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Clinical Features and Outcomes of Hospitalized Patients with Covid-19. Experience in a Mexican Third level Medical Facility

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Abstract:

Background:
Covid-19 is a novel coronavirus disease with a broad clinical spectrum that has spread globally. Regional information is needed to inform the decision making for health care providers.

Aim:
Describe the presenting characteristics, clinical course, and outcomes of hospitalized patients in a tertiary Mexican hospital.

Material and Methods:
Retrospective cohort study of 619 consecutive patients admitted to a Third Level Medical Facility in Puebla, between April 3rd and October 17th, 2020 with a confirmed diagnosis of Covid-19 by RT-PCR. The data included demographics, socioeconomic data, level of education, clinical data of the entire admission, and the outcome at the moment of discharge.

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Results:
All patients had pneumonia. Median age was 55 years, 91% had at least one comorbidity and the most frequent were: overweight/obesity (78.2%), hypertension (35.2%) and diabetes mellitus (20.5%). Fever, malaise, and cough were the most common presenting symptoms. D-dimer, fibrinogen, glucose calcium, blood gases and organ damage markers were the most frequent laboratory test values altered. Around 35.1% of patients required invasive ventilation. The overall mortality was 31% and the poorest outcome was seen in those mechanically ventilated outside ICU.

Conclusion:
Overweight, obesity, hypertension and diabetes mellitus were the most common comorbid conditions. Fever, malaise, and cough were the most common initial symptoms. Monocytopenia rather than lymphopenia was seen in this cohort. The highest mortality rate was seen in patients on mechanical ventilation outside UCI.

PALABRAS CLAVE

Neumonía Covid-19.
Hospitalización.
Pandemias.
SARS-CoV-2.

Características clínicas y resultados de pacientes hospitalizados con COVID-19. Experiencia en un Hospital de Tercer Nivel de Atención en México.

Resumen:

Antecedentes:
El Covid-19 es una enfermedad nueva por coronavirus con un amplio espectro clínico que se ha extendido a nivel mundial. Se necesita información regional para informar la toma de decisiones.

Objetivo:
Describir las características de presentación, curso clínico y resultados de los pacientes hospitalizados en un hospital terciario mexicano.

Material y métodos:
Estudio de cohorte retrospectivo de 619 pacientes consecutivos ingresados en un Centro Médico de Tercer Nivel en Puebla, entre el 3 de abril y el 17 de octubre de 2020, con diagnóstico confirmado de Covid-19 por RT-PCR. Los datos incluyeron datos demográficos, socioeconómicos, nivel de educación, datos clínicos de todo el ingreso y el resultado en el momento del alta.

Resultados:
Todos los pacientes tenían neumonía. La mediana de edad fue de 55 años, el 91% presentaba al menos una comorbilidad y las más frecuentes fueron: sobrepeso/obesidad (78,2%), hipertensión arterial (35,2%) y diabetes mellitus (20,5%). Fiebre, malestar y tos fueron los síntomas de presentación más comunes. El dímero D, el fibrinógeno, la glucosa cálcica, la gasometría y los marcadores de daño orgánico fueron los valores de laboratorio más alterados. Alrededor del 35,1% de los pacientes requirió ventilación invasiva. La mortalidad global fue del 31% y el peor resultado se observó en los pacientes con ventilación mecánica fuera de la UCI.

Conclusión:
El sobrepeso, la obesidad, la hipertensión y la diabetes mellitus fueron las enfermedades comórbidas más frecuentes. Fiebre, malestar y tos fueron los síntomas iniciales más comunes. En esta cohorte se observó monocitopenia en lugar de linfopenia. La tasa de mortalidad más alta se observó en pacientes con ventilación mecánica fuera de la UCI.

Clinical Features and Outcomes of Hospitalized Patients with Covid-19.

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Introduction

Covid-19 is a disease caused by a novel virus named severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). It belongs to the subgenus Sarbecovirus, genus Betacoronavirus, subfamily Orthocoronavirinae and family Coronaviridae. The periphery of coronaviruses resembles the solar corona in negative-stained electron microscopy, hence its name[1]. The disease was first identified in the city of Wuhan, China, and has spread globally, presenting a severe threat to global health.

The clinical presentation is heterogeneous, ranging from an asymptomatic disease to a life-threatening condition with respiratory failure. At present, specific therapies are lacking. In Mexico, the first cases were reported in February 2020, with pandemic disease levels peaking during July and August, starting to decrease during the following months.

However, as of January 2020, the Mexican health system faced a second wave with more lethality than the first one. During this time The Mexican Institute of Social Security (IMSS, after the initials in Spanish), carried the biggest burden of public health care and the highest mortality of patients hospitalized with Covid-19[2].

Because the mortality of hospitalized patients with this disease varies from country to country, it is important for the clinician to have data describing the features and behavior of this disease in different clinical settings. The aim of this study is to describe the demographics, presenting characteristics, clinical course and outcomes of hospitalized patients from a Mexican hospital dedicated to patients affected with Covid-19.

Methods

This is a retrospective cohort study conducted a Third Level Medical Facility in Puebla, Mexico. This site is a 315 bed multi-specialty hospital and a referral center for patients from the states of Puebla, Tlaxcala and Oaxaca. In March 2020 it was converted to a hybrid Covid-19 hospital. Data was collected from the charts of patients admitted between April 3rd and October 17th 2020 with a clinical diagnosis of Covid-19 and a positive SARS-Cov-2 RT-PCR nasopharyngeal swab. Patients transferred to other facilities were not included. This study was approved by the Hospital institutional review board (No. R-2020-785-126) as a minimal-risk research and informed consent was waived.

