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Anxiety in adults with allergic rhinitis during the coronavirus disease 2019 pandemic: A Canadian perspective

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ABSTRACT

Background: Despite the symptom overlap between allergic rhinitis (AR) and coronavirus disease 2019 (COVID-19), pandemic-time anxiety in people with AR remains an area of limited study.
Objective: To assess the AR-anxiety relationship in the unique context of the COVID-19 pandemic from a Canadian perspective.
Methods: The COVID-19 Associated Anxiety in patients with Asthma and AR Experiencing Symptoms survey was distributed on the "Qualtrics XM" platform, with 835 adult participants responding to the first iteration from April to August 2020. Anxiety was assessed on the Generalized Anxiety Disorder Assessment-7 (GAD-7), and AR burden of disease was assessed on the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). All analyses were conducted using IBM SPSS Statistics 27.
Results: High levels of anxiety were found, with 28.0% of the AR group and 27.5% of the control group meeting the diagnostic criteria for generalized anxiety disorder. After controlling for covariates, AR status had no significant predictive effect on GAD-7 in a hierarchal multiple regression model ($\Delta R^2 = .00$, $P = .69$). In the AR subgroup, there were significant positive correlations between anxiety and burden of disease for the total RQLQ score and all 7 domain scores ($P < .001$ for all), with the non-nose or eye symptom domain having the strongest correlation ($r = .63$). After controlling for covariates, total RQLQ score had a predictive effect on GAD-7 in a hierarchal multiple regression model ($\Delta R^2 = .049$, $P < .001$).
Conclusion: High levels of anxiety exist during the COVID-19 pandemic regardless of AR status, indicating the importance of early anxiety screening in all patients. This study also highlights the importance of non-nose or eye symptoms in AR management.

Introduction

Allergic rhinitis (AR), colloquially known as "hay fever," is an inflammatory disease of the nasal mucosa resulting from an immunoglobulin E-mediated response to allergen exposure. Clinically characterized by rhinorrhea, nasal congestion, nasal itching, and sneezing, AR is among the most common diseases worldwide and is estimated to affect approximately 1 in 4 Canadians.[1] Despite the high prevalence of AR, AR symptom control remains a major unmet need, with many patients with AR reporting inadequate relief with standard of care management.[1] Although historically trivialized and regarded as a nuisance disease, AR is now increasingly recognized as a condition with a substantial disease burden extending well beyond mere symptom burden, with evidence suggesting that uncontrolled AR has a major impact on quality of life, daily activities, school and workplace performance, and sleep.[2-4]

In addition to the burden of disease of AR alone, there is also evidence to imply a relationship between AR and anxiety symptoms and

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syndromes.[5-8] Previous literature suggests that AR may be linked to increased anxiety levels and that patients with AR may be more likely to have comorbid generalized anxiety disorder (GAD), although the body of literature on this topic remains somewhat conflicted about the nature and specifics of this potential relationship.[7-9] There remains debate about whether the AR-anxiety relationship exists across different AR subgroups and whether anxiety is associated with overall AR disease burden or with specific AR symptoms.[7-9]

In the novel context of the coronavirus disease 2019 (COVID-19) pandemic, the potential AR-anxiety relationship is of unique importance and relevance. The initial presentations of COVID-19 and AR share symptoms, including cough, rhinorrhea, nasal congestion, pharyngitis, and associated conjunctivitis.[10] From this symptom overlap, any number of worries may arise for patients with AR, including (but not limited to) the potential to mistake AR symptoms for symptoms of COVID-19 (or vice versa) and concern about being treated differently by those around them when patients experience AR symptoms. These worries may have been exacerbated by the spread of misinformation, with some health authorities proposing that those with allergic diseases may be at higher risk of contracting COVID-19 and of poorer prognoses after infection. Although there is emerging evidence that AR is not associated with poorer COVID-19 prognosis, patients with AR may have suffered negative psychological consequences from an increased perceived COVID-19 risk.[11] Compounded with a potential underlying AR-anxiety relationship, these COVID-19-specific concerns may put patients with AR at particular risk for increased pandemic-time anxiety.

The psychological impact of the COVID-19 pandemic is an emerging field of study, but there is a growing body of evidence suggesting that anxiety levels in the general population have increased during the pandemic, regardless of country.[12,13] A systematic review and meta-analysis by Salari et al[12] estimated the prevalence of anxiety in the general population to be 31.9%. In comparison, a prepandemic systematic review and meta-regression by Baxter et al[14] estimated the global prevalence of anxiety disorders to be 7.3%.

