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Article

Admission Hyperglycemia—An Early Predictor of Severity and Poor Prognosis in COVID-19

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Abstract

Background/Objectives: Admission hyperglycemia is frequent in COVID-19 and may serve as an early marker of severity. We assessed whether admission hyperglycemia predicts severe disease and poor outcomes in adults without diabetes. Methods: We performed a retrospective cohort study at the Clinical Hospital of Pneumophthisiology and Infectious Diseases, Brașov, Romania, including adults hospitalized with RT-PCR/antigen–confirmed COVID-19 between August 2020 and July 2021. Patients <18 or >80 years, with prior diabetes, or on corticosteroids were excluded. Hyperglycemia was defined as fasting glucose >106 mg/dL and classified as mild (107–180 mg/dL), moderate (181–300 mg/dL), and severe (>300 mg/dL). Clinical, laboratory, imaging, treatment, utilization, and cost parameters were analyzed. Results: Of 1,009 patients, 734 (72.7%) were hyperglycemic at admission. Compared with normoglycemic patients, hyperglycemics more often developed respiratory failure (67.7% vs. 38.2%), required CPAP (9.4% vs. 1.5%), had severe/critical disease (46.9% vs. 25.1%), ICU transfer (6.5% vs. 1.5%), and mortality (3.8% vs. 1.1%) (all p≤0.0256). They also showed lymphopenia, eosinopenia, higher inflammatory and coagulation markers, longer hospitalization (12.1 vs. 10.1 days), and increased costs (€1,846 vs. €1,043) (all p<0.001). Severe hyperglycemia (>300 mg/dL) strongly correlated with inflammation, coagulopathy, tissue injury, and radiologic severity. Conclusions: Admission hyperglycemia is a robust, easily measurable predictor of severe COVID-19 and adverse outcomes in non-diabetic adults and is associated with greater resource utilization and higher costs. Early identification may improve risk stratification, while prospective studies should assess whether glycemic control modifies prognosis.

Keywords: COVID-19; SARS-CoV-2; admission hyperglycemia; severity; mortality; ICU

1. Introduction

The COVID-19 pandemic caused by SARS-CoV-2 has posed a major global health threat. The virus continues to spread worldwide, producing heterogeneous clinical phenotypes whose severity is influenced by age, comorbidities, and vaccination status [1,2]. Although the respiratory tract is the primary portal of entry and site of viral replication, leading to diverse pulmonary manifestations, SARS-CoV-2 can also affect the cardiovascular, gastrointestinal, hepatic, pancreatic, renal, thyroid, and central nervous systems [3–8]. The continuous emergence of new variants further sustains the risk of severe disease, which may range from asymptomatic infection to mild, severe, or critical illness [9].

Patients with COVID-19, particularly older adults and those with comorbidities such as diabetes mellitus (DM), cardiovascular disease, or obesity, are at increased risk of severe disease, intensive care admission, and death [10–13]. Numerous studies have confirmed that diabetes confers a higher risk of severity and mortality compared with non-diabetic patients [14,15]. Hyperglycemia, the

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defining feature of DM, has also been associated with adverse outcomes in COVID-19 [16,17]. Importantly, several reports indicate that hyperglycemia at hospital admission is frequent even in patients without known diabetes [18,19].

It is increasingly recognized that hyperglycemia arising in the context of acute illness, independent of pre-existing diabetes, reflects more than a transient stress response and serves as a marker of disease severity and an independent predictor of mortality in a variety of infectious and inflammatory conditions, including COVID-19. Beyond stress hyperglycemia, SARS-CoV-2 infection appears to cause profound disruption of glucose homeostasis through mechanisms such as exaggerated systemic inflammation with massive cytokine release, direct pancreatic β-cell injury, and stress-related hormonal imbalances. Activation of the hypothalamic–pituitary–adrenal axis and increased secretion of cortisol, catecholamines, and glucagon contribute to transient hyperglycemia with negative prognostic impact, even in previously normoglycemic individuals [64,65].

Newly detected hyperglycemia after SARS-CoV-2 infection was one of the notable disturbances observed during the pandemic. However, it remains uncertain whether this represents unrecognized pre-existing dysglycemia, such as prediabetes unmasked by infection, or de novo diabetes directly caused by COVID-19 [66]. This hyperglycemia may present atypically, sometimes with severe forms, and survivors who experienced hyperglycemia during the acute phase have a significantly increased risk of developing diabetes within one year [20]. Consequently, long-term monitoring is essential for early identification of individuals at risk and for preventing late complications.

Stress-induced hyperglycemia is a well-described response to severe acute infections and correlates with systemic inflammation, endothelial dysfunction, thrombosis, and immune dysregulation. In SARS-CoV-2 infection, available evidence indicates that admission hyperglycemia may serve as an early and easily measurable marker of disease severity, being associated with higher complication rates, intensive care requirements, and mortality, even in patients without known diabetes [67].

The present study aimed to evaluate the prevalence and prognostic value of admission hyperglycemia in adult patients hospitalized with COVID-19 in a tertiary infectious diseases hospital. Specifically, we sought to assess its association with clinical severity, laboratory and imaging parameters, outcomes, resource utilization, and healthcare costs.

2. Materials and Methods

2.1. Study Design and Setting

We conducted a retrospective, single-center cohort study at the Clinical Hospital of Pneumophthisiology and Infectious Diseases, Brașov, Romania. The cohort was selected from the institutional database and included 1,127 patients hospitalized with COVID-19, confirmed by RT-PCR or antigen testing for SARS-CoV-2, between 1 August 2020 and 31 July 2021. The study was approved by the Ethics Committee of the Clinical Hospital of Pneumophthisiology and Infectious Diseases, Brașov (approval no. 9328/20.06.2024), and by the Ethics Committee of the "Lucian Blaga" University of Sibiu (approval no. 16/25.11.2022). COVID-19 diagnosis was based on clinical presentation and confirmed by RT-PCR or antigen testing. All patients were anonymized. Data were extracted from administrative databases and medical records by the first author.

2.2. Statistical Analysis

All analyses were performed using MATLAB R2024a (MathWorks), Microsoft Office 365 Excel, and dedicated Python scripts executed in a Jupyter Notebook environment. The following Python packages were employed:

- pandas: data wrangling, tabulation, and cohort filtering;
- numpy: numerical operations;
- scipy.stats: inferential statistics, including chi-square tests.

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Descriptive statistics, cross-tabulations, and hypothesis testing (e.g., chi-square tests of independence) were conducted with scipy.stats on data frames prepared using pandas and numpy. Plots and summary tables were generated in the same environment, with additional review and formatting in Excel.

2.3. Aim and Objectives

The primary aim was to evaluate admission hyperglycemia as an early predictor of severity and poor prognosis in non-diabetic patients with COVID-19.

- Primary objective: determine the prevalence of admission hyperglycemia and assess its association with epidemiologic, clinical, laboratory, and outcome parameters.
- Secondary objective: evaluate the financial impact of admission hyperglycemia.

The following characteristics were analyzed:

Epidemiologic variables: age, sex, history of chronic cardiovascular disease (hypertension, myocardial infarction with stent), pulmonary disease (asthma, COPD), metabolic disorders (obesity, hepatic steatosis), and chronic kidney disease.

Clinical aspects: clinical form of COVID-19, initial symptoms, time from symptom onset to admission, oxygen therapy requirement, CPAP need, use of antiviral and immunomodulatory therapies (remdesivir, tocilizumab, anakinra), and insulin therapy for hyperglycemia management.

Laboratory parameters: leukocytes, lymphocytes, platelets, C-reactive protein (CRP), ferritin, erythrocyte sedimentation rate (ESR), fibrinogen, D-dimer, interleukin-6 (IL-6), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and creatinine.

Imaging findings: extent of pulmonary involvement on chest CT or radiography.

Financial impact: length of hospital stay, ICU admission, and mean cost per case.

2.4. Specific Objectives

I. Prevalence of admission hyperglycemia and associated risk.

Patients were divided into two groups based on fasting blood glucose at the first measurement: >106 mg/dL (upper limit of the analyzer used) defined the hyperglycemic group, while <106 mg/dL defined the normoglycemic group. Serum glucose was measured using the Konelab 60i automated analyzer (Thermo Scientific, Finland) with the reference enzymatic glucose–hexokinase method and photometric detection. In this method, glucose is phosphorylated by hexokinase and subsequently oxidized by glucose-6-phosphate dehydrogenase (G6PD) in the presence of NAD^+/$NADP^+$. The reaction generates NADH/NADPH, directly proportional to glucose concentration, quantified at 340 nm. The analyzer automatically dispenses reagents, performs photometric measurements, and interprets the signal, reporting results in mg/dL. For each group, we analyzed epidemiologic, clinical, laboratory, imaging, and financial characteristics.

