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Clinical and laboratory COVID-19 features in hospitalized patients with concomitant diabetes mellitus type 2: A retrospective study

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Abstract

Objective: To investigate the prevalence of diabetes mellitus in comorbidity structures and its effect on the clinical course in hospitalized COVID-19 patients in south region of Kazakhstan.

Material and methods: A retrospective analysis of data from 918 patients with COVID-19 treated at the City Clinical Infectious Diseases Hospital was carried out. Pearson's Chi-square test and Student's t-test were conducted.

Results: In Kazakhstan, diabetes mellitus occupies the second position in the structure of comorbidities in patients with COVID-19 with a share of 20%. Diabetes mellitus in patients most often occurs in combination with cardiovascular diseases and arterial hypertension (20.3% and 16.3%, respectively). Combination of diabetes mellitus, arterial hypertension and other diseases was detected in 72.4% of patients. Combination of diabetes mellitus, cardiovascular and other diseases was detected in 32.5%.

In diabetes mellitus patients, COVID-19 was more severe, the hospital stay was longer, and patients over 60 years of age suffered. These patients had a combination of diabetes mellitus with arterial hypertension, obesity, and cardiovascular diseases. Hyperglycemia, elevated blood pressure, rapid breathing, and low saturation were more common for these patients.

Conclusion: Diabetes mellitus ranks second in the structure of comorbidities in COVID-19 in the south region of Kazakhstan and is characterized by a combination with cardiovascular diseases, arterial hypertension and obesity. In patients with diabetes, COVID-19 is more severe, which affects the length of stay in the hospital, the mortality rate and the need for transfer to the Intensive Care Unit.

Key words: pandemic, COVID-19, diabetes mellitus, comorbidities

Introduction

The disease, first registered in Wuhan (China) in 2019, caused by SARS-CoV-2 and named by the World Health Organization (WHO) as COVID-19, led to the development of a pandemic and caused enormous damage to the global community [1]. By September 2022, about 598 million cases with about 6.5 million deaths had been detected worldwide [2]. The COVID-19 epidemic in Kazakhstan, as well as throughout the world, was fluctuating in nature with a sharp increase in the first half of 2020 [3] with higher mortality in PCR-positive patients [4].

To date, a meta-analysis of data has shown that diabetes mellitus (DM) is one of the three most common

comorbidities in COVID-19 [5,6]. Previous studies in Kazakhstan showed a similar situation with diabetes mellitus [7]. At the same time, the proportion of diabetes mellitus in the structure of comorbidities differs somewhat by region [6].

The impact of diabetes on the formation of a more severe course of COVID-19 and mortality rates was also revealed [8-11]. In particular, Varikasuvu S.R. et al. showed that the risk of severe COVID-19 in patients with diabetes is 2.2 times higher than in non-diabetic individuals, while mortality is 2.5 times higher [10]. At the same time, the intensity of this influence also varies depending on the geographical region [6]. Thus, it is relevant to analyze the structure of comorbidities and assess their impact on the severity and mortality of COVID-19 in certain regions, which will contribute to the development of a more effective strategy for the rehabilitation of people who have had COVID-19 in a particular region. With regard to DM, this is the most appropriate, since, according to studies by Bhaskar Thakur et al. [6], there is no direct correlation between the incidence of diabetes mellitus and the mortality rate from COVID-19 by region.

In Kazakhstan, at the moment there is an unfavorable situation for diabetes mellitus. In particular, at the beginning of 2021, 382000 people were registered at the dispensary for «diabetes mellitus». For 15 years, the incidence of type 2 diabetes has increased by 3.5 times [12].

Thus, we believe that studying the impact of diabetes mellitus on the course of COVID-19 in Kazakhstan will contribute to the development of a personalized approach to the prevention and treatment of COVID-19 in patients with type 2 diabetes mellitus.

Purpose of the study: To investigate the prevalence of diabetes mellitus in comorbidity structures and its effect on the clinical course in hospitalized COVID-19 patients in south region of Kazakhstan

Material and methods

Participants

A retrospective case-control study was conducted. We studied the 918 COVID-19 patients case histories treated at the City Clinical Zhekenova Infectious Diseases Hospital in Almaty in 2020-2021. In all patients, the COVID-19 diagnosis was confirmed by PCR. PCR was performed by quantitative real-time PCR on nasopharyngeal swabs using the BGI kit (Beijing Genomics Institute, Shenzhen, China) in accordance with the manufacturer's instructions.

