Supplementary materials

Supplementary methods

Patient cohort classification

The target study sample was four hundred SARS-CoV-2-positive and four hundred SARS-CoV-2-negative patients. This sample size was determined to yield a level of precision, as measured by the width of the 95% confidence interval (CI), of at least ± 5%, to estimate the anosmia and ageusia rates in the SARS-COV-2 positive and negative patients. The phone interviews were conducted between May 6th and June 30th, 2020.

COVID-19 positive patients were defined as either patients who tested SARS-CoV-2-positive, or as patients who tested negative but presented with COVID-19-like symptoms and met clinical criteria for probable COVID-19 illness as determined by the treating physicians. The COVID-19 probable cases met the clinical criteria defined by CDC by having at least two of the following symptoms, fever, chills, rigors, myalgia, headache, sore throat, nausea or vomiting, diarrhea, fatigue, congestion or runny nose OR any one of the following symptoms, cough, SOB, difficulty in breathing, new olfactory disorder, new taste disorder.[(1)] Due to COVID-19 testing kit shortages during the study period, tests were not typically repeated when the degree of clinical suspicion for the disease was high. We deemed it important to include these unconfirmed but highly probable cases as COVID-19 positive cases because of the known rate of false negative RT-PCR test results.[(2)] The COVID-19 negative group was defined as patients who were tested for SARS-CoV-2 because of a clinical suspicion for possible COVID-19

at their presentation but were deemed negative for COVID-19 based on clinical evaluation in addition to the negative test results. Prior to calling COVID-19 negative patients, their charts were reviewed to confirm that patients were tested for SARS-CoV-2 based on suspicion for COVID-19.

Exclusion criteria

Patients with incomplete medical records, deceased patients, patients below the age of 18 years were initially excluded from the study. Those who did not have valid contact information, those who were unreachable after at least three call attempts or those who were unable to respond because of persistent healthcare issues and were receiving ongoing care in a medical facility were also eventually excluded from the study. Additional reasons for exclusion were as follows: Patients who were deceased during the call period of May 6th-June 30th, 2020, patients who were screened for SARS-CoV-2 prior to procedures (childbirth, surgeries, etc.), had no symptoms indicative for COVID-19 and tested negative, and those who could not remember getting tested

Data Collection

Demographics, relevant past medical history (e.g. asthma, chronic obstructive pulmonary disorder (COPD), diabetes, hypertension, and hypercholesterolemia) were obtained from the electronic medical records. Laboratory markers such as absolute eosinophil counts, absolute neutrophil counts, and the levels of markers of inflammatory response such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, ferritin, and serum lactate dehydrogenase (LDH) were obtained from the

time of the SARS-CoV-2 test. Length of hospital stay was defined as the duration of the patient stay in the hospital from the time of the presentation to emergency room to the time of the discharge from either emergency room or from the hospital.

The structured phone interviews were completed in either English or Spanish based on the subject's native language.

Statistical analysis:

Past medical history and laboratory variables that were statistically significant at the bivariate level, as well as those demographic characteristics that were considered clinically important *a priori* were considered for inclusion in an initial "full" model. A final model was also fit by using a backwards stepwise selection strategy, retaining only those variables which remained significant at $p<0{\cdot}05$. The goodness of fit of the logistic regression models was assessed using the Hosmer-Lemeshow test.

Patients who had not yet recovered their sense of smell or taste were censored at the time of the phone interview. Cox-proportional hazards regression models were also fit to the data to evaluate associations between demographic characteristics and time to recovery. The proportional hazards assumption was verified by evaluating the interaction term between the predictor variables of interest and the logarithm of the follow up time.

All statistical analyses were performed with STATA 15·1 software (StataCorp, College Station, TX) and SAS 9·4 (SAS Institute Inc., Cary, NC). A two-sided P-value $< 0{\cdot}05$ was considered significant for all analyses.

Appendix A.
Questionnaire in English

Did you have fever?
☐ Yes ☐ No
When did you notice it?
Date (exact or estimated):

Did you have body aches?
☐ Yes ☐ No
When did you notice it?
Date (exact or estimated):

Did you notice that you lose your sense of smell?
☐ Yes ☐ No
When did you notice it?
Date (exact or estimated):

If yes, was it complete or partial?
☐ Complete ☐ Partial

Did you notice that you lose your sense of taste?
☐ Yes ☐ No
When did you notice it?
Date (exact or estimated):

If yes, was it complete or partial?
☐ Complete ☐ Partial

Was the lack of smell and/or taste an early symptom – before other symptoms started?
☐ Yes ☐ No ☐ Unsure

If you still have partial loss of their sense of taste or smell, was there any specific change to any particular taste (sour, salty, sweet) and/or change in the type of smell (some things smell differently)?