The data gathered included demographics, baseline comorbidities, medications, vital signs on admission and initial laboratory test. Prescribed medications and laboratory results were also analyzed for the duration of the admission. Finally, pertinent clinical outcomes were recorded.

The Systematic COronary Risk Evaluation (SCORE) index was calculated, which gives the risk of developing fatal cardiovascular disease at 10 years. This score is endorsed by the European Society of Cardiology for high-risk patients and was used because of the high prevalence of cardiovascular risk factors in the Mexican population. The score considers age from 40 years, gender, systolic blood pressure, smoking, and total cholesterol level[3,4]. Socioeconomic level was classified in in high, medium-high, medium-low and low. For this, an ad-hoc scale was used obtaining a profile of the household which considered the educational level, current job position and the company where he or she works.

The statistical analysis was performed with the R programming language[5] and RStudio[6], with the packages tidyverse[7] and lubridate[8]. When appropriate, 95% confidence intervals were calculated with the binom package[9]. Unless otherwise stated, the results are reported as the median, the inter-quartile range (IQR), and the range of the values.

Results

Patient characteristics.
A total of 619 cases were included. Table I shows the somatometric and sociodemographic variables studied. The median age was 55 years, 50% of patients were between 44 and 64 years old. The median of body mass index (BMI) was 28.9 kg/m2 with an interquartile range (IQR) between 25.5 and 32; 62.2% were male. A total of 15.7% were health care workers, while 23.5% worked in a public space. Patients who were illiterate comprised 6.5% of the sample, while only 2.2% had postgraduate studies. A total of 69.3% had a socioeconomic level considered as medium-low or low. (Table I).

Table II summarizes the comorbidities reported. Figure 1 shows the distribution of the number of associated comorbidities. The maximum number of associated comorbidities in an individual was 8 (one patient); only 56 (9%) had no comorbidities; a total of 474 (76.5%) had either 1, 2 or 3 associated comorbidities.

Table I: shows the somatometric and sociodemographic variables studied.

Variable	Value	Missing cases
Somatic variables:	**Median, (IQR), [range]**	
Age	55, (44 - 64) [19 - 90]	0
Weight	77, (68 - 86) [39 - 136]	3
Height	1.6, (1.6 - 1.7) [1.4 - 2]	3
BMI	28.9, (25.5 - 32) [17.3 - 49.8]	3
Sociodemographic variables:	**No. (%)**	
Gender		0
Female	234(37.8)	
Male	385(62.2)	
Occupation:		2
Outdoor work	39(6.3)	
Health care worker	97(15.7)	
Unemployed	103(16.7)	
Office job	106(17.2)	
Work at home	128(20.7)	
Work in a public area	145(23.5)	
Schooling:		37
Illiteracy	38(6.5)	
Primary school	134(22.8)	
Junior high school	117(19.9)	
High school	140(23.9)	
College	145(24.7)	
Postgraduate studies	13(2.2)	
Socioeconomic level		1
Low	117(18.9)	
Medium-low	312(50.4)	
Medium-high	187(30.2)	
High	3(0.5)	

Table II: summarizes the comorbidities reported.

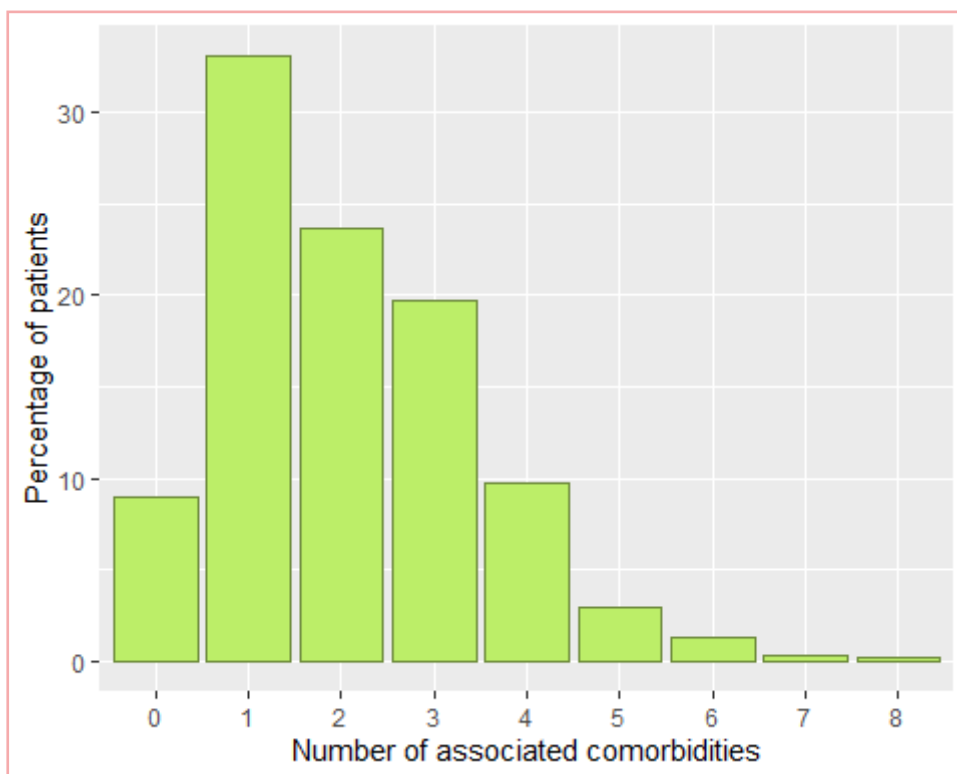| Comorbidity	No. (%)
Obesity	249(40.2)
Overweight	235(38)
Hypertension	218(35.2)
Diabetes mellitus	127(20.5)
Currently smoker	67(10.8)
Past smoker	42(6.8)
Renal disease	38(6.1)
Autoimmune disease	21(3.4)
Cancer	19(3.1)
Cardiovascular disease	18(2.9)
Cerebrovascular disease	11(1.8)
Use of dietary supplements	8(1.3)
Asthma	7(1.1)
Alergic rinhitis	6(1)
Insuline resistance	6(1)
COPD	5(0.8)
Lung disease other than COPD	5(0.8)
Conjunctivitis	1(0.2)
AIDS	1(0.2)