II. Relationship between the degree of admission hyperglycemia and risk of progression to severe COVID-19.

The hyperglycemic group was stratified into three subgroups according to admission glucose: mild (107–180 mg/dL), moderate (181–300 mg/dL), and severe (>300 mg/dL). We evaluated associations with disease severity, need for intensive interventions, inflammatory biomarker correlations, and healthcare resource utilization.

2.5. Inclusion and Exclusion Criteria

Inclusion criteria: (1) hospitalized patients diagnosed with SARS-CoV-2 infection; (2) age >18 years; (3) documented glucose levels at admission.

Exclusion criteria: (1) age <18 or >80 years; (2) prior diagnosis of type 1 or type 2 diabetes; (3) corticosteroid therapy prior to admission.

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2.6. Variables Collected

- Demographics: age, sex.
- Medical history: cardiovascular, pulmonary, renal, metabolic, hepatic comorbidities.
- Clinical data: presentation at onset, time from symptom onset to admission, COVID-19 severity, oxygen therapy, non-invasive ventilation, length of stay, costs, treatments administered, and clinical outcomes.
- Laboratory data: glycemia, inflammatory markers (CRP, ferritin, ESR), hematological and coagulation parameters (leukocytes, lymphocytes, platelets, D-dimer), tissue injury markers (AST, ALT, LDH), and renal function (urea, creatinine) at admission and discharge.
- Imaging: thoracic radiography or CT at admission, during hospitalization, and at discharge, used to assess pulmonary involvement.
- Respiratory function: lowest peripheral oxygen saturation (SpO_2, room air) recorded during hospitalization, regardless of timing.

2.7. Treatments

In-hospital management included oxygen therapy (low- or high-flow), non-invasive ventilation, and pharmacological treatments such as lopinavir/ritonavir, favipiravir, remdesivir, hydroxychloroquine, glucocorticoids, tocilizumab, anakinra, and insulin.

2.8. Clinical Severity Classification

Severity was established according to standard protocols [44,45]:

- Mild: upper respiratory tract symptoms without hypoxemia or pneumonia.
- Moderate: imaging-confirmed pneumonia without hypoxemia, SpO_2 >94%.
- Severe: imaging-confirmed pneumonia with at least one of the following: respiratory rate >30/min, severe respiratory distress, or SpO_2 <90%.
- Critical: severe respiratory failure requiring ventilatory support, ARDS, sepsis, septic shock, or acute thrombotic events.

3. Results

3.1. Prevalence of Admission Hyperglycemia and Associated Risk

From the initial cohort of 1,127 patients, those with incomplete or inconsistent data were excluded, yielding a final analytical cohort of 1,009 patients: 734 (72.7%) hyperglycemic at admission and 275 (27.2%) normoglycemic.

Over the course of hospitalization, using discharge values as a common reference, 34.4% of patients hyperglycemic at admission became normoglycemic by discharge, whereas 40% of those normoglycemic at admission developed hyperglycemia by discharge.

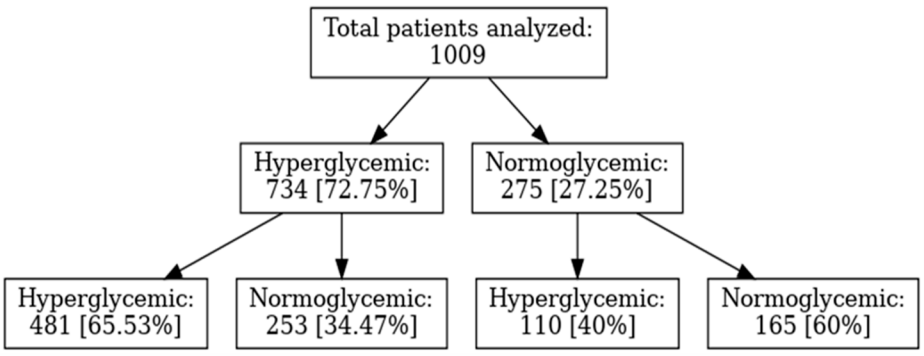

Figure 1. Temporal evolution of glycemic status at admission and discharge.

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Temporal analysis (August 2020–July 2021) showed a steady increase in admission hyperglycemia with a peak between February and May 2021. The November 2020 rise coincided with the beginning of the second pandemic wave, characterized by more severe cases, and the February–May 2021 peak corresponded to the Alpha wave—also marked by more severe disease. This suggests a possible association between hyperglycemia and severe COVID-19.

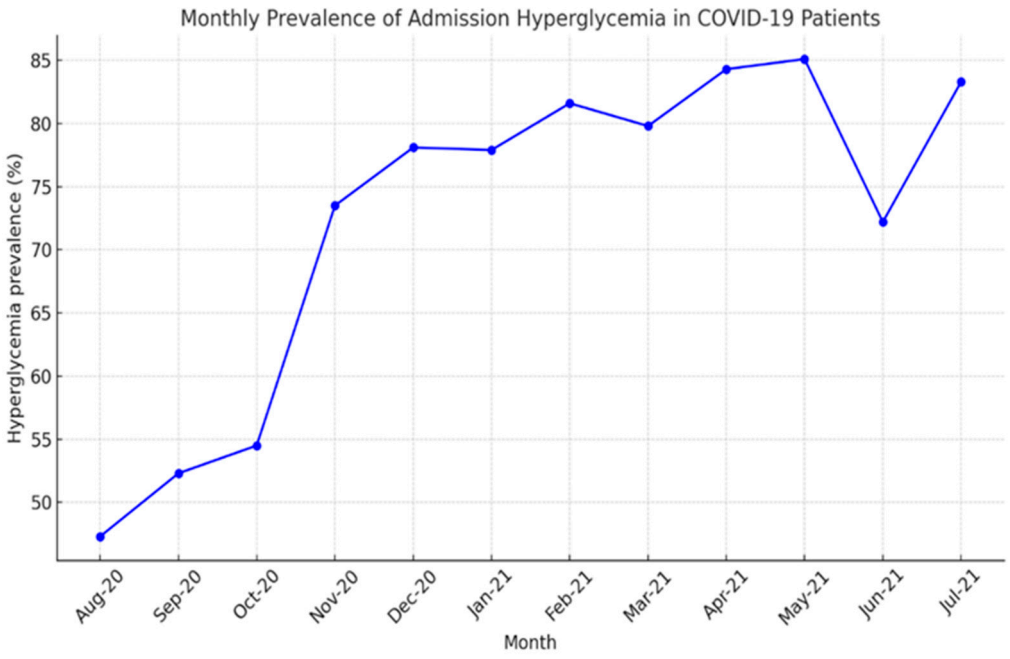

Figure 2.

3.2. Demographic Characteristics and Comorbidities

Sex distribution differed significantly: men predominated in the hyperglycemic group (58.3%), whereas women predominated in the normoglycemic group (54.5%). Hypertension was significantly more frequent in hyperglycemic than in normoglycemic patients (51.2% vs. 41.5%). Other cardiovascular conditions (myocardial infarction, coronary stent) were less common, without significant differences. COPD prevalence was similar between groups; asthma was slightly more frequent in normoglycemics, without statistical significance. Obesity was significantly more common in hyperglycemics (10.8% vs. 3.6%), underscoring the link between body weight status and dysglycemia at admission. Hepatic steatosis was infrequent, with no notable group differences.

Table 1. Demographic characteristics and comorbidities in patients with hyperglycemia versus normoglycemia at hospital admission.

Parameter	**Hyperglycemia (n = 734)**	**Normoglycemia (n = 275)**	**p-value**
Sex			0.0003 *
Male (%)	428 (58.3%)	125 (45.5%)	
Female (%)	306 (41.7%)	150 (54.5%)	
Comorbidities			
Arterial hypertension	376 (51.2%)	114 (41.5%)	0.0070

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Myocardial infarction/stent	21 (2.9%)	4 (1.5%)	0.2926
COPD	14 (1.9%)	4 (0.4%)	0.8283
Bronchial asthma	17 (2.3%)	9 (3.3%)	0.5281
Malignant neoplasms	8 (1.1%)	2 (0.7%)	0.8721
Obesity	79 (10.8%)	10 (3.6%)	0.0006
Hepatic steatosis	22 (3.0%)	5 (1.8%)	0.4154

Legend: Data are presented as number of patients (percentage). P-values were calculated using the Chi² test. Abbreviations: COPD = chronic obstructive pulmonary disease. * P-value refers to overall sex distribution between groups.