Did you have cough?
☐ Yes ☐ No
When did you notice it?
Date (exact or estimated):

Did you have a sore throat?
☐ Yes ☐ No
When did you notice it?
Date (exact or estimated):

Did you have belly aches?
▢ Yes ▢ No
When did you notice it?
Date (exact or estimated):

Did you have diarrhea?
▢ Yes ▢ No
When did you notice it?
Date (exact or estimated):

Did you have nausea/vomiting?
▢ Yes ▢ No
When did you notice it?
Date (exact or estimated):

Did you have fatigue?
▢ Yes ▢ No
When did you notice it?
Date (exact or estimated):

Did you have any other symptoms?
▢ Yes ▢ No
If yes, which ones?
When did you notice it?
Date (exact or estimated):

How long did your infection symptoms last?

Were you admitted to the hospital?
▢ Yes ▢ No

Did you require assistance with breathing?
▢ Yes ▢ No

If yes, what devices were used to assist your breathing?

Did you have to go to the intensive care unit?
▢ Yes ▢ No

Did you require a breathing tube/ventilator?
▢ Yes ▢ No

In which date did you start feeling symptoms?
Date:

What was the order of your symptoms?

Have you recovered your sense of taste and smell?

When did you do your COVID-19 testing?
Date:

How many days passed between the onset of symptoms and the date that you went to ER?
Number of days:

Appendix B
Questionnaire in Spanish

¿Le dio fiebre?
☐ Si ☐ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Sintió dolores musculares?
☐ Si ☐ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Noto pérdida del sentido de olfato?
☐ Si ☐ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

Si su respuesta fue sí, ¿Fue una pérdida completa o parcial?
☐ Completa ☐ Parcial

¿Noto pérdida del sentido del sabor?
☐ Si ☐ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

Si su respuesta fue sí, ¿Fue una pérdida completa o parcial?
☐ Completa ☐ Parcial

¿La falta del sentido del olfato o del sabor fue un síntoma temprano-antes de que comenzaran otros síntomas ?

▢ Si ▢ No▢ No está seguro(a)
Si todavía tiene pérdida del sentido del olfato o del sabor, ¿hubo algún cambio específico de un sabor en particular (agrio, salado, dulce) y/o cambio en el tipo de olor (algunas cosas le huelen distintas) ?

¿Tuvo tos ?
▢ Si ▢ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Tuvo dolor de garganta ?
▢ Si ▢ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Sintió malestar abdominal?
▢ Si ▢ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Tuvo diarrea?
▢ Si ▢ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Tuvo náuseas o vómito?
▢ Si ▢ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Sintió fatiga?
▢ Si ▢ No
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Tuvo algún otro síntoma?
▢ Si ▢ No
Si su respuesta fue si, ¿cuál otro síntoma ?
¿Cuándo lo noto?
Fecha (exacta o aproximada)

¿Cuánto tiempo duró sus síntomas de infección ?

¿Fue ingresado al hospital?
▢ Si ▢ No

¿Requirió asistencia para poder respirar?
☐ Si ☐ No
Si su respuesta fue si, ¿cuál aparato fue usado para asistirle a respirar ? ¿Estuvo en la unidad de cuidados intensivos?
☐ Si ☐ No

¿Requirió de intubación/ventilación mecánica?
☐ Si ☐ No
¿En qué fecha comenzó a sentir síntomas?
Fecha:
¿En qué orden sucedieron sus síntomas?

¿Ha recobrado su sentido del sabor y sentido de olfato?

¿Cuándo fue a hacerse la prueba del COVID-19?

¿Cuántos días pasaron desde el inicio de los síntomas a la fecha en que acudió a la sala de emergencia?
Número del días:

Supplementary results:

Pre-existing conditions

Pre-existing conditions such as asthma, COPD, and diabetes were not significantly associated with the presence or absence of the sense of smell or taste among COVID-19 patients (data not shown). However, hypertension and hypercholesterolemia were significantly less frequent in those with anosmia (Table 1) but not in patients with ageusia (Table 2).

Severity

There was a significantly shorter length of hospital or emergency room stay among the COVID-19 patients with self-reported anosmia (4 (IQR 2-8) days vs. 6 (IQR 3-10) in patients without anosmia, p=0·002, Table 1) but there was no significant difference in the length of stay between patients with and without ageusia (Table 2). There was no significant difference in frequency of ICU admission or endotracheal intubation in those with and without anosmia or ageusia (Tables 1 and 2).