The study was approved by the Ethics Committee of the Asfendiyarov Kazakh National Medical University (No.1293, 01/26/2022). Inclusion Criteria: All hospitalized COVID-19 patients. The clinic administration is informed, the clinic employees took part in the study, and there are no objections to the publication of data in the open press.

Inclusion Criteria: Participants were included in the study based on the protocol (National Clinical Protocol: "Coronavirus Infection COVID-19 in Adults" No.1. dated 03/02/2020) [12].

Exclusion criterion: persons not included in the protocol.

Data collection

Hospitalization indications

- Moderate Covid-19 infection: patients with following risk factors, symptoms and vital signs. Risk factors are age over 60 years, diabetes, hypertension, etc.; Respiratory rate (RR) 20-24, SpO2 - 93-95%, lung damage volume above 25%.

- Extremely severe or critical severity of COVID-19 (formation of acute respiratory distress syndrome, sepsis, septic shock, etc.)

- Patients with a fever of 380C and above for 3 days, resistant to antipyretic drugs.

- RR >24; increasing shortness of breath during normal household stress, talking; decrease in SpO2 <93%.

Clinical data included life and disease history, results of objective examination.

The study included individuals with a history of diabetes mellitus, who were registered with specialists at the dispensary.

Data analysis

The obtained results were processed in the IBM SPSS Statistics 17 statistical package. The following variables were used for the analysis: qualitative (disease history, presence of concomitant diseases, gender) and quantitative (age, length of stay in the hospital, hospitalization time from the onset of symptoms, clinical and laboratory values). Quantitative and qualitative data were shown using descriptive statistics. Comparison of the two groups by qualitative characteristics was performed by using Pearson's Chi-square test. To compare several groups at the same time, we used the $\chi 2$ test for arbitrary tables. Comparison of quantitative data was conducted using Student's t-test for unrelated variables. Differences were considered statistically significant at $p \leq 0.05$.

Results

Study population

The study population is presented in Table 1.

All patients with COVID-19 were over 18 years of age. The average age of patients with coronavirus infection was 54.4±17.02 years. There were 43% men and 57% women in the study group. A history of lung disease, hypertension, diabetes mellitus and obesity were noted in 10,5%, 39,4%, 13,4% and 6,2%, respectively. Leukopenia was detected in 238 (25,9%) patients, lymphopenia in 408 (44,4%) and thrombocytopenia in 311 (33,9%) patients, while 75 patients had leukocytosis, 31 had lymphocytosis and 88 had thrombocytosis (8,2%, 3,4% and 9,6% respectively). Low fibrinogen level was noted in 413 (45%) patients. The number of patients with a temperature above 38°C on admission was 116 (12,6%), while subfebrile temperature was noted in 802 (87,4%) patients. A normal level of systolic blood pressure was detected in 845 (92.1%) patients. Pneumonia on admission was noted in 639 (69.6%) patients. Deceleration of the frequency of RR and HR was detected in 795 (86.6%) and 18 (2%) patients, respectively. An increase in the number of heartbeats was noted in 114 (12,4%) patients. Patients with a low saturation level accounted for 34,3%.

The results of the analysis of the comorbidities structure COVID-19 patients are presented in Table 2. The number of patients with comorbidities was 609 (66%), while 309 (34%) patients did not have any. Arterial hypertension (AH) (59.4%), diabetes mellitus (DM) (20%), and cardiovascular diseases (CVD) (18.5%) occupy leading positions in the structure of comorbidities. In addition, gastrointestinal diseases (GD) (16.4%), bronchitis (10.8%), obesity (9.3%), anemia (3.4%), chronic kidney disease (1.8%) and other diseases (28.2%), which include thyroid diseases, rheumatoid diseases, eye diseases, autoimmune diseases, diseases of the upper respiratory tract, etc. have been identified. The structure of comorbidities in patients with COVID-19 is shown in Figure 1.

Our analysis of the comorbidities structure in patients with COVID-19 also showed that DM is most common in combination with CVD and AH (20.3% and 16.3%, respectively) (Table 3).