Figure 1: Number of associated comorbidities per patient.

Table III: summarizes drugs received prior to admission. A total of 35.1% of the patients had no drugs prescribed prior to admission for Covid-19 (Figure 2). In contrast, 46.7% of admitted patients were taking 2 or more drugs. The median of number of drugs employed was 1, IQR of 0 - 3, polypharmacy (use of 5 or more drugs in the same individual) was present in 6.8% of the patients.

Table III: summarizes drugs received prior to admission.

Medication	No. (%)
Acetaminophen	267(43.13)
Antibiotic	212(34.25)
Macrolide	146(23.59)
Oral or parenteral corticoid	88(14.22)
Aspirin or indomethacin	64(10.34)
Ivermectin	63(10.18)
Enoxaparin	44(7.11)
Oseltamivir	34(5.5)
Ibuprofen	30(4.85)
Hydroxy-or chloroquine	16(2.58)
Bronchodilator	16(2.58)
Clopidogrel	12(1.94)
Colchicine	10(1.62)
Statins	6(0.97)
Inhaled corticoid	6(0.97)
Vitamin D	5(0.81)
Nitazoxanide	4(0.65)
Nasal corticoid	2(0.32)
Chlorine dioxide	1(0.16)
Ribavirin	1(0.16)

Clinical presentation

All patients were admitted with clinical diagnosis of Covid-19 pneumonia and an abnormal CAT scan. Fever, malaise and cough were the most frequent initial symptoms, with 67.2% of the cases reporting any of these symptoms. Dyspnea was reported as the first symptom in 78 patients (12.7%). (Table IV).

Laboratory values on admission are in table V. The organ damage markers most commonly employed were aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH). Inflammation markers such as ferritin and erythrocyte sedimentation rate (ESR) were used in only 4 and 31 patients respectively.

Clinical measures during hospitalization

Table VI shows the drugs employed during hospitalization. A total of 18 different drugs were used reflecting the lack of a standard of treatment. This trend is also seen in the number of drugs administered per patient (Figure 3).

The median of the number of drugs used to treat the disease was 5, IQR of 4 - 6, polypharmacy was used in 63.8% of cases.

A summary of the laboratory tests performed during hospitalization is presented in table VII. The day when a battery of tests was ordered was registered; The median of studies per patient was 3, IQR[2,3], range [1- 21].

In the last report before outcome, lymphocytes, neutrophils, D-dimer, fibrinogen, ALT, LDH, gamma-glutamyltransferase, ferritin and ESR had median values above the normal range, while monocytes, bicarbonate, PaCO2, paO2 and calcium were below the reference values.
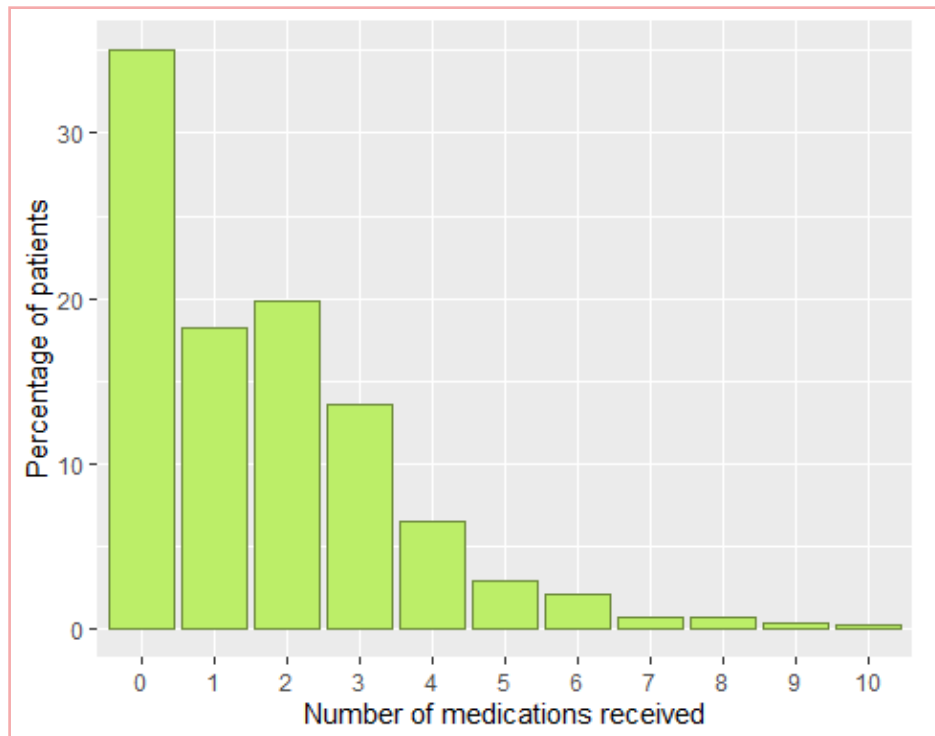
Figure 2: Number of medications used before admission to the hospital.