Age distribution showed clear differences: younger patients (36–50 years) were more often normoglycemic, whereas older patients (66–80 years) were predominantly hyperglycemic, with statistically significant results.

Table 2. Age distribution by admission glycemic status.

Age group (years)	Hyperglycemia (n = 734)	Normoglycemia (n = 275)
18–35	20 (2.7%)	21 (7.6%)
36–50	129 (17.6%)	68 (24.7%)
51–65	307 (41.8%)	113 (41.1%)
66–80	278 (37.9%)	73 (26.5%)

3.3. Clinical Presentation and Disease Severity

Regarding symptoms, the most common (in descending order) were fever, cough, dyspnea, fatigue, and myalgia. Cough was significantly more prevalent in hyperglycemics, and dyspnea far more frequent in the same group (47.3% vs. 27.6%), with highly significant differences. Headache, pharyngitis, and taste/smell disturbances were more common in normoglycemics, without statistical significance. Gastrointestinal symptoms (nausea, vomiting, diarrhea) were significantly more frequent in normoglycemics.

Table 3. Comparison of Symptom Prevalence Between Hyperglycemic and Normoglycemic COVID-19 Patients.

Symptom	Hyperglycemia (n = 734)	Normoglycemia (n = 275)	p-value
Fever	534 (52.9%)	196 (19.4%)	0.697453
Cough	491 (48.7%)	164 (16.3%)	0.037819
Dyspnea	347 (34.4%)	76 (7.5%)	0.0
Fatigue	339 (33.6%)	118 (11.7%)	0.389855
Myalgia	191 (18.9%)	69 (6.8%)	0.825703

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Headache	173 (17.1%)	81 (8.0%)	0.066295
Sore throat	16 (1.6%)	11 (1.1%)	0.168757
Anosmia/Ageusia	37 (3.7%)	23 (2.3%)	0.066097
GI symptoms	137 (13.6%)	66 (6.5%)	0.072793

Legend: Data are presented as number of patients (percentage). P-values were calculated using the Chi² test. Abbreviations: GI = gastrointestinal symptoms (nausea, vomiting, diarrhea).

Age-stratified CPAP need showed that patients <35 years did not require ventilatory support regardless of glycemic status. In the 51–65 and 66–80 age groups, CPAP need was significantly higher in hyperglycemics.

Table 4. Age-Stratified CPAP Requirement in COVID-19 Patients According Glycemic Status at Admission.

Age group (years)	Hyperglycemic CPAP	Normoglycemic CPAP	p-value
18–35	0 / 20 (0.0%)	0 / 21 (0.0%)	–
36–50	8 / 129 (6.2%)	1 / 68 (1.5%)	0.2488
51–65	24 / 307 (7.8%)	1 / 113 (0.9%)	0.0150
66–80	37 / 278 (13.3%)	2 / 73 (2.7%)	0.0188

Legend: Data are presented as number of patients requiring CPAP / total number in age group (percentage). P-values were calculated using the Chi² test. Abbreviation: CPAP = continuous positive airway pressure.

Acute respiratory failure was much more frequent in hyperglycemics (67.7% vs. 38.2%). CPAP need was also higher (9.4% vs. 1.5%). Mild forms predominated in normoglycemics (40.4% vs. 14.4%), whereas severe and critical forms were significantly more frequent in hyperglycemics. ICU transfer was more common in hyperglycemics (6.5% vs. 1.5%), and mortality was higher (3.8% vs. 1.1%).

Table 5. Comparison of Clinical Characteristics Between Hyperglycemic and Normoglycemic Patients.

Clinical Parameter	Hyperglycemia (n = 734)	Normoglycemia (n = 275)	p-value
Acute respiratory failure	497 (67.7%)	105 (38.2%)	0
CPAP therapy	69 (9.4%)	4 (1.5%)	0
Mild clinical form	106 (14.4%)	111 (40.4%)	0
Moderate clinical form	282 (38.4%)	94 (34.2%)	0.2151
Severe clinical form	295 (40.2%)	66 (24.0%)	0
Critical clinical form	50 (6.8%)	3 (1.1%)	0.0003
Transfer to ICU	48 (6.5%)	4 (1.5%)	0.0011
Death	28 (3.8%)	3 (1.1%)	0.0256

Legend: Data are presented as number of patients (percentage). P-values were calculated using the Chi² test. Abbreviations: CPAP = continuous positive airway pressure; ICU = intensive care unit.

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Length of stay was significantly longer in hyperglycemics (12.1 vs. 10.1 days), and mean hospitalization costs were substantially higher (€1,846 vs. €1,043). The mean interval from symptom onset to admission did not differ significantly (6.8 vs. 6.3 days).

Table 6. Comparison of Hospital Stay Duration and Hospitalization Costs Between Patients With Hyperglycemia and Normoglycemia at Admission.

Variable	Hyperglycemia (n=734)	Normoglycemia (n=275)	p-value
Mean hospital stay duration	12.14 days	10.1 days	< 0.001
Mean hospitalization cost per case	€1846	€1043	< 0.001

3.4. Laboratory Findings

Laboratory parameters differed significantly. Leukopenia and thrombocytopenia had similar frequencies. Lymphopenia (<1000/µL) was much more frequent in hyperglycemics (60.1% vs. 24.7%, p<0.001), as was eosinopenia (84.5% vs. 45.1%, p<0.001). Inflammatory and severity markers were significantly more often elevated in hyperglycemics: ESR >10 mm/h (82.4% vs. 69.5%, p<0.001), CRP >10 mg/L (77.8% vs. 63.3%, p<0.001), ferritin >250 ng/mL (83.5% vs. 59.3%, p<0.001), and LDH >245 U/L (90.5% vs. 81.1%, p<0.001). Coagulation/inflammation parameters were more often abnormal: D-dimer >243 ng/mL (63.6% vs. 50.9%, p<0.001) and fibrinogen >450 mg/dL (59.7% vs. 46.9%, p<0.001). ALT >45 U/L (48.6% vs. 30.3%, p<0.001) and AST >45 U/L (38.5% vs. 25.5%, p<0.001) were also more frequent with hyperglycemia. Creatinine did not differ significantly.

Table 7. Laboratory abnormalities in patients with hyperglycemia versus normoglycemia at hospital admission.

Parameter	Hyperglycemia (n = 734)	Normoglycemia (n = 275)	p-value (Chi² test)
Leukocytes < 4000/µL	139 (18.9%)	52 (18.9%)	1.0
Lymphocytes < 1000/µL	441 (60.1%)	68 (24.7%)	0.0
Platelets < 150,000/µL	105 (14.3%)	37 (13.5%)	0.8069
Eosinophils = 0/µL	620 (84.5%)	124 (45.1%)	0.0
ESR > 10 mm/h	605 (82.4%)	191 (69.5%)	<0.001
CRP > 10 mg/L	571 (77.8%)	174 (63.3%)	<0.001
Ferritin > 250 ng/mL	613 (83.5%)	163 (59.3%)	0.0
LDH > 245 U/L	664 (90.5%)	223 (81.1%)	<0.001
D-dimers > 243 ng/mL	467 (63.6%)	140 (50.9%)	<0.001
Fibrinogen > 450 mg/dL	438 (59.7%)	129 (46.9%)	<0.001
ALT (GPT) > 45 U/L	383 (48.6%)	101 (30.3%)	<0.001
AST (GOT) > 45 U/L	304 (38.5%)	85 (25.5%)	<0.001

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Creatinine > 1.2 mg/dL	146 (19.9%)	47 (17.1%)	0.3591

Legend: Data are presented as number of patients (percentage). P-values were calculated using the Chi² test. Abbreviations: ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; LDH = lactate dehydrogenase; ALT (GPT) = alanine aminotransferase; AST (GOT) = aspartate aminotransferase.

3.5. Treatments

3.5.1. Antiviral Therapy

Antiviral treatments differed by group: remdesivir and favipiravir were used more often in hyperglycemics, whereas lopinavir/ritonavir (Kaletra) was prescribed more frequently in normoglycemics. Hydroxychloroquine use was similar.(Table 8)

3.5.2. Immunomodulatory Therapy

Immunomodulatory therapy for cytokine storm control (tocilizumab, anakinra) was significantly more common in hyperglycemics, suggesting more frequent systemic inflammatory responses in this group. (Table 9)

3.5.3. Corticosteroid Therapy and Steroid-Induced Hyperglycemia

Among the 275 patients who were normoglycemic at admission, 40% developed hyperglycemia during hospitalization, and 94.5% of these had received corticosteroid therapy New-onset hyperglycemia was not associated with poor outcomes, as only 16.2% progressed to severe or critical disease, and 0.9% required non-invasive ventilation or ICU transfer. At discharge, 29.3% of patients had glucose levels >140 mg/dL, indicating persistent metabolic alterations and the potential need for long-term follow-up and preventive interventions (Table 10)

Table 8. Comparison of Antiviral Treatments Used in COVID-19 Between Hyperglycemic and Normoglycemic Patients.