Table 1 Characteristics of patients with COVID-19

Parameters		Patients with COVID-19 N (%)
Total		918 (100%)
Sex	Male	395 (43%)
	Female	523 (57%)
Age (years) M ± m		54,4±17,02
Having a history of lung disease, n (%)	Yes	96 (10,5%)
	No	822 (89,5%)
Having a history of hypertension, n (%)	Yes	362 (39,4%)
	No	556 (60,6%)
Having a history of diabetes, n (%)	Yes	123 (13,4%)
	No	795 (86,6%)
Presence of obesity, n (%)	Yes	57 (6,2%)
	No	861 (93,8%)
Leukocytes, n (%)	Up to 3,9x109/l	238 (25,9%)
	4 - 9x109/l	605 (65,9%)
	Over 9,1x109/l	75 (8,2%)
Lymphocytes, n (%)	Up to 0,9x109/l	408 (44,4%)
	1,0-3,2x109/l	479 (52,2%)
	Over 3,3x109/l	31 (3,4%)
Fibrinogen, n (%)	Up to 4 g/l	413 (45%)
	Over 4,1g/l	505 (55%)
Platelets, n (%)	Up to 179 x 109/l	311 (33,9%)
	180-320x 109/l	519 (56,5%)
	Over 321x109/l	88 (9,6%)
Temperature at admission, n (%)	<38°C	802 (87,4%)
	>38°C	116 (12,6%)
Systolic blood pressure on admission, mmHg, n (%)	Up to 139	845 (92,1%)
	140 -160	47 (5,1%)
	Over 160	26 (2,8%)
Presence of pneumonia on admission, n (%)	Yes	639 (69,6%)
	No	279 (30,4%)
RR*, n (%)	Below 20	795 (86,6%)
	Over 21	123 (13,4%)
HR**, n (%)	Up to 59	18 (2%)
	60-100	786 (85,6%)
	Over 101	114 (12,4%)
Saturation on admission, n (%)	Below 94%	315 (34,3%)
	Over 95%	603 (65,7%)

Abbreviation:
RR* – respiratory rate
HR** – heart rate

Figure 1 - The structure of comorbidities in patients with COVID-19

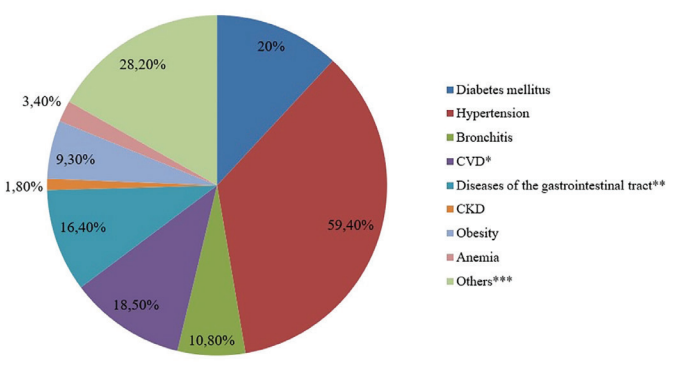

Table 2 The structure of comorbidities in patients hospitalized with COVID-19

Total - 918			
Of which:	N	%	
No comorbidities	309	34	
There are comorbidities	609	% of total	% of comorbidities
Of which:			
Diabetes mellitus	123	13,3	
	20,0		
Hypertension	362	39,4	
	59,4		
Bronchitis	66	7,1	10,8
CVD*	113	12,3	18,5
Diseases of the gastrointestinal tract**	100	10,8	16,4
CKD	11	1,1	1,8
Obesity	57	6,2	
	9,3		
Anemia	23	2,5	
	3,4		
Others***	172	18,7	28,2

Abbreviation:
CVD - cardiovascular diseases
GIT - gastrointestinal tract
CKD - chronic kidney disease
**CVD - ischemic heart disease, angina pectoris, cardiac arrhythmias
**Diseases of the gastrointestinal tract - stomach ulcers, gastritis, pancreatitis, cholecystitis, colitis, enteritis, hepatosis, hepatitis
***Others - thyroid disease, rheumatoid disease, eye disease, autoimmune disease, upper respiratory tract disease, etc.