Table IV: Dyspnea was reported as the first symptom.

Variable	Value	Missing values
First symptom	*No. (%)*	*3*
Fever	162(26.3)	
Malaise	139(22.56)	
Cough	113(18.34)	
Dyspnea	78(12.66)	
Sore throat	44(7.14)	
Headache	35(5.68)	
Diarrhea	22(3.57)	
Chest pain	14(2.27)	
Muscular weakness	3(0.49)	
Anosmia	2(0.32)	
Incapability to move	2(0.32)	
Rash	2(0.32)	
Vitals	Median, (IQR) [range]	
Heart rate	98, (86.5-110.5) [38-160]	4
Respiratory rate	24, (22-28) [16-44]	4
Temperature	37, (36.5-37.7) [35-40]	4
Systolic pressure	123, (110-134) [40-202]	4
Diastolic pressure	76, (69-83) [20-120]	4
Severity score	1, (0-2) [0-16]	7
Oxygen saturation	90, (86-93) [31-100]	4

Table V: Laboratory values on admission.

Test	No.	Values[a]	reference ranges
Hemogram			
Hemoglobin (g/dL)	610	14.4; (13.1-15.7) [7.8-20.5]	12.21-15.10
Red blood cells (10x6 cell/μL)	610	4.9; (4.5-5.3) [1.3-7.5]	4.04-6.13
Platelets (10x3 cell/μL)	610	252; (191-326) [0.62-864]	150-450
White blood cells (cell/μL)	610	8,895; (6,422.5-12,467.5) [651-44,810]	4,400-10,200
Monocytes (cell/μL)	609	490; (257-793) [0-7,000]	600-3,400
Eosinophils (cell/μL)	609	0; (0-50) [0-2,000]	0-900
Basophils (cell/μL)	609	0; (0-80) [0-1,040]	0-200
Neutrophils (cell/μL)	610	7,275; (4,855-10,720) [40-41,673]	1,070-6,470
Lymphocytes (mmol/L)	610	920; (620-1,160) [0-4,104]	600-3400
Coagulation tests			
D-dimer (ng/mL)	594	440; (244.2-899.8) [8-80,223]	0-243
Protrombin time (seg)	488	13; (12-15.0) [0-106]	41913
Fibrinogen (mg/dL)	3	775; (754.5-808.5) [734-842]	200-400
Arterial blood gases			
pH	567	7.4; (7.4-7.5) [6.8-7.6]	7.35-7.45
PaCO2 (mmHg)	567	27; (23-32) [10-115]	34-37
HCO3 (mmHg)	567	18; (15.2-20) [3-35]	19-21
PaO2 (mmHg)	567	64; (51-83) [0-194]	60-70
Metabolic panel			
Urea (mg/dL)	610	28; (16-42) [6-3,402]	16.6-48.5
Glucose (mg/dL)	610	122; (99-164.8) [9.8-725]	74-106
Serum creatinine (mg/dL)	610	0.84; (0.71-1.1) [0.26-16.8]	0.5-1.2
Blood urea nitrogen (mg/dL)	610	13; (7.6-19.5) [0.50-140]	8.00-23
Potassium (mmol/L)	596	4; (3.7-4.4) [2.2-10]	3.5-5.5
Sodium (mmol/L)	596	137; (134-139) [102-151]	132-144
Chlorine (mmol/L)	596	104; (101-107) [64-137]	98-110
Calcium (mg/dL)	43	7.7; (7.4-8.1) [0-9.7]	8.9-10.3
Organ damage markers			
Aspartate aminotransferase (UI/L)	573	42; (29-60) [7-1,493]	15-40
Alkaline phosphatase (UI/L)	45	80; (61-112) [14-214]	38-126
Gamma-glutamyltransferase (UI/L)	2	70.5; (52.8-88.2) [35-106]	9.0-35
Alanine aminotransferase (UI/L)	566	37; (25.2-62) [6-744]	0-34
Lactate dehydrogenase (UI/L)	491	379; (292-518.5) [108-3,029]	120-243
CK (UI/L)	276	86; (49.8-178.8) [2-1,945]	32-294
CK-MB (UI/L)	228	25; (19-35) [0-360]	0.0-25

Troponin T (ng/dl)	3	0.05; (0.05-4.5) [0.05-9]	
Troponin 1 (ng/dl)	3	0.05; (0.05-1.0) [0.05-2]	0-0.4
Inflammation markers			
Ferritin (ng/mL)	4	956.5; (524-13,503.5) [371-50,000]	11-306.8
Erythrocyte sedimentation rate (mm/h)	31	37; (28-49.5) [1-62]	1.070- 6.470

[a]Median, (IQR), [range]. The values where the median is out of the reference range are highlighted.

Table VI: drugs employed during hospitalization.