Antiviral Treatment	**Hyperglycemia (n=734)**	**Normoglycemia (n=275)**	**p-value**
Remdesivir	233 (31.7%)	42 (15.3%)	0.0
Kaletra	208 (28.3%)	119 (43.3%)	<0.001
Plaquenil	152 (20.7%)	71 (25.8%)	0.0976
Favipiravir	258 (35.1%)	75 (27.3%)	0.0217
No antiviral treatment	20 (2.7%)	23 (8.4%)	<0.001

Table 9. Administration of immunomodulatory treatment depending on glycemic status upon admission.

Immunomodulator treatment	Hyperglycemic (n=734)	Normoglycemic (n=275)	p-value (χ^2 test)
Tocilizumab (IL-6 inhibitor)	121 (16.48%)	18 (6.54%)	< 0.001
Kineret (IL-1 inhibitor)	192 (26.15%)	34 (12.36%)	< 0.001

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Table 10. Steroid use and new-onset hyperglycemia among normoglycemic patients at admission.

Variable	Normoglycemics who developed hyperglycemia (n, %)
Developed hyperglycemia during hospitalization	110 (40.0%)
Received corticosteroids	104 (94.5%)
Progressed to severe/critical disease	18 (16.2%)
Required non-invasive ventilation / ICU transfer	1 (0.9%)
Glucose >140 mg/dL at discharge	29.3%

3.6. Relationship Between Degree of Admission Hyperglycemia and Risk of Progression to Severe COVID-19

Among hyperglycemics (N=734), 571 (77.7%) had 107–180 mg/dL, 141 (19.2%) had 181–300 mg/dL, and 22 (2.9%) had >300 mg/dL at admission. To better understand the impact of hyperglycemia on clinical and inflammatory profiles, Spearman correlations among biological and clinical parameters were analyzed across the three glycemic strata. Severe hyperglycemia (≥300 mg/dL) was associated with an accentuated systemic inflammatory response and more severe pulmonary, vascular, and hematologic involvement compared with moderate or mild hyperglycemia.

Table 11. Comparative Analysis of Spearman Correlations Across Glycemic Groups.

No.	**Domain / Observation**	**Blood Glucose ≥ 300 mg/dL**	**Blood Glucose 181–300 mg/dL**	**Blood Glucose 107–180 mg/dL**
1	Symptomatology	Dyspnea–myalgia, fever–ferritin	Dry cough	Dry cough
2	Chest X-ray (CXR)	CXR with ferritin, CRP, D-dimer	CXR with saturation	CXR with LDH, saturation
3	Oxygen saturation	Saturation with chest X-ray, LDH, CRP	Saturation with chest X-ray, LDH	Saturation with chest X-ray, LDH
4	Systemic inflammation (CRP, ESR, fibrinogen)	CRP with oxygen saturation, chest X-ray, D-dimer	CRP–ESR, CRP–fibrinogen	CRP–ESR, CRP–fibrinogen
5	Inflammation / Ferritin	Ferritin with chest X-ray, fever	Ferritin with AST, ALT, LDH	Ferritin with LDH, CRP, AST
6	CRP and LDH	Not observed	Not observed	Strong positive correlation
7	Ferritin and LDH	Not observed	Correlation present	Correlation present

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8	D-dimer	D-dimer with symptom onset days, chest X-ray	D-dimer with age	D-dimer with LDH
9	LDH (tissue injury)	LDH with oxygen saturation, dyspnea	LDH with AST (TGO)	LDH with AST, CRP, chest X-ray, ferritin
10	Liver involvement (AST/ALT)	Not observed	ALT–AST	ALT–AST, AST–ferritin, AST–LDH

Correlation network analysis demonstrated a progressive increase in structural complexity from mild to severe hyperglycemia. In mild hyperglycemia (Figure 3), the network remained relatively simple, with correlations primarily restricted to inflammatory markers (CRP, ESR, fibrinogen, ferritin, LDH) and hematological parameters (leukocyte and lymphocyte counts). Clinical symptoms appeared scattered and weakly connected.

In moderate hyperglycemia (Figure 4), the inflammatory–hematological cluster became more consolidated and expanded through the integration of coagulation markers (D-dimer) and renal function parameters (creatinine), particularly among older patients. Clinical symptoms remained heterogeneous, with limited interconnections.

In severe hyperglycemia (Figure 5), the correlational structure was markedly dense, comprising numerous positive and negative associations. Inflammatory, hematological, and coagulation markers formed a central cluster interconnected with demographic variables and clinical manifestations such as fever, dyspnea, and asthenia. Negative correlations, including those between lymphocytes and platelets, were more frequent, suggesting profound immunological and hematological imbalance.

Heatmap analyses corroborated this progression, showing moderate associations and a clearly delineated inflammatory cluster in mild hyperglycemia (Figure 6), stronger integration of inflammatory and hematological parameters in moderate hyperglycemia (Figure 7), and an intricate pattern in severe hyperglycemia (Figure 8), characterized by inverse relationships and broader involvement of clinical symptoms.

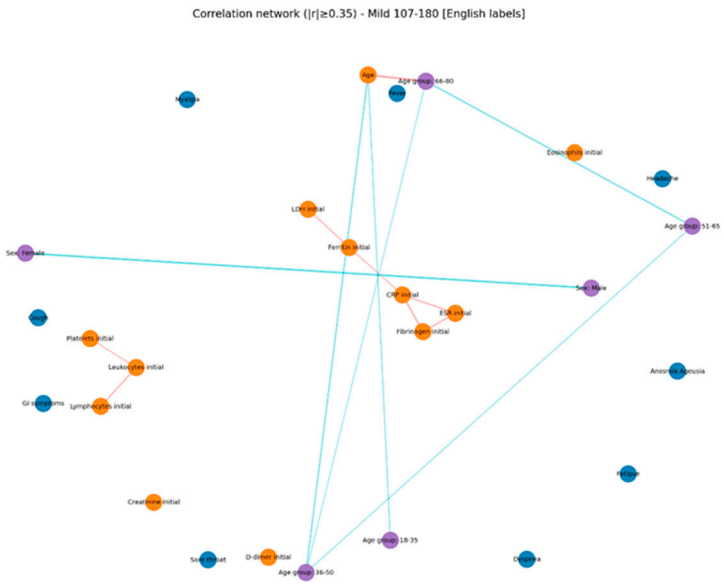

Figure 3.

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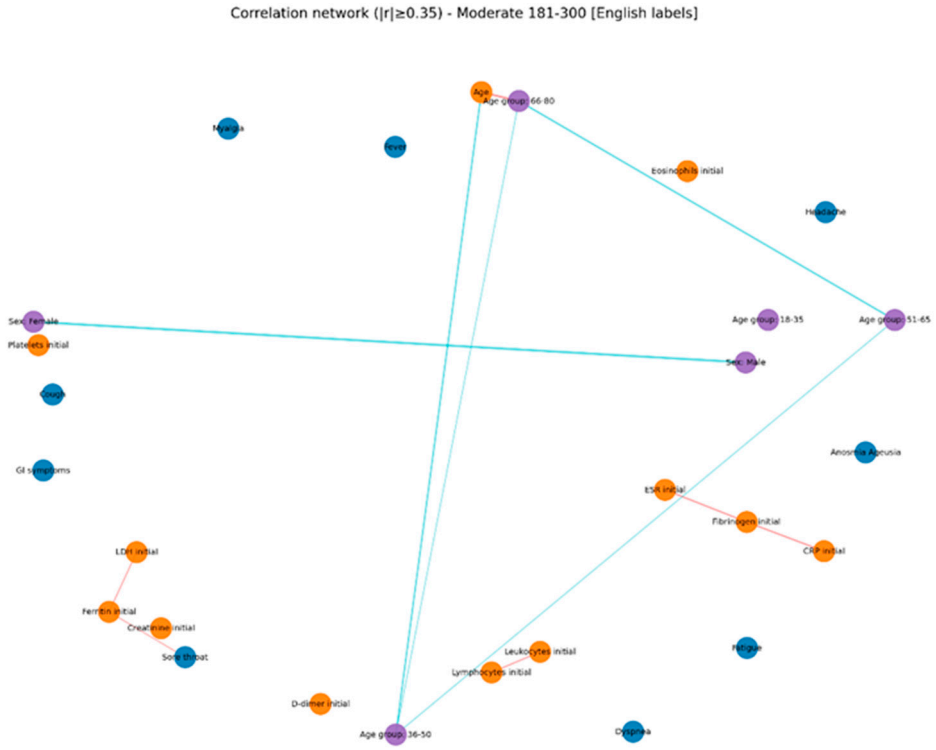

Figure 4.