Table S1- Characteristics of COVID-19 patients and the control cohort

	Characteristics	COVID-19 patients, N=486	COVID-19-negative patients, N=103	*p*-value
Demographics	Age, years (±SE)	57 (±0.7)	55.1 (±1.8)	0.3
	Gender, N (%) women	230 (47)	63 (61)	***0.01***
	Race/ethnicity, N (%)			0.09
	White	46 (9)	6 (5)	
	Black	193 (40)	44 (43)	
	Latino	160 (33)	43 (43)	
	Asian	10 (2)	1 (1)	
	Unknown	77 (16)	8 (8)	
Reported Symptoms	Anosmia*, N (%)	162 (34)	8 (8)	***<0.001***
	Ageusia*, N (%)	242 (51)	10 (10)	***<0.001***
	Fever*, N (%)	244 (51)	34 (33)	***0.001***
	Body aches*, N (%)	219 (51)	34 (33)	***0.001***
	Cough*, N (%)	287 (67)	30 (30)	***<0.001***
	Pneumonia*, N (%)	55 (11)	1 (1)	***<0.001***
	Sore throat*, N (%)	108 (23)	11 (11)	***0.009***
	Diarrhea*, N (%)	195 (41)	20 (20)	***<0.001***
	Loss of appetite*, N (%)	70 (14)	5 (5)	***0.008***
	Headache*, N (%)	62 (14)	9 (9)	0.2
	Fatigue or weakness*,	323 (68)	38 (37)	***<0.001***
	BMI▲, kg/m2 (IQR)	30 (26-36)	28(25-33)	***0.02***
	Number of days from the onset of symptoms to the SARS-CoV-2 test, median (IQR)	7 (3-12)	3 (2-9)	***0.001***
	Number of days from SARS-CoV-2 test to the phone interview, median (IQR)	46 (36-62)	44 (26-63)	0.2
Patient past medical history	History of asthma▲, N (%)	84 (17)	31 (30)	***0.003***
	History of hypertension▲, N (%)	232 (48)	60 (58)	***0.05***
	History of COPD▲, N (%)	39 (8)	12 (12)	0.2
	History of diabetes▲, N (%)	166 (34)	41 (40)	0.3

	History of hypercholesterolemia▲, N (%)	167 (34)	39 (38)	0.5
Laboratory markers at the time of SARS-CoV-2 test	Absolute neutrophil counts▲, K/μL (±SE)	6.1 (±0.16)	8.1 (±0.6)	***<0.001***
	Eosinophil counts▲, K/μL (±SE)	0.04 (±0.004)	0.2 (±0.04)	***<0.001***
	C-reactive protein▲, mg/dL	8.1 (4.1-15.5)	4.2 (0.6-18.1)	***0.05***
	Erythrocyte sedimentation rate▲, mm/h (±SE)	76 (±3.8)	82 ((±11.5)	0.6
	Lactic dehydrogenase▲, U/L (±SE)	420 (±10.1)	307 (±26.0)	***<0.001***
	Fibrinogen▲, mg/dL (±SE)	657 (±12.0)	530 (±51.0)	***0.02***
	Ferritin▲, ng/mL (IQR)	610 (349-1231)	783 (340-1423)	0.1
Outcomes	Length of emergency department or hospital stay, days (IQR) ▲	5 (3-10)	3 (2-6)	***<0.001***
	Admission to ICU▲	52 (11)	8 (8)	0.5
	Endotracheal intubations▲, N (%)	32 (7)	4 (4)	0.4

*Patient reported. ▲ Extracted and verified through medical record data extraction and review