Medication	No. (%)
Enoxaparin	570(92.08)
Antibiotics[a]	563(90.95)
Macrolide	496(80.13)
Oral or parenteral corticoid	473(76.41)
Acetaminophen	440(71.08)
Colchicine	115(18.58)
Statins	85(13.73)
Bronchodilators	81(13.09)
Hydroxy- or chloroquine	80(12.92)
Clopidogrel	76(12.28)
Aspirin or indomethacin	66(10.66)
Nasal corticoid	61(9.87)
Nitazoxanide	40(6.46)
Vitamin D	28(4.52)
Ivermectin	14(2.26)
Oseltamivir	6(0.97)
Ibuprofen	4(0.65)
Ribavirin	1(0.16)

[a]Other than macrolides.

Analysis of the outcomes

From the 619 patients admitted, 192 died, thus[9] the overall mortality rate was 31% [CI95% (27.4-34.7)]. The median length of stay was 8, IQR (5–12). A total of 217 patients (35.1%) required invasive ventilation. Table VIII shows mortality and length of stay, according to the level of care and type of ventilatory support. Figure 4 is a Kaplan-Meier plot which depicts the survival probability depending on these variables.

The worst outcome was seen in patients with mechanical ventilation outside the ICU, 85 out of 90 (94.4%). Patients treated in ICU without ventilatory support showed the best chance of survival.

Figure 5 shows the smooth density plots for the age, oxygen saturation at the moment of admission, length of stay and the time elapsed between the first symptoms and hospital admission, separated by living status. The distribution of age, oxygen saturation and length of stay was different between survivors and non-survivors, but not for the days of delay between first symptoms and admission. While the median of the age of the survivors was 51, IQR (42-61), for the deceased was 61, IQR (54-68).
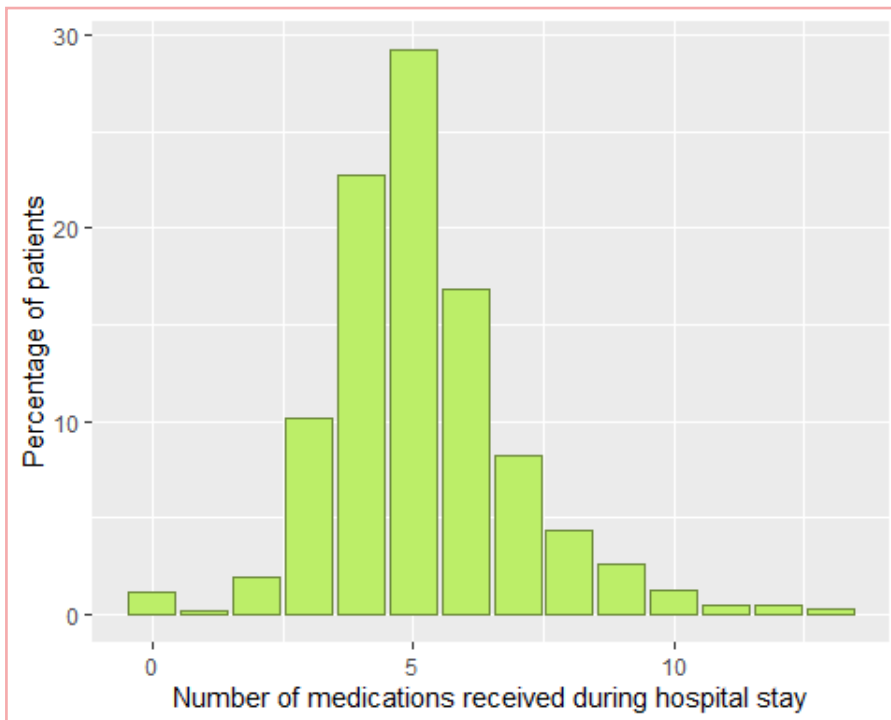
Figure 3: Number of medications per patient for treating Covid-19 during hospitalization.
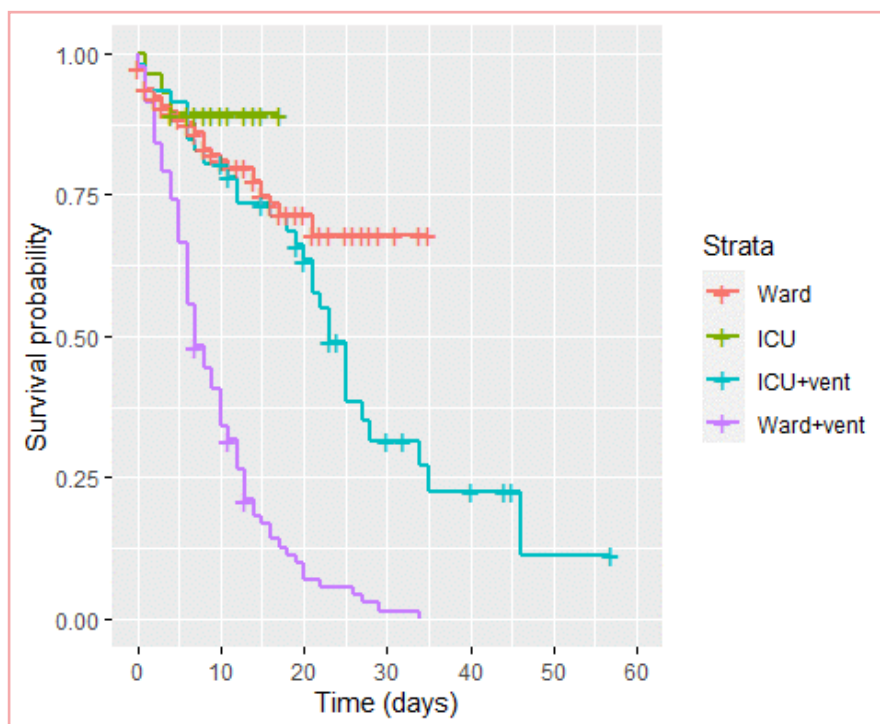

Figure 4: Survival of hospitalized patients according to the level of care and the need for mechanical ventilation. Ward: Patients which did not need ICU and/or mechanical ventilation, the whole stay occurred in the ward. ICU: patients which needded intensive care but were not mechanically ventilated. ICU+vent: patients admitted in ICU requiring mechanical ventilation. Ward+vent: patients mechanically ventilated in the ward.