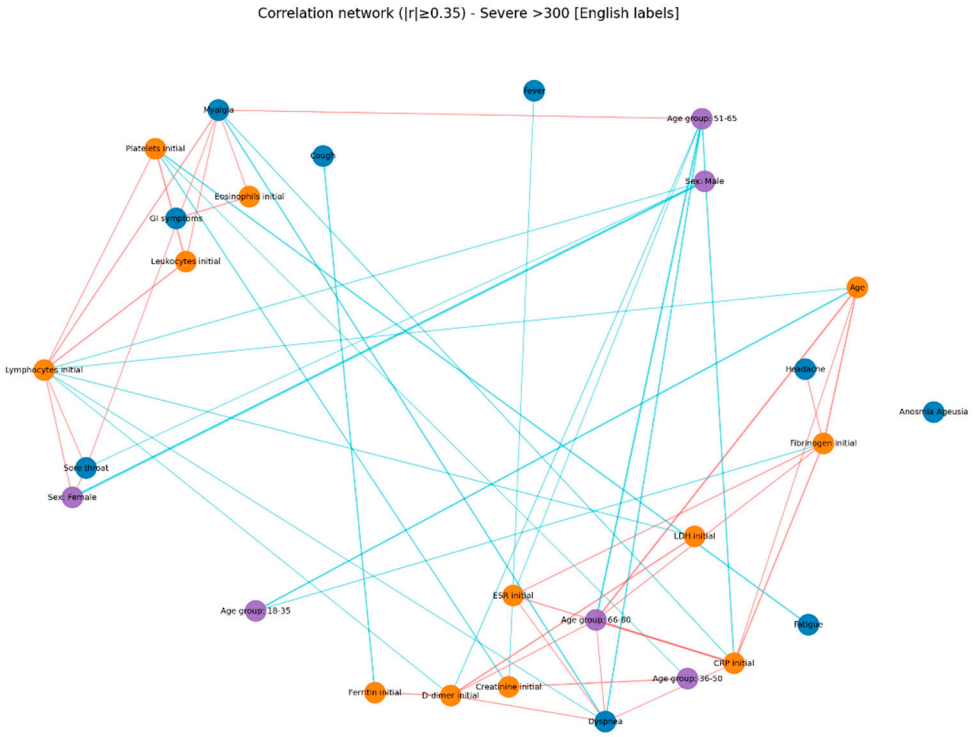

Figure 5.

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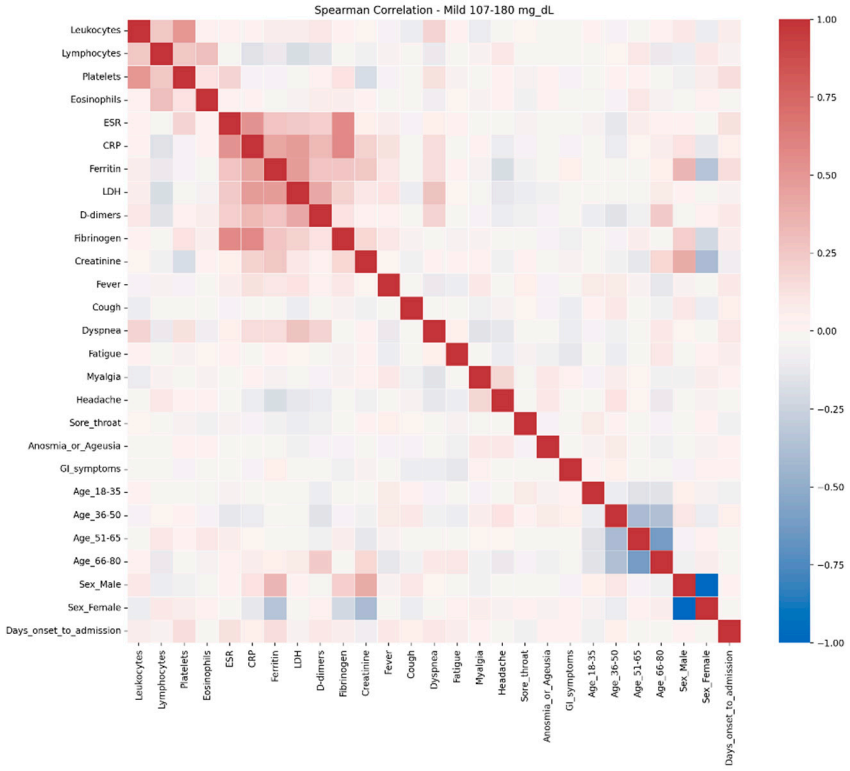

Figure 6.

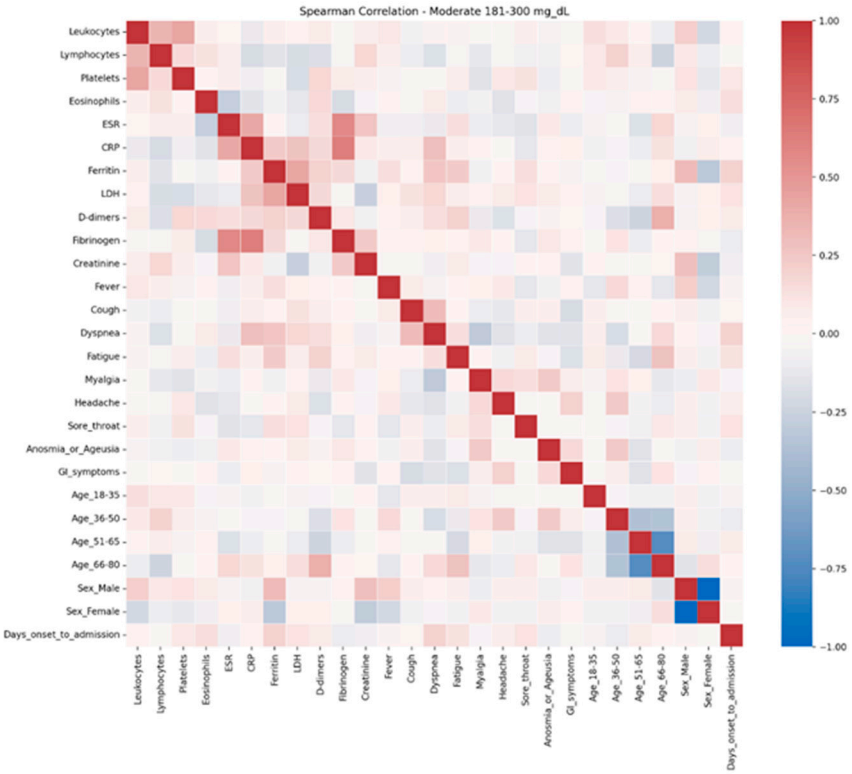

Figure 7.

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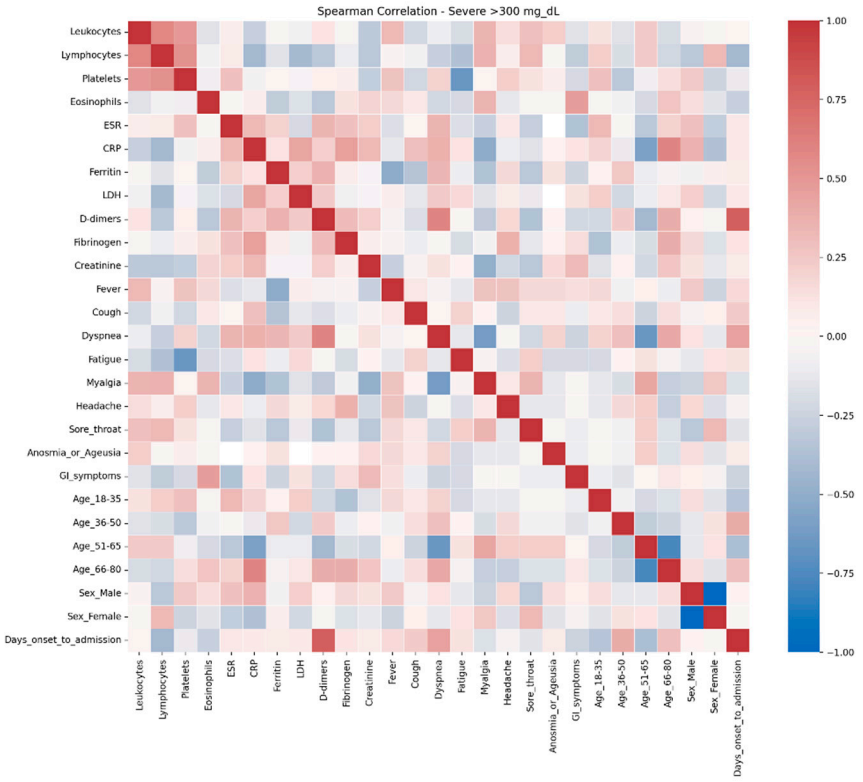

Figure 8.