Table 3 The structure of comorbidities in patients of diabetes mellitus having COVID-19

Parameters	Amount, n	%
The total number of patients with diabetes mellitus in combination of all concomitant diseases	123	100
In which:		
Diabetes mellitus (isolated)	12	9,8
Presence of diabetes mellitus + hypertension	20	16,3
Presence of diabetes mellitus + hypertension + other diseases	89	72,4
Presence of diabetes mellitus + lung disease	4	3,3
Presence of diabetes mellitus + lung diseases + other diseases	15	12,2
Presence of diabetes + obesity	4	3,3
Presence of diabetes mellitus + obesity + other diseases	13	10,6
Presence of diabetes mellitus + CVD	25	20,3
Presence of diabetes mellitus + CVD + other diseases	40	32,5
Presence of diabetes mellitus + gastrointestinal diseases	9	7,3
Presence of diabetes mellitus + gastrointestinal diseases + other diseases	13	10,6
Presence of diabetes mellitus + other diseases*	26	21,1

*Others - thyroid disease, rheumatoid disease, eye disease, autoimmune disease, upper respiratory disease, etc.

At the same time, the presence of DM, AH and other diseases was detected in 72.4% of patients, and the number of patients with a combination of diabetes mellitus, cardiovascular and other diseases was 32.5%. The number of patients with only DM was identified in only 9.8% of patients. The combination of DM with gastrointestinal diseases was detected in 7.3% of patients. At the same time, the number of patients with diabetes, gastrointestinal disease and other diseases was 10.6%. The combination of DM with lung diseases, as well as the combination of DM with

Table 4 Comparative characteristics of demographic and clinical-laboratory parameters of COVID-19 patients with and without diabetes mellitus

