Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

angiotensin-converting enzyme 2 expression levels correlate with allergic sensitization, higher levels of total immunoglobulin E, and type 2 inflammatory cytokines.[3-5] Interleukin 13, a major type 2 inflammatory cytokine, is found to significantly reduce angiotensin-converting enzyme 2 expression in airway epithelial cells.[5] Our findings of the association of AR and eczema with decreased need of hospitalization for COVID-19 provide robust clinical data to support these mechanistic findings.

The role of asthma and its association with COVID-19 severity is more complicated.[6,7] Asthma was not reported in previously published cohorts of COVID-19 from China[1,2]; although data from the Centers for Disease Control indicate that asthma is present in as high as 27% of hospitalized COVID-19 patients in the United States in the 20 to 49 year age range.[6] This could be explained by the lower rates of asthma in China (2%-4%) than those in the United States (8%-11%).[8,9] In the current report, allergic asthma was not associated with any COVID-19 outcome variable despite AR being protective against hospitalization. Furthermore, nonallergic asthma was associated with a prolonged intubation time which confirms an earlier study.[10] It is possible that asthma, as a chronic pulmonary disease susceptible to viral-induced exacerbations, places those with more severe COVID-19 illness at risk for more prolonged lung involvement. However, a coexisting atopic background may mitigate the severe inflammatory response syndrome of COVID-19 in those with allergic asthma, leading to the absence of the prolonged intubation time reported in individuals with nonallergic asthma.

The knowledge that atopy is associated with less severe COVID-19 outcomes can be instructive in clinical risk stratification. Further studies are needed to understand the underlying mechanism of these apparent protective physiological factors that may prove advantageous in future prevention and treatment strategies.

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Smell loss is a prognostic factor for lower severity of coronavirus disease 2019

Check for updates

Coronavirus disease 2019 (COVID-19) can present with a myriad of symptoms.[1] Guidelines from the People's Republic of China, the United Kingdom, and Italy had focused screening efforts on patients with fever and cough, excluding anosmia from similar scrutiny.[1] However, the screening of individuals with reported anosmia and dysgeusia has been associated with a greater likelihood of a positive COVID-19 result than other indicators of an upper respiratory tract infection.[2-4] The relative predictive value of presenting COVID-19 symptoms is under current investigation.[3-6] This study seeks to ascertain the role of smell loss in risk stratification and predicting COVID-19 patients' prognosis.

Adult patients with COVID-19 who were evaluated at a university medical center between February 1, 2020 and April 3, 2020 were identified by an electronic medical records query and included in our initial series. Complete data on demographic variables, clinical characteristics, COVID-19 symptoms, COVID-19 treatments, and clinical evaluations were retrieved. Through a predesigned screening questionnaire for COVID-19, the patients were evaluated through telemedicine, in-person, or at the emergency department and were asked about their symptoms during the history taking, including whether they had acute smell loss. Patients with incomplete clinical data or whose smell loss was not recorded were excluded.

The retrieved information included the following: (1) demographics; (2) body mass index (BMI); (3) comorbid conditions (asthma, allergic rhinitis, chronic rhinosinusitis, eczema, food allergy); (4) preexisting smell dysfunction; (5) COVID-19–related inflammatory laboratory values (complete blood cell counts, C-reactive protein, albumin, creatinine, ferritin, and erythrocyte subdimension rate); (6) COVID-19 outcomes (need for hospitalization, intensive care unit admission, intubation); and (7) development of acute respiratory disease syndrome. To identify and confirm comorbidities and other clinical variables, all charts were reviewed by 2 independent trained

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researchers, and 20% of the charts were randomly checked by the principal investigator. Data points with a lack of concordant information were reviewed again by an independent investigator, and if needed, were excluded from the analysis.

The Statistical Product and Service Solutions version 23 (SPSS Inc, Chicago, Illinois) was used for all analyses. Results with continuous variables were presented as mean plus or minus SD unless otherwise specified and were compared using parametric analysis if normally distributed (Student's t test). The χ^2 test was performed to analyze the correlation among the categorical parameters. Logistic regression was conducted to calculate the odds ratio (OR) of smell loss in association with nominal dependent variables such as preexisting comorbidities and COVID-19 outcome was adjusted for possible confounders (demographics and BMI). The adjusted ORs were presented with their 95% confidence intervals (CIs). Analysis of covariance was conducted to compare the adjusted means of continuous variables such as laboratory values in association with smell loss, adjustment for demographics, and BMI. This research study was approved by the institutional review board.

The initial series consisted of 1013 patients who were evaluated and received positive test results for COVID-19. Sufficient data on smell loss, demographic variables, comorbidities, and outcomes were available for 949 patients (93.7%), who were included for the analysis. The cohort consisted of 55.2% of women with a mean (SD) age of 48.42 (±15.67) years. In this series, 54.3% of patients were Black, 25.0% were non-Latino White, 22.9% were Latino, and 14.3% were identified as other race or ethnicity.