4. Discussion

In this retrospective study of 1.009 adult inpatients with COVID-19, admission hyperglycemia was associated with significantly more severe clinical courses, higher medical resource consumption, and worse prognosis than normoglycemia. Our results align with the literature identifying admission hyperglycemia as an important predictor of severity and mortality in COVID-19 [1–3]. Admission glucose correlates directly with risk of progression to severe disease and death [39,40]. The risk factors identified here are consistent with prior research, highlighting robust correlations between systemic immune responses and inflammation with potential multiorgan involvement that contributes to worsening disease [1–3].

4.1. Metabolic Profile and Risk Factors

Sex distribution differed significantly by admission glycemia, with men predominating among hyperglycemics (58.3% vs. 41.7%; p=0.0003) and women among normoglycemics (54.5% vs. 45.5%). This matches epidemiologic data indicating higher prevalence and worse outcomes in men with SARS-CoV-2 infection [50]. Age was also significantly associated with admission glycemia: patients aged 36–50 years were more often normoglycemic (24.7% vs. 17.6%), whereas those aged 66–80 years were predominantly hyperglycemic (37.9% vs. 26.5%; p<0.001), in line with evidence that advanced age is a risk factor for hyperglycemia and poor prognosis in SARS-CoV-2 infection [55,56]. CDC guidance likewise emphasizes substantially higher risks of severe disease, complications, and mortality in those ≥65 years [57]. Early glycemic monitoring and metabolic control strategies are therefore crucial in older patients.

Hypertension and obesity were significantly more frequent among hyperglycemics (51.2% vs. 41.5%, p=0.007; and 10.8% vs. 3.6%, p=0.0006, respectively). These comorbidities are well-known for worsening COVID-19 course, being associated with higher mortality and severe complications. Respiratory comorbidities did not differ significantly, suggesting metabolic comorbidities (hypertension, obesity) are most relevant for hyperglycemic COVID-19 patients [51–54].

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Mechanistically, hyperglycemia impairs immune responses and increases susceptibility to severe infections; obesity, hypertension, and diabetes contribute to severe disease through factors such as increased ACE2 expression in adipose tissue and exacerbation of systemic inflammation [40,41,52].

4.2. Clinical Severity and Respiratory Involvement

In our non-diabetic cohort (n=1009), a remarkable 72.7% presented with disordered glucose metabolism at admission, with values from 107 mg/dL (106 mg/dL being the analyzer's upper normal limit) up to 620 mg/dL (the latter in a 50-year-old woman).

A temporal analysis of COVID-19 hospitalizations and admission hyperglycemia revealed that, in the first months (August–October 2020), hyperglycemia was present in 47–55% of patients, a lower percentage compared to subsequent months. The sharp increase observed between November 2020 and January 2021 (73–78%) coincided with the second pandemic wave and a growing number of severe cases, suggesting that hyperglycemia may represent a marker of COVID-19 severity. The peak values recorded between February and May 2021 (82–85%) corresponded to the wave driven by the Alpha variant and indicated that more than four out of five hospitalized patients presented with admission hyperglycemia, supporting the hypothesis of a bidirectional relationship between SARS-CoV-2 and hyperglycemia: the viral variant associated with more severe forms induces hyperglycemia, while metabolic disturbances, in turn, influence the clinical phenotype of COVID-19. The 38-percentage-point difference between the minimum and maximum values is statistically significant and highlights the clinical relevance of admission hyperglycemia as a prognostic indicator. These findings suggest that admission hyperglycemia is closely associated with COVID-19 severity; thus, early monitoring and glycemic control may be essential to improve outcomes in hospitalized patients [4–6,39].

Likewise, in our cohort, severe forms of COVID-19 were more frequent in hyperglycemic patients, and acute respiratory failure was nearly twice as common compared to normoglycemic patients, suggesting more pronounced pulmonary involvement associated with hyperglycemia. Although the overall incidence of critical forms was low, these were more than five times more frequent in hyperglycemics. The need for non-invasive ventilation was nearly five times higher among hyperglycemics, whereas mild forms predominated in normoglycemics. The probability of ICU admission was more than five times higher in hyperglycemic patients, noting that some patients used CPAP in the infectious diseases ward due to ICU bed shortages. Mortality was also significantly higher among hyperglycemics. These data show that admission hyperglycemia is not only a marker of severity but also a possible independent negative prognostic factor, contributing to clinical decompensation and increased risk of death [5,65,66]. The associations persist even in the absence of a previous diagnosis of diabetes, suggesting that stress hyperglycemia or newly diagnosed diabetes may have similar clinical implications [63,67]. In 60.4% of hyperglycemic patients, hyperglycemia persisted during hospitalization; 12.4% required insulin therapy for glycemic control. Among patients with admission glucose > 180 mg/dL, 77.5% developed severe or critical forms with respiratory failure, 16.5% required non-invasive ventilation, and 7% died. In a retrospective study (Inner-City Hospital, 2020), patients without diabetes but with admission glucose > 200 mg/dL had significantly higher mortality; moreover, stress hyperglycemia in the absence of pre-existing diabetes was associated with even greater risks than in patients with known diabetes [41]. Consequently, admission glucose levels correlate directly with clinical severity and risk of death, as reported both in our study and in other research [17,18,40].

Similar results were reported by Fadini et al. in a retrospective analysis of 413 COVID-19 patients, which highlighted a strong correlation between admission glucose and clinical severity/complications, with a significantly stronger association ($p < 0.001$) in newly diagnosed diabetes (HbA1c ≥ 6.5% or random glucose ≥ 11.1 mmol/L [≥ 200 mg/dL] in the presence of hyperglycemia symptoms) compared to pre-existing diabetes. Each 2 mmol/L (36 mg/dL) increase in fasting admission glucose was associated with a 21% relative increase in the risk of severe disease [17]. Similarly, Coppelli et al., in a retrospective study of 271 patients, showed that admission

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hyperglycemia remained the only independent predictor of mortality (p = 0.04); mortality was significantly higher in patients with "new" hyperglycemia (≥ 140 mg/dL) without diabetes compared to normoglycemics (< 140 mg/dL): 39.4% vs. 16.8% [18].

Age-stratified analysis of CPAP requirement adds further nuance: in patients ≤ 50 years, the need was low and similar between groups, likely reflecting better respiratory reserve; in those aged 51–65 years, hyperglycemia was associated with an eightfold higher risk of requiring CPAP, while in patients ≥ 66 years the rate was about 4.5 times higher than in normoglycemics, suggesting a possible additive effect of hyperglycemia on age-related pulmonary vulnerability [23].

4.3. Immune Dysfunction and Inflammatory Profile in Hyperglycemia

Accumulating evidence indicates that hyperglycemia is associated with profound immune dysfunction, including lymphopenia, elevated CRP and D-dimer, and coagulation abnormalities (21,25). Recent meta-analyses confirm significantly higher levels of ferritin, CRP, IL-6, fibrinogen, and D-dimer in hyperglycemic/diabetic patients compared with normoglycemics, reflecting an amplified proinflammatory and prothrombotic state [22,24].