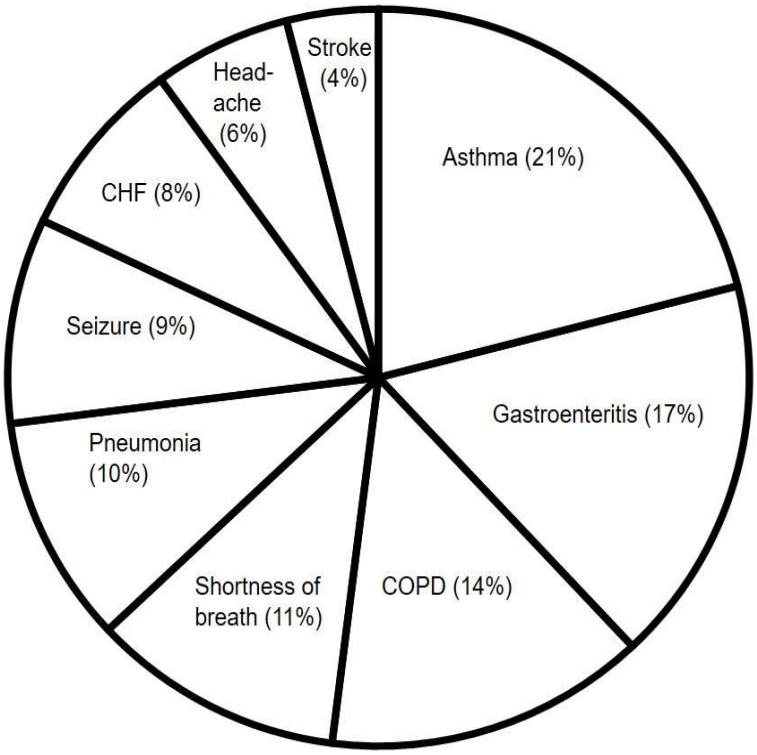

Figure S1: Admission diagnoses of COVID-19 negative patients (N=103), CHF-Congestive Heart failure, COPD-Chronic Obstructive Pulmonary Disease

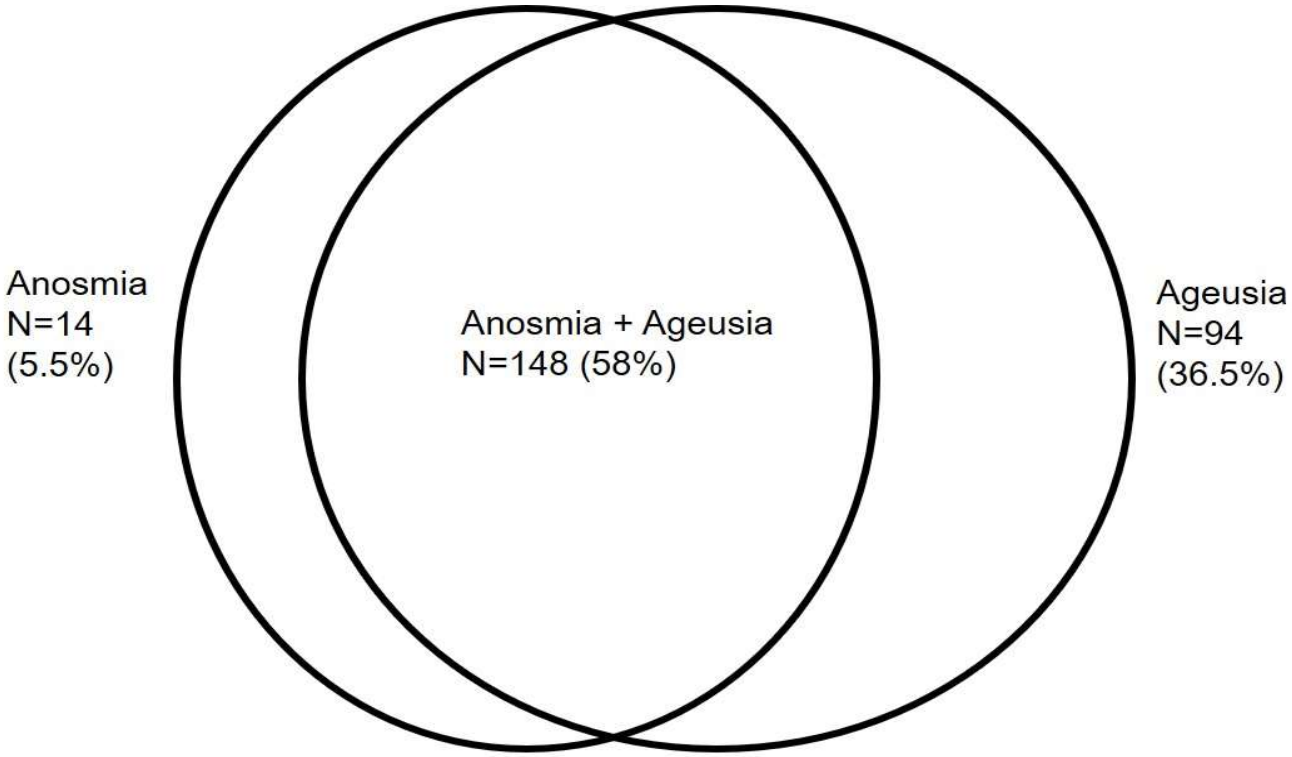

Figure S2: Anosmia and ageusia overlap in COVID-19 patients.

References:

1. CDC-definition of COVID-19 probable cases: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/faq-surveillance.html.
2. Xiao AT, Tong YX, Zhang S. False negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. J Med Virol. 2020.