of the materials presented in the reporting data and the statistical register, which makes it difficult to conduct a larger study with the inclusion of predictors in the analysis.

Conclusion

The main conclusion that can be drawn is that during the COVID-19 pandemic in the Kazakhstan population, the incidence, the prevalence of diabetes (E10-E14), mortality increased, and survival in this pathology shifted.To a greater extent, the increase in morbidity and terminal outcomes occurred due to non-insulin-dependent type diabetes (E11), mainly in the female population.At the same time, the average survival rates in the female population are significantly higher than in the male population.

An additional study to assess the accounting for E10-E14 deaths comorbid withCOVID-19 is recommended.

This knowledge can be useful in the development of differentiated measures to improve the health of the Kazakhstan population suffering from diabetes.

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None.

Conflict of Interests

The authors declare that they have no competing interests.

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