In our cohort, laboratory findings consistently linked hyperglycemia with heightened immune/inflammatory responses. Severe lymphopenia (< 1000/μL) occurred in nearly 60% of hyperglycemics versus 23% of normoglycemics, underscoring marked cellular immune impairment. Hyperglycemia may exacerbate this dysfunction through mechanisms such as abnormal protein glycosylation and impaired T-cell activation, thereby limiting viral clearance. Supporting these observations, a recent study in Diseases (2024) reported that hyperglycemic COVID-19 patients exhibited reduced lymphocytes, lower oxygen saturation, and increased LDH and ferritin, all markers of severe disease [21]. Other reports similarly noted that hyperglycemia and diabetes are associated with profound lymphopenia and elevated CRP, IL-6, TNF-α, and PCT compared with non-diabetic patients [27]. Complete eosinopenia, observed in 84% of hyperglycemics in our study, further supports an intense acute inflammatory response; its predictive value for ICU admission and respiratory support has been described elsewhere (28). Consistent with these hematologic abnormalities, hyperglycemic patients showed significantly higher levels of ESR, CRP, ferritin, and fibrinogen, suggesting a pronounced proinflammatory milieu driven by oxidative stress, endothelial dysfunction, and activation of the IL-6/TNF-α cytokine axis [21,29]. Elevated D-dimer and LDH indicated increased thrombotic risk and extensive tissue injury, particularly pulmonary, in line with previous reports identifying hyperglycemia as an independent risk factor for thromboembolic complications and alveolo-capillary damage [21,29].

Transaminase elevations (ALT, AST) were also more frequent in hyperglycemics, possibly reflecting systemic inflammatory injury, viral-induced hepatic involvement, metabolic toxicity, or muscle damage [21,27]. In contrast, creatinine did not differ significantly between groups, suggesting that renal impairment at admission is more likely attributable to factors such as hypotension, hypoxia, or nephrotoxic drugs rather than hyperglycemia itself [42].

Taken together, these findings indicate that hyperglycemic patients display a markedly more severe inflammatory and hematologic profile than normoglycemics, characterized by lymphopenia, eosinopenia, and elevated inflammatory and coagulation markers, thereby supporting the concept of hyperglycemia as both a marker and amplifier of severe COVID-19.

4.4. Comparative Analysis by Hyperglycemia Severity

The comparative analysis of clinical and biological profiles according to hyperglycemia severity highlights a graded progression of the inflammatory response and hematologic parameters as glucose levels rise. Three distinct subgroups — mild hyperglycemia (107–180 mg/dL), moderate hyperglycemia (181–300 mg/dL), and severe hyperglycemia (> 300 mg/dL) — showed significant quantitative and qualitative differences, with important clinical and prognostic implications.

Even in the absence of a prior diabetes diagnosis, elevated glucose levels can amplify systemic inflammation and alter hematologic and coagulation functions (58). In the severe hyperglycemia

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group (> 300 mg/dL), notable correlations were observed: CRP was inversely associated with oxygen saturation and positively with radiologic severity and D-dimer levels, suggesting an intense systemic inflammatory syndrome with pulmonary and vascular involvement. D-dimers correlated with time to hospitalization and radiologic score, indicating an early, aggressive vascular inflammatory process associated with rapid disease progression. Markers of cellular injury, particularly LDH, showed negative correlations with O_2 saturation and positive associations with dyspnea in severe hyperglycemia, suggesting extensive pulmonary damage [59].

Across all groups, LDH correlated positively with ferritin, AST, and CRP, but these correlations were strongest in the moderate hyperglycemia subgroup, pointing to multisystem cellular injury. A retrospective study by Kumar et al. (2025) [60] demonstrated that CRP, D-dimer, and IL-6 are independent risk factors for COVID-19 severity, while CRP, D-dimer, LDH, ferritin, and the neutrophil-to-lymphocyte ratio (NLR) are independent predictors of mortality. D-dimer emerged as the most sensitive and specific marker of severity, while LDH was the most reliable predictor of mortality [68–70]. Hepatic involvement was evident in moderate hyperglycemia, reflected by correlations between transaminases and inflammatory markers; however, in extreme hyperglycemia these associations disappeared, possibly indicating less pronounced secondary hepatic injury or a clinical picture dominated by pulmonary and systemic involvement. Diaz-Louzao C. et al. (2022) examined the temporal relationships between inflammatory markers (CRP, IL-6, D-dimer, lymphocyte count) and hepatic injury markers (AST, ALT, GGT), showing different patterns depending on disease evolution and prognosis [71]. Notably, deceased patients had elevated hepatocellular markers positively correlated with inflammatory markers, whereas in survivors these correlations became inverse after one week of hospitalization [63,71].

Oxygen saturation decreased in parallel with negative correlations to CRP, LDH, and chest radiologic score across all subgroups, with maximum intensity in patients with glucose ≥ 300 mg/dL, reflecting severe hypoxemia and extensive pulmonary involvement. In this group, the radiologic score was the most interconnected marker, correlating with CRP, ferritin, and D-dimer, supporting the suspicion of severe viral pneumonia and intense inflammation [32].

Correlations between inflammatory markers (CRP–LDH, ferritin–LDH) were evident in groups with lower glucose levels but disappeared in extreme hyperglycemia, possibly reflecting a “saturated” inflammatory response in which traditional biological relationships become attenuated due to profound systemic dysfunction.

These results support the hypothesis that elevated glucose levels, even without pre-existing diabetes, can amplify systemic inflammatory responses and induce hematologic and coagulation changes [61,62]. Patients with glucose > 300 mg/dL showed tighter integration of clinical symptoms with biological parameters, which may explain their higher risk of complications and the need for more aggressive monitoring and intervention.

The persistence of isolated symptoms (anosmia, fatigue), even at high glucose levels, suggests that not all clinical manifestations are directly influenced by metabolic status. In contrast, inflammatory and hematologic parameters appear to be more sensitive indicators of hyperglycemia severity and may serve as prognostic markers.

These observations provide an integrated perspective on the interaction between glucose metabolism and the inflammatory response, supporting a stratified management approach in patients with acute hyperglycemia. In practice, early identification of patients with complex networks of correlations (inflammatory, hematologic, and clinical) may guide timely therapeutic interventions and prevent progression to severe forms or major metabolic decompensation.

Overall, the data support the concept that admission hyperglycemia in COVID-19 is more than a simple metabolic marker, representing an indicator of disease severity. Multiple correlations between glucose, inflammation, pulmonary involvement, and tissue injury suggest that early glycemic control may have significant prognostic implications. These findings align with other studies demonstrating the clear association between hyperglycemia and mortality in COVID-19, even in patients without pre-existing diabetes [15,21,29–31].

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In the present study, correlation network analysis revealed that hyperglycemia severity is associated with a progressive increase in the complexity of interactions among biological, clinical, and demographic variables. In mild hyperglycemia, the profile was dominated by correlations between inflammatory markers and hematologic parameters, suggesting that even slightly elevated glucose levels can trigger a detectable inflammatory response. As hyperglycemia advanced to moderate levels, the inflammatory–hematologic cluster became more consolidated, with additional connections to coagulation markers and renal function, particularly in older patients, indicating broader systemic activation and increased vulnerability to metabolic and endothelial dysfunction. In severe hyperglycemia, the correlation structure became dense, with numerous positive and negative associations, reflecting greater immunologic and hematologic dysregulation. The integration of respiratory and general symptoms (fever, dyspnea, fatigue) into the biological core of the network reflects a more severe clinical expression and a closer interplay between inflammatory responses and clinical manifestations. These patterns suggest that hyperglycemia is not merely a marker of severity but actively contributes to remodeling the inflammatory and hematologic response, with direct implications for the clinical phenotype and patient prognosis. Ceriello A. (2020), in "Hyperglycemia and COVID-19: what was known and what is really new?", supports the hypothesis that hyperglycemia is not just a marker but an active factor exacerbating inflammation and the procoagulant state [72].

4.5. Pathophysiological Considerations

The relationship between hyperglycemia and poor prognosis in COVID-19 is complex and bidirectional. SARS-CoV-2 infection can induce hyperglycemia through increased release of counter-regulatory hormones, severe systemic inflammation, and possibly by direct injury to pancreatic β-cells. In turn, hyperglycemia worsens immune dysfunction, increases oxidative stress, promotes endothelial damage, and induces a prothrombotic state, thereby amplifying the pathogenic cascades involved in severe disease [5,6,26].

A major mechanism involves viral binding to the ACE2 receptor, expressed in pancreatic β-cells, hepatocytes, and adipose tissue [9]. Viral entry may exert direct cytotoxic effects, impairing insulin production and secretion. Systemic inflammation and the acute "cytokine storm" may further aggravate insulin resistance, leading to disruption of glucose metabolism [10,11].

