SUPPLEMENTARY MATERIAL

Presenting prevalence, characteristics and outcome of asthmatic patients with T2 diseases in hospitalized subjects with COVID-19 in Madrid, Spain

SUPPLEMENT

Introduction.

The first confirmed case of coronavirus disease 2019 (COVID-19) in Spain was reported in Madrid at the end of February 2020. Soon after, Madrid reported an outbreak, and cases in Spain increased dramatically, as one of the countries had more cases in the world.

Material and Methods.

Demographic data, smoking status, non-atopic comorbidities, presence of atopy, symptoms, clinical, radiological and laboratory data on-admission and discharge, need of ICU (Intensive Care Unit) admission days of hospitalization and death were analyzed. Severity of COVID-19 on-admission was classified according to the FIO_2 required: A0 (FIO_2 21%), A1 (FIO_2 up to 35%), A2 (35% >FIO_2≤60%) and A3 (FIO_2> 60%).

For asthmatic patients, data related to severity [9], treatment, compliance, and control before COVID-19 were collected together with exacerbation during hospitalization. Compliance was based on refill medication data on electronic prescription during the last year, good compliance was considered as ≥ 80% of refills. Asthmatic patients were categorized as non-allergic and allergic (by positive prick test to aeroallergens).

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Statistical methods.

Categorical variables were described as frequencies and percentages. Continuous variables were summarized as mean ± standard deviation (SD). To compare the frequencies, we used two-sided *Fisher's* exact test. Continuous variables from asthmatic and non-asthmatic groups were compared by two-tailed Mann-Whitney test for non-parametric data. Normality was analyzed using the Shapiro-Wilk test and Kolgomorov-Smirnov test as appropriate. $P < 0.05$ was considered significant. Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software Inc, San Diego, CA, USA).

Treatment Protocol for every COVID-19 hospitalized patient.

All patients received treatment with lopinavir 200mg/ritonavir 50mg two pills every 12hrs for 7 days and cyclosporine A initiated based on weight (<60kg: 50mg-0-50mg; between 60-80kg: 100mg-0-50mg; over 80kg: 100mg-0-100mg); the dose was augmented every 48hrs to reach 5mg/kg/day and treatment was maintained during at least 15 days. All patients also received hydroxychloroquine 400mg every 12hrs for 5 days, low molecular weight heparin at prophylactic dose, intravenous methylprednisolone 250mg every day for 3 days and 80mg the next 2 days. During hospitalization, one of the patients with intermittent asthma received LABA/low-medium dose GCI and the other five patients did not receive any anti-asthmatic treatment. From the five moderate asthma patients, two of them received LABA/ medium dose GCI during hospitalization to treat the asthma exacerbation on admission; the other three didn´t receive LABA/GCI.

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Table S1. Epidemiological, demographic and clinical characteristics of hospitalized patients with COVID-19.

	NON-ASTHMA GROUP (n=178)	ASTHMA GROUP (n=11)	*p* VALUE
Age-Mean ± SD	68.12 ± 13.73	57.73 ± 14.63	n.s.
Age-Range	28-88	36-85	n.s.
Age groups-No (%)			
<30 y	1 (0.56)	0 (0.00)	n.s.
30-49 y	28 (15.73)	3 (27.27)	n.s.
50-69 y	84 (47.19)	5 (45.45)	n.s.
≥ 70 y	65 (36.52)	3 (27.27)	n.s.
Sex-No (%)			
Female	72 (40.45)	8 (72.73)	*p* = 0,0559 RR = 0.2752 CI 95%=0.07535-1.005
Male	106 (59.55)	3 (27.27)	
BMI (body mass index)			
BMI-Mean ± SD	28.23 ± 5.20	29.94 ± 4.62	n.s.
BMI-groups-No (%)			
Unknown	72 (40.45)	3 (27.27)	n.s
Underweight (< 18.5)	0 (0.00)	0 (0.00)	n.s
Normal (18.5-24.99)	31 (17.42)	2 (18.18)	n.s
Overweight (25-29.9)	42 (23.60)	2 (18.18)	n.s
Obese (BMI ≥ 30)	33 (18.54)	4 (36.36)	n.s.
Smoking status-No (%)			
Current smokers	18 (10.11)	1 (9.10)	n.s.
Ex-smokers	35 (19.66)	4 (36.36)	n.s.
Never smokers	125 (70.22)	6 (54.55)	n.s.
Non T2-comorbidities-No (%)			
Hypertension	84 (47.19)	3 (27.27)	n.s.
Diabetes mellitus	29 (16.29)	3 (27.27)	n.s.
Hyperlipidemia	63 (35.39)	2 (18.18)	n.s.
Heart disease	20 (11.24)	0 (0.00)	n.s.
Chronic renal disease	11 (6.18)	0 (0.00)	n.s.
Active cancer	16 (8.99)	0 (0.00)	n.s.
Surgery experience	77 (43.26)	5 (45.45)	n.s.
COPD	5 (2.81)	0 (0.00)	n.s.
T2-comorbidities- No (%)			
Allergic rhinitis	9 (5.06)	5 (45.45)	*p* = 0,0004; RR = 10.417; CI 95% = 3.627-29.912
Food allergy	3 (1.68)	1 (9.10)	n.s.
Drug hypersensitivity	25 (14.04)	1 (9.10)	n.s.
Nasal polyps	1 (0.56)	0	n.s.
Atopic Dermatitis	1 (0.56)	0 (0.00)	n.s.
Chronic urticaria	2 (1.12)	0 (0.00)	n.s.
Sensitization to aeroallergens- No (%)			
Pollens	7 (3.93)	6 (54.54)	*p* < 0,0001 RR = 16.246 CI 95% = 5.714-46.188
Epithelia	0 (0.00)	2 (18.18)	*p* = 0.0031 RR = 20.778 CI 95% = 10.983-39.309