Overall, 198 (20.9%) patients reported smell loss during their initial evaluation for COVID-19. Smell loss was significantly associated with younger age, female sex, and higher BMI: the mean age was 46 vs 49 years in those with and without smell loss, respectively ($P = .02$); 64.7% of patients with smell loss vs 52.8% of those without smell loss were women ($P = .003$); and the mean BMI was 33.6 vs 31.5 in those with and without anosmia, respectively ($P = .001$). There was a significant association between smell loss and history of preexisting smell dysfunction (OR, 4.66; 95% CI, 2.07-10.46, $P < .001$), allergic rhinitis (OR, 1.79; 95% CI, 1.12-2.87, $P = .02$), and chronic rhinosinusitis (OR, 3.70; 95% CI, 1.29-10.67, $P = .02$) compared with patients without smell loss.

Sufficient data on laboratory markers was available for 419 (41.8%) patients. Compared with patients without smell loss, patients with smell loss exhibited less lymphopenia (the mean ± SD of lymphocyte count was 1.84 ± 3.69 vs 1.11 ± 0.81 in those with and without smell loss, respectively; $P = .001$) and higher albumin counts (3.02 ± 0.83 vs 2.77 ± 0.83, $P = .02$). Other laboratory values and inflammatory markers were not associated with smell loss among patients with COVID-19. These results did not change after adjusting for demographics and BMI.

Smell loss was also significantly associated with decreased hospitalization (OR, 0.69; 95% CI, 0.47-0.99, $P = .04$), intensive care unit admission (OR, 0.38; 95% CI 0.20-0.70, $P = .002$), intubation (OR, 0.43; 95% CI, 0.21-0.89, $P = .02$), and acute respiratory distress syndrome (OR, 0.45; 95% CI, 0.23-0.89, $P = .02$) after adjustment for demographics and BMI (Table 1). These results remained significant after further adjustment for allergic rhinitis and chronic rhinosinusitis.

Our data implicate smell loss as an independent positive prognostic factor of a less severe COVID-19 infection. It was significantly associated with decreased hospitalization, intensive care unit admission, intubation, and acute respiratory distress syndrome rates compared with the lack of smell loss (Table 1). In further support, smaller studies of 169 and 34 patients who received a positive COVID-19 diagnosis found an association between anosmia with outpatient care as opposed to hospitalization.[7] Our data aligns with these findings. In addition, smell loss was associated with less lymphopenia and higher levels of albumin, suggesting a less severe reaction to COVID-19 in patients with smell loss than those with an intact smell.

Table 1
Preexisting Conditions and COVID-19–related Outcomes in 949 COVID-19 Patients in Association With Smell Loss

Conditions	Number of cases with condition among the series	Odds ratio (95% CI) of having smell loss in patients with the condition compared with those without the condition	Adjusted P value[a]
History of smell dysfunction	27	4.66 (2.07-10.46)	<.001[b]
Allergic rhinitis	101	1.79 (1.12-2.87)	.02[c]
Food allergy	71	1.64 (0.95- 2.83)	.08
Atopic dermatitis (eczema)	42	1.22 (0.59-2.50)	.60
Asthma	243	1.18 (0.82-1.70)	.36
Chronic rhinosinusitis	15	3.70 (1.29-10.67)	.02[c]
GERD	60	0.67 (0.29-1.58)	.36
Diabetes	243	0.86 (0.57-1.29)	.46
Hypertension	391	1.14 (0.77-1.68)	.52
Emergency department visit for COVID-19	520	0.83 (0.59-1.16)	.28
Hospitalized	311	0.69 (0.47-0.99)	.04[c]
ICU-admitted	131	0.38 (0.20-0.70)	.002[c]
Intubated	86	0.43 (0.21-0.89)	.02[c]
ARDS	93	0.45 (0.23-0.89)	.02[c]

Abbreviations: ARDS, acute respiratory distress syndrome; BMI, body mass index; COVID-19, coronavirus disease 2019; GERD, gastroesophageal reflux disease; ICU, intensive care unit.
[a]Odds ratios and adjusted P values are calculated by logistic regression adjusting for age, sex, and BMI.
[b]P value less than .001.
[c]P value less than .05.