Several studies have shown that SARS-CoV-2 infection can significantly disrupt glucose metabolism, leading to hyperglycemia, insulin resistance, and in some cases, new-onset diabetes, even in individuals without prior metabolic disorders. These alterations may persist beyond the acute phase, contributing to post-acute sequelae (PASC, or "long COVID") [4–8]. SARS-CoV-2 may also stimulate glycolysis in monocytes, increasing lactate production and consequently serum LDH levels, which are characteristic of severe forms [26]. For example, Chen et al. (2022) demonstrated that even patients with mild disease exhibited persistent metabolic alterations 2–3 months after recovery (elevated fasting glucose, reduced insulin sensitivity) [19]. Similarly, Montefusco et al. described persistent hyperglycemia and altered insulin secretion dynamics during convalescence, suggesting that the virus may act both as a trigger and as an accelerator of metabolic dysfunction [20].

4.6. Therapeutic Implications

The differences observed in antiviral use in our study likely reflect both the greater severity among hyperglycemic patients and the evolution of therapeutic protocols throughout the pandemic. Remdesivir was administered significantly more often in the hyperglycemic group (31.7%) compared with normoglycemics (15.3%) ($p < 0.001$), suggesting that these patients, being more severely affected (as shown by clinical and biological analyses), more frequently met the criteria for administration in moderate-to-severe forms requiring oxygen therapy. One study explored factors associated with hyperglycemic complications following remdesivir use, reporting more frequent administration in severe cases [33]. In contrast, Kaletra (lopinavir/ritonavir) was prescribed significantly more often in normoglycemics (43.3%) than in hyperglycemics (28.3%) ($p < 0.001$), suggesting that antiviral

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selection was influenced not only by glycemic status but also by treatment availability and protocol changes during the pandemic. The observed differences therefore reflect the temporal context of pandemic waves and resource availability rather than a direct effect of hyperglycemia. During the same period, admission hyperglycemia was less prevalent, and many normoglycemics were hospitalized earlier, when Kaletra was more commonly prescribed. Favipiravir was used more frequently in hyperglycemics (35.1% vs. 27.3%), but without statistical significance. Since it was introduced in later waves and indicated for mild-to-moderate forms, its higher use in hyperglycemics may reflect the need for early treatment in a high-risk population and the limited availability of remdesivir. A meta-analysis showed that favipiravir did not significantly reduce the need for ICU admission or oxygen therapy [34]. Lack of antiviral treatment was more common among normoglycemics (6.1%) compared with hyperglycemics (1.4%) ($p < 0.001$), suggesting milder forms or hospitalizations during early phases when access to antivirals was limited.

Regarding immunomodulatory therapy, our data showed significantly greater use of tocilizumab and anakinra in patients with admission hyperglycemia (16.5% and 26.2% vs. 6.5% and 12.4%, $p < 0.001$). This suggests that these patients more frequently developed severe inflammatory responses requiring IL-6 or IL-1 blockade to control cytokine storm. Hyperglycemia has previously been associated with a proinflammatory state and immune dysfunction, which may exacerbate COVID-19 severity and increase the need for immunomodulatory therapies [46–49]. Thus, the observed differences support the hypothesis that admission hyperglycemia may serve as a marker of more severe forms of COVID-19, necessitating both broader-spectrum antivirals and intensive immunomodulation. A study published in Düzce Medical Journal compared the two drugs, suggesting that both can reduce the risk of clinical deterioration; high-flow oxygen requirements and non-invasive ventilation were lower, and hospital stays were shorter in the tocilizumab-treated group ($p < 0.001$; $p = 0.002$; $p = 0.027$) [36].

The frequent use of corticosteroids in moderate-to-severe forms may contribute to hyperglycemia and requires careful management to avoid iatrogenic complications [35]. Among the 275 normoglycemic patients at admission, 40% developed hyperglycemia during hospitalization; 94.5% of these received corticosteroids. Newly developed hyperglycemia was not associated with poor prognosis (only 16.2% developed severe/critical forms; 0.9% required non-invasive ventilation/ICU transfer). Furthermore, patients with persistent metabolic alterations may benefit from early lifestyle interventions, nutritional counseling, and pharmacological support to prevent progression to overt diabetes, considering that 29.3% of study patients had glucose > 140 mg/dL at discharge [43].

4.7. Length of Hospital Stay and Costs

Patients with admission hyperglycemia had a mean hospital stay approximately two days longer than normoglycemics (12.14 vs. 10.1 days; $p < 0.001$), suggesting that hyperglycemia may serve as a marker of more severe disease or delayed recovery. The risk of prolonged hospitalization was significantly higher among hyperglycemics (HR = 1.72; $p < 0.001$). At the same time, the mean hospitalization costs were about €800 higher per patient (€1846 vs. €1043; $p < 0.001$), reflecting longer admissions, the need for additional investigations, more expensive therapies, and a higher probability of complications [38].

The mean time from symptom onset to admission did not differ significantly between groups (6.8 vs. 6.3 days; $p = 0.087$), suggesting that differences in hospital stay and costs cannot be attributed to delayed presentation but rather to disease severity and management complexity. Similarly, a study of 1122 patients across 88 U.S. hospitals reported that those with diabetes or uncontrolled hyperglycemia at admission had higher mean glucose levels (202 vs. 114 mg/dL; $p < 0.001$), increased mortality (28.8% vs. 6.2%; $p < 0.001$), and longer hospital stays (5.7 vs. 4.3 days), supporting the association of hyperglycemia with more severe disease and a more complex clinical course [37].

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4.8. Limitations and Future Directions

This study has several limitations. First, the retrospective and observational design precludes establishing a causal relationship between admission hyperglycemia and COVID-19 outcomes and may introduce recording bias. Second, as a single-center study conducted during a specific period (August 2020 – July 2021), the results may not be generalizable to other populations, regions, viral variants, or therapeutic regimens. In the absence of data on HbA1c, C-peptide, or pancreatic autoantibodies, it was not possible to differentiate the underlying mechanism of hyperglycemia (stress-induced vs. insulin resistance vs. autoimmune insulin deficiency). Likewise, a clear distinction between stress hyperglycemia and newly diagnosed diabetes could not be made.

Nevertheless, the findings indicate admission hyperglycemia as a clinically relevant and easily measurable prognostic marker. Hyperglycemia at admission may reflect both an accentuated systemic inflammatory response and pre-existing metabolic imbalance, being associated with more severe forms of disease, prolonged clinical course, and higher costs. New-onset hyperglycemia and diabetes increase cardiovascular risk and mortality if not managed promptly [12,13]. Systematic monitoring of glucose levels at admission and the implementation of careful glycemic control could enable early identification of high-risk patients, optimize therapeutic strategies, and improve resource allocation. Prospective studies and clinical trials are needed to determine whether early intervention and strict glycemic control can improve outcomes and reduce complications, thereby consolidating hyperglycemia as an integrated prognostic factor in COVID-19 management.

5. Conclusions

In this large retrospective cohort of non-diabetic adults hospitalized with COVID-19, admission hyperglycemia was highly prevalent and strongly associated with disease severity, systemic inflammation, respiratory failure, ICU transfer, and mortality. Hyperglycemia also correlated with prolonged hospital stay and higher healthcare costs, underscoring its role as both a prognostic marker and a driver of resource utilization.

The severity of hyperglycemia was directly related to the complexity of inflammatory, hematologic, and clinical interactions, suggesting that glucose dysregulation contributes actively to disease progression. Corticosteroid-induced hyperglycemia was frequent but had limited short-term prognostic impact; nevertheless, the persistence of hyperglycemia at discharge highlights the need for post-COVID metabolic follow-up.

These findings support admission glucose as a simple, inexpensive, and robust biomarker for early risk stratification in COVID-19. Routine glycemic monitoring and proactive management strategies should be integrated into the care of hospitalized patients, regardless of diabetes history. Prospective studies are warranted to evaluate whether targeted glycemic control can improve outcomes and reduce complications in COVID-19 and future infectious disease settings.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Clinical Hospital of Pneumophthisiology and Infectious Diseases, Brașov, Romania (approval no. 9328/20.06.2024), and by the Ethics Committee of the "Lucian Blaga" University of Sibiu (approval no. 16/25.11.2022).

Informed Consent Statement: Patient consent was waived due to the retrospective nature of the study and the use of anonymized data.

Data Availability Statement: The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

- COVID-19 Coronavirus Disease 2019
- SARS-CoV-2 Severe Acute Respiratory Syndrome Coronavirus 2
- DM Diabetes Mellitus
- ICU Intensive Care Unit
- CRP C-Reactive Protein
- ESR Erythrocyte Sedimentation Rate
- LDH Lactate Dehydrogenase
- AST Aspartate Aminotransferase
- ALT Alanine Aminotransferase
- CT Computed Tomography
- CPAP Continuous Positive Airway Pressure

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