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The values of oxygen saturation depicted in figure V were adjusted subtracting the amount of oxygen administered (l/min) to the actual oxygen saturation reported, thus reflecting the severity of the disease. The distribution of this variable is more spread in the non-survivors, with a median of 78, IQR (71-84), while the median of survivors was 88, IQR (83-91).

The duration of hospital stay was also different between survivors (median 8, IQR [6-12]) and non-survivors (median 6, IQR [2-12]); it is worth noting that 17 patients stayed less than 24 hours, and from these, 15 (88.2%) died. Finally, the days of delay were similar between survivors and non-survivors, both with a median of 7 days.

Table VII: laboratory tests performed during hospitalization.

Test	Values of the mean[a]	Values of the last test[a]	No.[b]	Reference range
Hemogram				
Basophils (cell/µL)	40; (0-70) [0-1,000]	23; (0-86) [0-1,040]	606	0-200
Eosinophils (cell/µL)	25; (0-80) [0-1,941]	0; (0-90) [0-1,941]	607	0-900
Hemoglobin (g/dL)	14; (12.7-15.3) [6.88-20.1]	13.9; (12-15.2) [5.49-19.9]	608	12.21-15.10
White blood cells (cell/µL)	9,274.8; (6,861.2-12,199.0) [1,471-44,810]	8,700; (6,482.5-11,847.5) [1,600-44,810]	608	4,400-10,200
Lymphocytes (mmol/L)	991.2; (700-1,340.5) [40-12,247.7]	1,031; (650-1,580.8) [0-24,222]	608	600-3400
Monocytes (cell/µL)	538.5; (362.5-752.1) [0-4,759]	530; (329-747.8) [0-9,048]	608	600-3,400
Neutrophils (cell/µL)	7,370.9; (5,142-10,348.5) [305-53,954.8]	6,625; (4,228-9,960) [570-48,886]	608	1,070-6,470
Platelets (10x3 cell/µL)	273.8; (219.9-349.6) [35.09-677.7]	285; (213.5-380) [15.40-740]	608	150-450
Red blood cells (10x6 cell/µL)	4.7; (4.2-5.1) [1.73-2,124.0]	4.6; (4.1-5.1) [0.60-6,360]	608	4.04-6.13
Coagulation tests				
D-dimer (ng/mL)	465; (260.5-1,028) [0.84-158,333]	448; (236-920) [0.97-158,333]	597	0-243
Fibrinogen (mg/dL)	707; (547.8-838.8) [16-1,274]	707; (547.8-838.8) [16-1,274]	30	200-400
Protrombin time (seg)	12.8; (11.8-14.7) [9.78-106]	12.5; (11.5-14.3) [8.80-106]	515	41913
Arterial blood gases				
HCO3 (mmHg)	18.6; (16-21) [3-135]	18.6; (16-21) [3-135]	569	19-21
PaCO2 (mmHg)	29; (25-35) [10-115]	29; (25-35) [10-115]	569	34-37
PaO2 (mmHg)	68; (53-85.3) [0-194]	68; (53-87) [0-218]	569	60-70
pH	7.4; (7.4-7.5) [6.80-7.9]	7.4; (7.4-7.5) [6.80-7.9]	569	7.35-7.45
Oxygen saturation (%)	92.0; (88.8-94) [31-103]	93; (90-95) [31-130]	615	90-99

Metabolic panel

Blood urea nitrogen (mg/dL)	12.7; (7.8-20.3) [0.50-108]	11.5; (7-18.7) [0.22-190]	609	8.00-23
Calcium (mg/dL)	8.0; (7.5-8.3) [4.40-9.7]	8; (7.5-8.4) [4.40-9.7]	232	8.9-10.3
Chlorine (mmol/L)	104.5; (102-107) [67.33-125.8]	105; (102-108) [86-132]	604	98-110
Serum creatinine (mg/dL)	0.80; (0.68-1.0) [0.26-14.7]	0.74; (0.62-0.93) [0.26-48]	609	0.5-1.2
Glucose (mg/dL)	113.2; (94-157.7) [45.33-725]	100; (81-140) [24-725]	609	74-106
Potassium (mmol/L)	4.0; (3.8-4.4) [2.55-10]	4; (3.7-4.4) [2.40-10]	604	3.5-5.5
Sodium (mmol/L)	138; (135.7-140) [91.67-156]	139; (136-141) [110-163]	604	132-144
Urea (mg/dL)	27.5; (16.5-42.2) [5.50-231]	24.1; (14.7-39) [3.70-408]	609	16.6-48.5