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Dust mites	5 (2.80)	0 (0.00)	n.s.
Symptoms on Admission-No (%)			
Fever	146 (82.02)	9 (81.81)	n.s.
Cough	140 (78.65)	9 (81.81)	n.s.
Dyspnea	105 (58.99)	6 (54.54)	n.s.
Chest tightness	16 (8.99)	2 (18.18)	n.s.
Wheezing	4 (2.25)	0 (0.00)	n.s.
Rhinitis	8 (4.50)	0 (0.00)	n.s.
Odynophagia	14 (7.87)	0 (0.00)	n.s.
Myalgia	67 (37.64)	3 (27.27)	n.s.
Headache	19 (10.67)	0 (0.00)	n.s.
Conjunctivitis	4 (2.25)	0 (0.00)	n.s.
Weight loss	13 (7.30)	0 (0.00)	n.s.
Gastrointestinal symptoms	55 (30.90)	4 (36.36)	n.s.
Hypogeusia	5 (2.81)	0 (0.00)	n.s.
Anosmia	4 (2.25)	0 (0.00)	n.s.
FIO_2 required on admission- No (%)			
21%	57 (32.02)	4 (36.36)	n.s.
≥ 21-35%	99 (55.62)	5 (45.45)	n.s.
≥35% -60%	14 (7.87)	1 (9.10)	n.s.
>60%	8 (4.49)	1 (9.10)	n.s.
Chest radiograph´s infiltrates on admission- No (%)			
Normal	10 (6.62)	2 (18.18)	n.s.
Single lung	29 (16.29)	1 (9.10)	n.s.
Bilateral lung	139 (78.1)	8 (72.72)	n.s.
Blood laboratory findings on admission-Average ± SD			
Leukocytes (cls/mm^3)	7014.6 ± 3684.865	5993.63 ± 2733.37	n.s.
Lymphocytes (cls/mm^3)	927.53 ± 599,23	909.10 ± 610.6	n.s.
Eosinophils (cls/mm^3)	28,39 ± 105.06	23.55 ± 25.50	n.s.
C protein reactive (mg/dL)	10.40 ± 8.23	10.55 ± 12.88	n.s.
Ferritin (ng/mL)	1958.50 ± 8586.63	928.89 ± 722.43	n.s.
D-dimer (µg/L)	2508.23 ± 14064.81	593.55 ± 680.92	$p = 0.0846$
Days of hospitalization-Average ± SD			
	10.9 ± 9.67	9.72 ± 8.14	n.s.
Admission in ICU care-No (%)			
	30 (16.85)	2 (18.18)	n.s.
Blood laboratory findings prior to discharge- Average ± SD			
Leukocytes (cls/mm^3)	8506.33 ± 4749.31	8182.73 ± 5813.22	n.s.
Lymphocytes (cls/mm^3)	1349.72 ± 1120.53	1690.91 ± 2553.99	n.s.
Eosinophils (cls/mm^3)	64.42 ± 106.65	34.48 ± 48.42	n.s.
C protein reactive (mg/dL)	24.18 ± 126.80	3.37 ± 2.70	n.s.
Ferritin (ng/mL)	1122.10 ± 1228.85	1055.37 ± 998.7	n.s.
D-dimer (µg/L)	2230.57 ± 5574.53	5469.25 ± 9655.82	n.s.
Outcomes-No (%)			
Life discharge	149 (83.70)	9 (81.82)	n.s.
Death	22 (12.36)	2 (18.18)	n.s.
Hospitalization on-going- (as of May 20, 2020)	7 (3.93)	0 (0.00)	n.s.

No: number. SD: standard deviation. COPD: chronic obstructive pulmonary disease. RR: relative risk. CI: confidence interval

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