Parameters	DM absence (n=795)	DM presence	p (n=123)
Indicators			
Demographic and general clinical indicators			
Sex, n (%)			
Female	445 (56%)	78 (63%)	0,121
Male	350 (44%)	45 (37%)	
Age, n (%)			
18 to 44 years old	277 (34,8%)	8 (6,5%)	<0,001
45 to 59 years old	189 (23,8%)	26 (21,1%)	
60 and older	329 (41,4%)	89 (72,4%)	
Hospitalization time from the onset of symptoms, n (%)			
Until 10 days	661 (83,1%)	94 (76,4%)	0,070
More than 10 days	134 (16,9%)	29 (23,6%)	
The course of the disease, n (%)			
Severe	171 (22%)	59 (48%)	<0,001
Medium severity	624 (78%)	64 (52%)	
Lethal outcome, n (%)			
Yes	6 (1%)	5 (4%)	0,002
No	789 (99%)	118 (96%)	
Length of stay in hospital (bed days), n (%)			
Until 10 days	631 (79,4%)	70 (56,9%)	<0,001
More than 10 days	164 (20,6%)	53 (43,1%)	
Transfer to the intensive care unit, n (%)			
Yes	10 (1,3%)	12 (9,8%)	<0,001
No	785 (98,7%)	111 (90,2%)	
Comorbidities			
Hypertension, n (%)			
Yes	272 (34%)	90 (73%)	<0,001
No	523 (66%)	33 (27%)	
Having a history of lung disease, n (%)			
Yes	79 (10%)	17 (14%)	0,191
No	716 (90%)	106 (86%)	
Presence of obesity, n (%)			
Yes	41 (5%)	16 (13%)	<0,001
No	754 (95%)	107 (87%)	
A history of kidney disease, n (%)			
Yes	10 (1%)	4 (3%)	0,094
No	785 (99%)	119 (97%)	
The presence of diseases of the gastrointestinal tract in history, n (%)			
Yes	106 (13,3%)	13 (10,6%)	0,396
No	689 (86,7%)	110 (89,4%)	
Having a history of CVD, n (%)			
Yes	73 (9,2%)	40 (32,5%)	<0,001
No	722 (90,8%)	83 (67,5%)	
Having a history of anemia, n (%)			
Yes	18 (2,3%)	6 (4,9%)	0,091
No	777 (97,7%)	117 (95,1%)	
Presence of other diseases in history, n (%)			
Yes	110 (13,8)	16 (13%)	0,804
No	685 (86,2%)	107 (87%)	
Laboratory indicators			
The level of glucose in the blood at the time of admission, n (%)			
<4,0 mmol\l	31 (4%)	3 (2,5%)	p<0,001
4,1-6,1 mmol\l	559 (70%)	40 (32,5%)	
>6,2 mmol\l	205 (26%)	80 (65%)	
Leukocytes, n (%)			
Up to 3,9x109/l	210 (26%)	28 (23%)	0,097
4 - 9x109/l	526 (66%)	79 (64%)	
Over 9,1x109/l	59 (8%)	16 (13%)	
Lymphocytes, n (%)			
Up to 0,9x109/l	359 (45%)	49 (40%)	0,390
1,0-3,2x109/l	408 (51%)	71 (58%)	
Over 3,3x109/l	28 (4%)	3 (2%)	
Fibrinogen, n (%)			
Up to 4 g/l	363 (46%)	50 (41%)	0,299
Over 4,1 g/l	432 (54%)	73 (59%)	
Platelets, n (%)			
Up to 179 x 109/l	260 (33%)	51 (42%)	0,079
180-320x 109/l	461 (58%)	58 (47%)	
Over 321x109/l	74 (9%)	14 (11%)	
Activated partial thromboplastin time, n (%)			
Up to 24 sec	25 (3%)	1 (1%)	0,226
25-35 sec	497 (63%)	84 (68%)	
Over 36 sec	273 (34%)	38 (31%)	
Prothrombin index, n (%)			
Up to 79 %	134 (17%)	19 (15%)	0,803
80-100%	590 (74%)	91 (74%)	
Over 101%	71 (9%)	13 (11%)	
Data of an objective clinical and instrumental study			
Temperature at admission, n (%)			
<38°C	693 (87%)	109 (89%)	0,653
>38°C	102 (13%)	14 (11%)	
Blood pressure on admission, n (%)			
Up to 139 mmHg	733 (92%)	112 (91%)	0,002
140-159 mmHg	45 (6%)	2 (2%)	
Over 160 mmHg	17 (2%)	9 (7%)	
Pneumonia, n (%)			
Yes	549 (69%)	90 (73%)	0,356
No	246 (31%)	33 (27%)	
Respiratory rate per minute on admission, n (%)			
16-20	696 (87,5%)	96 (78%)	0,015
Less than 15	2 (0,3%)	1 (1%)	
More than 21	97 (12,2%)	26 (21%)	
Heart rate per minute on admission, n (%)			
Up to 59	16 (2%)	2 (2%)	0,536
60-100	684 (86%)	102 (83%)	
More 101	95 (12%)	19 (15%)	
Saturation on admission, n (%)			
Up to 94	251 (32%)	64 (52%)	p<0,001
More 95	544 (68%)	59 (48%)	

obesity, was the same (3.3%). At the same time, the number of patients with diabetes, lung diseases and other diseases, as well as the number of patients with diabetes, obesity and other diseases was 12.2% and 10.6%, respectively.

A comparative analysis of the demographic and clinical and laboratory characteristics of COVID-19 patients with and without diabetes mellitus showed a number of significant differences between the indicators (Table 4).

Thus, among patients with diabetes, persons over the age of 60 met 1.7 times more often compared with persons not suffering from DM (72,4% and 41,4%, respectively). The severe course of the COVID-19 in patients with DM was observed 2.18 times more often than in patients without DM (48% versus 22%). Fatal outcome was also 4 times more common among diabetic patients (4% vs. 1%). The presence of arterial hypertension in history in patients with DM was noted 2.14 times more often (73% vs. 34%), while an increased level of blood pressure at admission in patients with DM was registered 7 times more often (7% vs. 1%). In addition, the presence of cardiovascular diseases in patients with diabetes was detected 3.5 times more often (32.5% versus 9.2%). Obesity occurred in DM patients 2.6 times more often (13% versus 5%). The presence of kidney pathology in history in patients with DM was noted 3 times more often, however, the significance was not revealed.

As for laboratory parameters, significant differences were noted only in the level of glucose in the blood at the time of admission. In patients with diabetes mellitus, the glucose level n the blood above the norm was observed 2.5 times more often than in patients without diabetes (65% vs. 26%).