Organ damage markers

Aspartate aminotransferase (UI/L)	40; (28.5-60) [10-1,493]	36; (23-57) [8-1,493]	595	15-40
Alanine aminotransferase (UI/L)	44; (28-68) [6.50-840]	42.5; (26-73) [5-840]	592	0-34
CK-MB (UI/L)	25; (18.7-36) [0-344.7]	25; (18-37) [0-322]	297	0.0-25
CK (UI/L)	91; (48-225) [2-17,516.5]	82; (46-205) [2-33,388]	344	32-294
Lactate dehydrogenase (UI/L)	341; (262.6-451) [17-2,079]	302; (225-439) [17-2,079]	545	120-243
Alkaline phosphatase (UI/L)	76; (61-100) [14-1,098]	76; (60-100) [14-1,098]	225	38-126
Gamma-glutamyltransferase (UI/L)	126.5; (72.4-287.9) [30.50-969]	126.5; (76.8-253.8) [26-969]	16	9.0-35
Troponin 1 (ng/dl)	0.05; (0.05-2) [0.05-14]	0.05; (0.05-2) [0.05-14]	5	0-0.4
Troponin T (ng/dl)	0.05; (0.05-0.05) [0.05-3.3]	0.05; (0.05-0.05) [0.05-0.50]	5	

Inflammation markers

Ferritin (ng/mL)	340.5; (46-1,245.8) [10-50,000]	340.5; (49-1,245.8) [10-50,000]	24	11-306.8
Erythrocyte sedimentation rate (mm/h)	40; (27-47.2) [1-1,775]	40; (26.8-48) [1-1,775]	112	1.070- 6.470

[a]Median, (IQR), [range]. The values where the median of the last value is out of the reference range are highlighted.
[b]Number of patients to whom the tests were made

Table VIII: mortality and length of stay, according to the level of care and type of ventilatory support.

	Mortality[a]	Total[a]	Days of stay[b]
Overall	192(31)	619	8; (5-12) [0-57]
ICU care	32(43.2)	74(12)	12; (8-22.8) [0-57]
Mechanical ventilation	107(84.3)	127(20.6)	10; (6-19.5) [0-57]
Mechanical ventilation outside ICU	85(94.4)	90(14.6)	8; (5-13.8) [0-40]
Non-invasive ventilation	6(60)	10(1.6)	9; (8-13.5) [6-29]

[a]Number of patients (percentage).
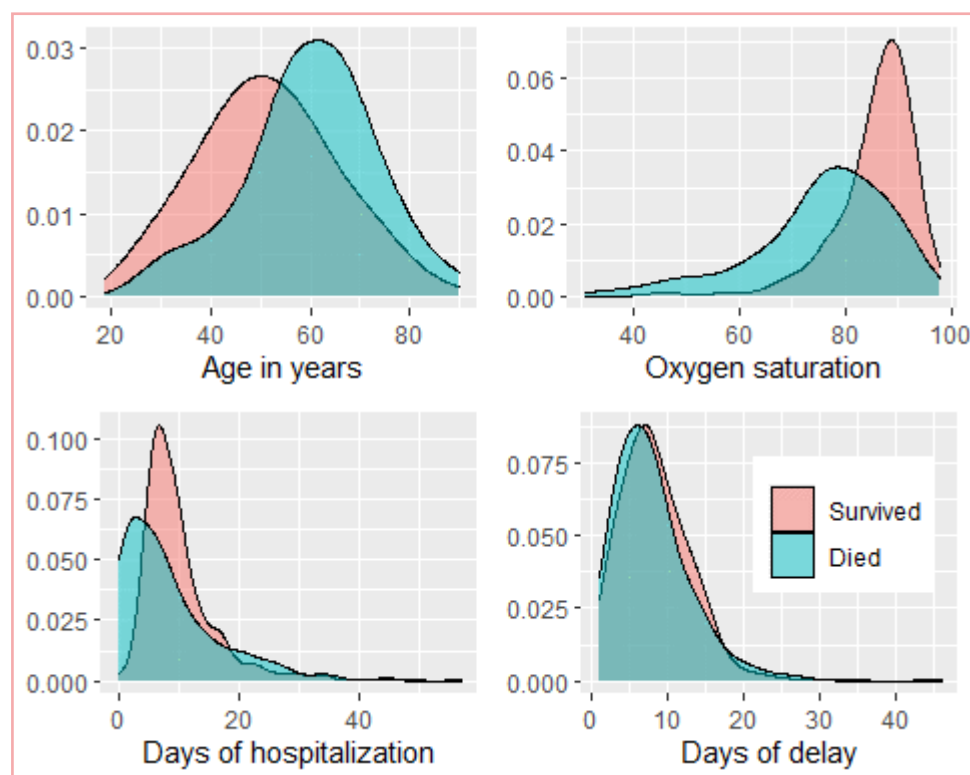[b]Median; (IQR), [range].

Figure 5: Smooth density plots for the age, oxygen saturation at the moment of admission, days of stay and the time elapsed between the first symptoms and the hospital admission, separated by vital status at the moment of discharge.

Discussion

Covid-19 is described as a novel coronavirus disease which affects several organs, mainly the lungs. Its clinical presentation varies from asymptomatic to a life-threatening disease which may progress to acute respiratory distress syndrome (ARDS), multiple organ failure (MOF) and death. This work provides a detailed description of the clinical presentation and outcomes in a tertiary Mexican hospital.

As for March 1st 2021, the General Directorate of Epidemiology of the Mexican Ministry of Health (MMH) reported a global mortality of 2.2%; in Mexico, according to the MMH daily technical report on covid-19, the lethality of the disease is around 9%[10]. A meta-analysis published in July 2020, reported an overall fatality rate of 6%, but does not give information about the in-hospital mortality rate[11].