A history of preexisting smell dysfunction, allergic rhinitis, or chronic rhinosinusitis was associated with a greater chance of acute smell loss in patients with COVID-19. However, because most patients who experience smell loss in the setting of COVID-19 report a return of smell with clinical resolution of illness,[8] and an initial neuroimaging study seemed to indicate an absence of acute visible size changes to the neural olfactory system,[9] COVID-19 is not associated with permanent anosmia. Positive and negative predictive values could not be calculated because the basal rates of hyposmia and anosmia, the prevalence of COVID infection, and the individual phases of illness of each infected patient were not established for the studied population; however, they have been evaluated in further detail elsewhere.[6] Female sex, lower age, higher BMI, history of previous smell loss, and preexisting allergic rhinitis and chronic rhinosinusitis appeared as important predictors of smell loss in the setting of COVID-19 infection. The main limitations of our study were its retrospective nature, subjective nature of smell loss, and focused nature of the data collection that did not include the patients' current medications.

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Food allergy and growth from late childhood to early adolescence

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Immunoglobulin E–mediated food allergy may be associated with diminished growth but obesity has also been proposed to be associated with food allergy.[1-3] This study examined the association between food allergy and growth in a population of Canadian children and adolescents using data from the Study of Asthma, Genes, and Environment (SAGE).[4]

A survey was provided in 2002 to all households in the province of Manitoba with children born in 1995 and residents of the province at 7 years old (N = 13,980); 3681 surveys were returned. A nested case-control study of 723 participants was created.[4] Those participants were seen between ages 7 and 10 years and again between 11 and 14 years for clinical assessments for food allergy, asthma, atopic dermatitis, and allergic rhinitis by 1 of 2 pediatric allergists. Height and weight were measured at both assessments and body mass index (BMI) were calculated. Those data were converted to height- (H/A), weight- (W/A), and BMI-for-age (B/A) z scores.[5] World Health Organization (WHO) criteria were used to define obesity, overweight or obesity, wasting, and stunting.[6] Health care records, caregiver reports and surveys were used to collect data for a number of variables around the time of the first assessment.

Regression was used for analyses with statistical significance set at $P < .05$. Participants with no missing data were included. Similar to a study by Beck et al,[7] the region of residence, ethnicity, household income, gestational age, and birthweight were included as a priori variables in adjusted models. Other variables were systematically tested for inclusion.[7] All adjusted models ultimately included duration of breastfeeding in addition to the a priori variables. For adjusted linear regression models with H/A, W/A, and B/A at 7 to 10 years as outcomes and food allergy at 7 to 10 years as the exposure of interest, asthma, atopic dermatitis, and allergic rhinitis at 7 to 10 years were also included. For adjusted linear regression models with H/A, W/A, and B/A at 11 to 14 years as outcomes and persistent food allergy as the exposure of interest, persistent asthma, persistent atopic dermatitis, and persistent allergic rhinitis were also included. To be classified as persistent, a diagnosis had to be made at both assessments. Logistic regression models, both adjusted and not, included obesity and obesity or overweight as outcomes and food allergy at 7 to 10 years and persistent food allergy at 11 to 14 years as the exposures of interest. Sensitivity analyses excluded participants with H/A, W/A, or B/A categorized as biologically implausible by the WHO (H/A <-6 or >6, W/A <-6 or >5, B/A <-5 or >5).[5] Stata version 15.1 (StataCorp, College Station, Texas) was used for analyses. SAGE was approved by the University of Manitoba's Health Research Ethics Board (HS14742 [H2002:078]).

Complete data were available for 415 participants in which 46 and 37 participants had food allergy at the first and both assessments, respectively. Those with food allergy at 7 to 10 years were more likely to neither identify as indigenous nor white, had diagnoses of atopic dermatitis, asthma, and allergic rhinitis and reported inhaled corticosteroid use (Table 1). For the sensitivity analyses, 6 children were excluded because of W/A greater than 5, B/A greater than 5, or both at 7 to 10 years.

In unadjusted models, children with food allergy at 7 to 10 years had lower H/A at 7 to 10 years in both primary (β: −0.336, 95% confidence interval [95% CI]: −0.656 to −0.017, $P = .039$) and sensitivity analyses ($P < .05$). In the sensitivity analysis, such children also had lower W/A at 7 to 10 years in the unadjusted model (β: −0.366, 95% CI: −0.724 to −0.008, $P = .045$). For models with H/A, W/A, and B/A as outcomes, there were no other statistically significant relationships but there were consistently negative associations between outcomes and food allergy exposures. This finding was robust to sensitivity analyses. In all analyses, there were no statistically significant associations between food allergy exposures and overweight- and obesity-related outcomes.

Consistent with previous research, this study indicates that, in a population of Canadian children aged 7 to 10 years (in unadjusted models), those having a clinical diagnosis of food allergy were shorter than those without and were also noted to have lower weight when extremes of W/A and B/A were removed.[1,2] Although not statistically significant, there were consistently negative associations between food allergy exposures and H/A, W/A, and B/A outcomes.

This study also indicates that, in a population of Canadian children at ages 7 to 10 and 11 to 14 years, there were no statistically significant relationships between food allergy exposures and overweight- and obesity-related outcomes. Elevated

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