According to the indicators of clinical and instrumental studies, there were significant differences in the RR and the saturation level at admission. Thus, the saturation level below 94% in diabetic patients was observed 1.62 times more often than in patients without diabetes (52% vs. 32%), and RR above 21 in diabetic patients was recorded 1.72 times more often (21% versus 12.2%).

Discussion

The results of the analysis of the comorbidities structure in COVID-19 patients in our study showed that 66% of COVID-19 hospitalized patients had comorbidities. Previously, Hui Poh Goh et al showed the structure of comorbidities in COVID-19 in different regions of the world. The share of diabetes in the comorbidities structure in COVID-19 was 31% in the USA, 20% in Europe, 18% in Latin America and 14% in Asia [6]. In our study, diabetes mellitus is in second place (20%) after arterial hypertension (59.4%). Cardiovascular diseases are in third place (18.5%). This distribution of positions is consistent with the data for the Asian region [6].

At the same time, the proportion of diabetes mellitus in the structure was 20%, which is closer to the figures for the European Region (20%) and higher than in the Asian Region (14%), which causes concern.

An analysis of the comorbidities structure in DM patients showed that comorbidities were 1.4 times more common for DM patients compared to the general population of COVID-19 patients (90.2% vs. 66.0%). At the same time, diabetes mellitus was more often combined with arterial hypertension (72.4%), cardiovascular diseases (32.5%), lung diseases (12.2%), as well as obesity and gastrointestinal diseases (in equal combination in 10, 6% of cases).

It should be noted that all these diseases associated with diabetes are independent risk factors for the formation of a severe COVID-19 [13-17].

Moreover, the combination of arterial hypertension, obesity and cardiovascular disease has been shown to be the main condition for the development of the metabolic syndrome, which can lead to severe COVID-19 [18-22].

Thus, it can be assumed that the previously identified role of diabetes mellitus in the development of severe COVID-19 [23-25] is due not only to the pathogenesis of diabetes mellitus [26-28], but also the presence of a large number of diseases associated with diabetes, which increase the impact on the severity of COVID-19.

We also found a wide range of differences in the characteristics of hospitalized COVID-19 patients with and without diabetes mellitus, confirming the role of diabetes in the formation of severe COVID-19. Thus, among COVID-19 patients, DM people over 60 years of age accounted for almost half of the total number of patients, which is associated with the characteristics of type 2 diabetes mellitus that mainly occurred in old age [29, 30].

According to our data, in patients with concomitant DM, COVID-19 was more severe, and a lethal outcome was noted more often than in its absence. In addition, according to the results of the analysis, it was revealed that patients with diabetes mellitus stayed in the hospital longer than patients without it.

Also, patients with diabetes mellitus were much more likely to have high blood pressure on admission. As noted above, this is because COVID-19 often has a combination of diabetes mellitus, hypertension, and cardiovascular disease. Also, patients with diabetes mellitus were much more likely to have high blood pressure on admission. As noted above, this is because COVID-19 often has a combination of diabetes mellitus, hypertension, and cardiovascular disease [18-22].

It is interesting that in the absence of differences in the incidence of pneumonia at admission in groups of patients with and without diabetes mellitus, dyspnea was more common in patients with diabetes mellitus and the saturation level was significantly lower. We believe that this is related with the more severe nature of lung damage in diabetic patients due to the presence of angiopathy with increased vascular permeability and collapse of the alveolar epithelium. On the other hand, in DM, there is usually a significant decrease in forced vital capacity and forced expiratory volume in one second, which is associated with increased plasma glucose levels [31].

The limitation of this study is the use of the results obtained in one hospital, and therefore additional studies are needed to objectively assess the situation in Kazakhstan.

Conclusion

The results of our retrospective analysis confirm the role of diabetes mellitus in the development of severe COVID-19. A high degree of combination of concomitant diabetes mellitus in patients with COVID-19 with other diseases was shown, which has a synergistic aggravating effect on the course of COVID-19. Our statistical analysis of the incidence of diabetes mellitus in the structure of comorbidities in hospitalized patients with COVID-19 in the southern region of Kazakhstan, as well as data on the structure and combination of comorbid pathology in patients with diabetes mellitus, will help optimize the treatment and rehabilitation of this category of patients.

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