There also have been limited reports of increased pandemic-time anxiety in patients with allergic diseases—Gonzalez-Diaz et al found that individuals with allergic diseases reported more posttraumatic stress disorder (PTSD) and depressive symptoms than did nonallergic controls, with participants with respiratory allergies reporting more depressive symptoms than participants with nonrespiratory allergies and similar levels of PTSD symptoms.[15] However, it is worth noting that this study was conducted in Mexico, did not stratify between asthma and AR within the respiratory allergies group, and did not assess risk of GAD or anxiety symptoms beyond those encompassed in PTSD. Similarly, a cross-sectional survey study of adults with asthma in the US found that COVID-19-related anxiety was associated with uncontrolled asthma.[16]

Reports studying pandemic-time anxiety in patients with AR are scarce—Wang et al conducted a survey study of 98 participants with AR and 56 healthy controls in Wuhan, China, finding that participants with AR reported more anxiety than healthy controls.[17] However, this study had a limited sample size and only studied participants in Wuhan. This geopolitical context is relevant because Wuhan had a different set of COVID-19 regulations, policies, and a distinct socio-cultural milieu compared with North America during the pandemic.[18] Considering the conflicting literature surrounding the prepandemic AR-anxiety relationship, the AR-COVID-19 symptom overlap, and emerging evidence of increased pandemic-time anxiety, COVID-era anxiety in the population of patients with AR is an important topic that currently remains completely unstudied from a North American perspective. For specialists in Clinical Allergy and Immunology and other medical practitioners caring for patients with AR, a better understanding of pandemic-time anxiety would provide invaluable insight into best practices for management of AR disease burden both during and after the COVID-19 pandemic.

Methods

Survey Design

Data were collected using the COVID-19 Associated Anxiety in Allergic Rhinitis and Asthma patients Experiencing Symptoms (CAAARES) survey, which was conducted online on the "Qualtrics XM" platform. The CAAARES survey was distributed to the participant database of an allergy research group in Southeastern Ontario and to a broader online audience through social media promotion. The first iteration of the CAAARES survey collected responses from April to August 2020 during the spring and summer allergy season, when weed pollen, tree pollen, and mold spores are at their annual peak levels. This allowed the CAAARES survey to capture responses over the overlapping course of the peak seasonal AR period and the COVID-19 pandemic. Participants gave their written informed consent through a Letter of Information before completion of the online survey. The CAAARES study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

Participants

A total of 835 adult respondents participated in the first iteration of the CAAARES survey. Participants were excluded if they did not report a location of residence within Canada or if they did not report a valid response to AR status, GAD-7, or demographic data (sex, age, employment status, asthma diagnosis, previous anxiety diagnosis, past or current access of mental health services) (Fig 1).

Measures of Interest

Anxiety was measured on the Generalized Anxiety Disorder Assessment-7 (GAD-7), a self-report screening tool for GAD.[19] Generalized Anxiety Disorder Assessment-7 scores range from 0 to 21, with a score of 10 or higher suggested as the diagnostic threshold for GAD.[19]

Burden of disease of AR was assessed on the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), a self-report quality of life instrument assessing functional impairment experienced by adult patients with AR, with scores ranging from 0 (no impairment) to 6 (severe impairment).[20] The RQLQ can be further categorized into 7 domains: activity limitations, sleep problems, nose symptoms, eye symptoms, non-nose or eye symptoms, practical problems, and emotional function.[20]

Data Analysis

To maximize the sample size and power of each statistical test, responses were selectively excluded if they had missing responses for the variables being tested. No adjustment was made for multiple comparisons, and all analyses used a P value cutoff of $P \leq .05$ to determine statistical significance, including χ^2 tests, t tests, regressions, and correlations. All regression coefficients reported are standardized regression coefficients. All participant data were deidentified, and all analyses were conducted with IBM SPSS Statistics 27.

Results

Case-Control Analysis

A cross-sectional case-control analysis was conducted to compare anxiety in a group of participants with AR with that of a control

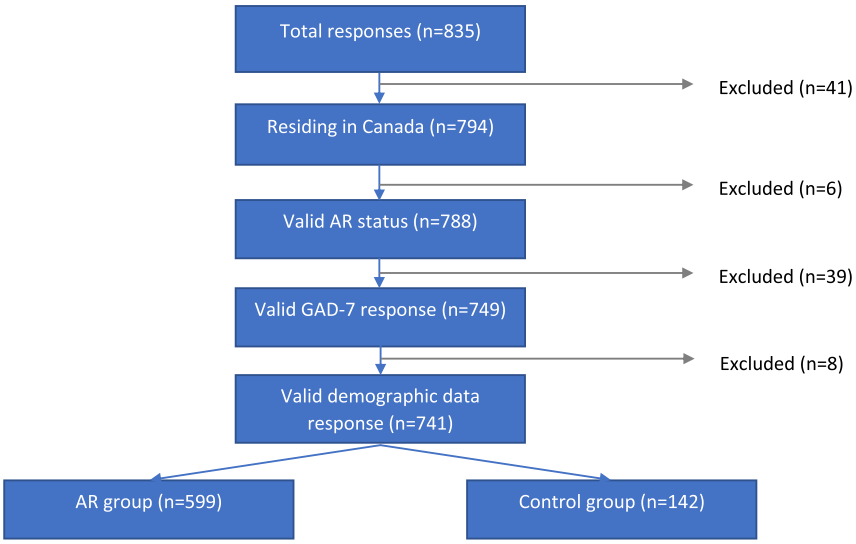

Figure 1. Flow chart of included and excluded responses from the first iteration of the CAAARES survey forming the present study population. AR, allergic rhinitis; CAAARES, COVID-19 Associated Anxiety in patients with Asthma and AR Experiencing Symptoms; COVID-19, coronavirus disease 2019; GAD-7, Generalized Anxiety Disorder Assessment-7.

group, defined as participants self-identifying as not having AR. A total of 741 responses were included, 599 participants with AR (80.8% of total included responses) and 142 participants without AR (19.2% of total included responses). The baseline demographic characteristics of the AR group and the control group are summarized in Table 1. χ^2 Testing showed a significant difference between the AR and control groups in age and asthma diagnosis.