A recent paper reported some of the features of patients with covid-19 in Mexico[12], using the open data source provided by the *Epidemiological Surveillance System of Respiratory Viral Diseases (ESSRV)* of the Mexican government. We analyzed the ESSRV database (accessed on March, 2021) and found that around 91% of deaths by covid-19

occur in hospitals. The overall in-hospital mortality was 43.7%. Table IX shows hospitalization and mortality rates reported by different sectors of the Mexican Health System, and a considerable difference can be seen among them. It is worth noting that the IMSS received more than 50% of the patients requiring hospitalization in Mexico.

Table IX: hospitalization and mortality rates reported by different sectors of the Mexican Health System, and a considerable difference can be seen among them.

Health care sector	Number of patients admitted (%)[1]	Number of deaths	Mortality rate (%)
IMSS	208,969 (50.6)	105,68	50.6
SSA	125,640 (39.2)	49,257	39.2
ISSSTE	33,727 (39.4)	13,288	39.4
Private Hospitals	14,251 (21)	2,996	21.0
SEDENA	9,742 (21.1)	2,058	21.1
PEMEX	6,932 (36.9)	2,56	36.9
State Hospitals	6,920 (40.3)	2,788	40.3
IMSS-Bienestar	3,700 (38.6)	1,428	38.6
SEMAR	1,982 (27.2)	540	27.2
Municipal Hospitals	990 (6.6)	65	6.6
University Hospitals	885 (39.8)	352	39.8
Red Cross	19 (31.6)	6	31.6
DIF[2]	19 (5.3)	1	5.3

Source: open database of the Epidemiological Surveillance System of Respiratory Viral Diseases, Ministry of Health, Mexico (accessed 26/03/2021).
[1]Total of patients hospitalized: 413,776.
[2]Children's hospital.

These numbers are in contrast with the mortality seen in hospitalized patients in other countries. In a report of 5700 patients admitted to 12 hospitals in the New York City area, a mortality rate of 21% was observed[13]. An initial report of 1590 hospitalized patients in China from 575 hospitals showed an overall mortality rate of 3.2%[14], while another paper from the RECOVERY Collaborative Group reported 25.7% in 4716 patients from 176 hospitals in the United Kingdom[15].

High body mass index, type II diabetes mellitus (DM) and hypertension are preexisting conditions that have been associated with the severity of disease[16]. According to the National Survey of Health and Nutrition 2018[17], in Mexico 75.2% of adults are either overweight or obese (39.1% and 36.1% respectively).

The 95% confidence intervals of the frequencies reported in this study include these values, thus reflecting the distribution of these conditions in the general population (CI95% for overweight 34.1-34.7%, CI 95% for obesity 36.4-44.1%). This is not the case for diabetes mellitus and hypertension. The aforementioned survey reports a prevalence for DM of 10.3% (9.1% in men and 11.4% for women) and for hypertension of 18.4% (20.9% for women and 15.3% for men).

The proportion of DM in the sample is more than two-fold the reported in the general population (CI95% for DM 17.3-23.7%). The prevalence of hypertension was also higher than in the general population (CI95% for hypertension 31.5-39%).

Laboratory findings overall are in line with what has been reported elsewhere in the literature with the notable exception of an absence of lymphopenia seen in this sample. Inflammatory markers such as D-dimer, ferritin, fibrinogen, CRP and ESR have been shown to be almost universally elevated and may reflect severity[18]. During admission a decrease in some of these inflammatory markers may suggest recovery[19]. *Lymphopenia* has been suggested as predictor of illness severity and recovery, but is unclear if it results from direct viral infection or incidentally in the course of the disease[20,21]. In contrast, monocytopenia was observed in our patient population and has been reported to be associated specifically in patients with type 2 diabetes[22]. The presence of monocytopenia with absence of lymphopenia in our study is of unclear significance and it may need further research.

Management of severe covid-19 demands a specialized care and the use of considerable resources. Accordingly, treatment options may be limited in low and

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middle-income countries, leading to an increased mortality. A previous report on hospital mortality in mechanically ventilated Covid-19 patients in Mexico, shows a difference when compared with other countries such as the United Kingdom or Germany[23], but this was a retrospective study using the ESSRV database. In a prospective observational study by the Mexico COVID-19 Critical Care Collaborative Group, the overall mortality rate observed in 164 patients admitted to ten ICUs was 51.8%[24].

Results presented in this study underline the difference in mortality when patients are mechanically ventilated outside ICU premises. In October 2020, the Mexican government issued a set of recommendations for treatment of hospitalized covid-19 patients[25]. Recently, the European Respiratory Society published a guideline for the management of hospitalized adults with covid-19[26].

In general, the panel recommends the use of anticoagulation in all hospitalized patients and in cases requiring supplementary oxygen or ventilatory support, the use of systemic corticosteroids, IL-6 receptor antagonist monoclonal antibody, and non-invasive ventilatory support, including high-flow nasal cannula and non-invasive CPAP, when no immediate indication for invasive mechanical ventilation is present.

This work has some limitations. Due to its retrospective nature, some data were not available for all patients. The influence of some variables on the outcome were not analyzed deliberately, as we are working on a different paper to address this.

In conclusion, the results presented give a snapshot of the clinical presentation, evolution and clinical outcomes of Covid-19 patients in a representative Mexican hospital. Overweight, obesity, hypertension and diabetes mellitus were the most common comorbid conditions. Fever, malaise and cough were the most common initial symptoms. Monocytopenia rather than lymphopenia was seen in this cohort. The highest mortality rate was seen in patients on mechanical ventilation outside ICU. Future interventions to improve outcomes may be evaluated taking into account these results.

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