Figure 2 compares the percentage of participants in the AR and control groups reporting GAD-7 scores indicating minimal anxiety (0-4), mild anxiety (5-9), moderate anxiety (10-14), and severe anxiety (15-21).[20] Participants meeting the diagnostic criteria for GAD are indicated by the red boxes (GAD-7 score ≥ 10).[20] In the AR group, 28.0% of respondents met the diagnostic criteria for GAD, compared with 27.5% of respondents in the control group. The mean GAD-7

Table 1
Baseline Demographic Characteristics of the AR Group and the Control Group Including Comparisons With χ^2 Tests

Characteristic	n (% of group)		
	AR group (n = 599)	Control group (n = 142)	χ^2 results
Sex			*P* = .59
Man	108 (18.0)	26 (18.3)	
Woman	485 (81.0)	113 (79.6)	
Nonbinary or prefer not to disclose	6 (1.0)	3 (2.1)	
Age			*P* < .001
18-25	82 (13.7)	51 (35.9)	
26-35	141 (23.5)	36 (25.4)	
36-45	158 (26.4)	17 (12.0)	
46-55	112 (18.7)	25 (17.6)	
56-65	90 (15.0)	8 (5.6)	
≥ 65	16 (2.7)	5 (3.5)	
Employment status			*P* = .11
Full time	161 (26.9)	40 (28.2)	
Full time working from home	113 (18.9)	27 (19.0)	
Part time	40 (6.7)	7 (4.9)	
Part time working from home	28 (4.7)	3 (2.1)	
Unemployed	24 (4.0)	5 (3.5)	
Recently laid off owing to COVID-19	68 (11.4)	16 (11.3)	
Retired	48 (8.0)	10 (7.0)	
Student	50 (8.3)	24 (16.9)	
Other	67 (11.2)	10 (7.0)	
Asthma diagnosis			*P* < .001
Yes	222 (37.1)	22 (15.5)	
No	377 (62.9)	120 (84.5)	
Previous anxiety symptom or syndrome diagnosis			*P* = .83
Yes	314 (52.4)	73 (51.4)	
No	285 (47.6)	69 (48.6)	
Currently receiving mental health services			*P* = .66
Yes	72 (12.0)	19 (13.4)	
No	527 (88.0)	123 (86.6)	
Received mental health services in the past			*P* = .52
Yes	347 (57.9)	78 (54.9)	
No	252 (42.1)	64 (45.1)	

Abbreviations: AR, allergic rhinitis; COVID-19, coronavirus disease 2019.
NOTE. Values in red indicate results showing a statistically significant difference between groups.

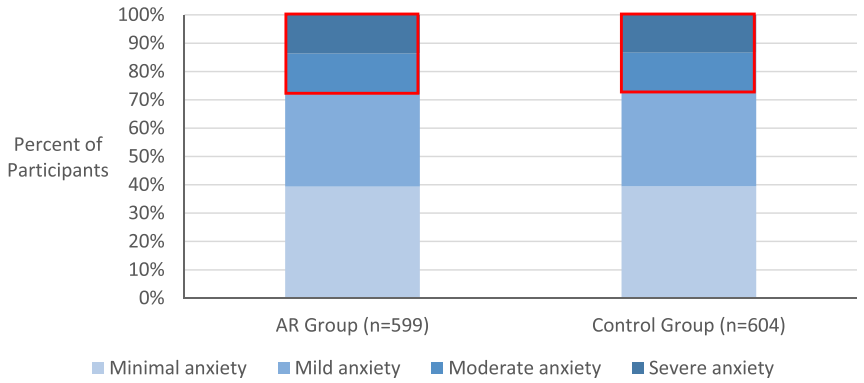

Figure 2. High levels of anxiety were found in both the AR group (n = 599) and the control group (n = 604). Red boxes indicate Generalized Anxiety Disorder Assessment-7 (GAD-7) scores meeting diagnostic criteria for generalized anxiety disorder (GAD-7 ≥ 10). There was no significant difference in mean GAD-7 scores between groups (t (739) = −.036; *P* = .97). AR, allergic rhinitis; GAD-7, Generalized Anxiety Disorder Assessment-7.

scores in the AR and control groups were 6.96 (SD = 5.64) and 6.98 (SD = 5.42), respectively. There was no significant difference in mean GAD-7 scores between the 2 groups when compared with a 2-tailed *t* test (t [739] = −.036; *P* = .97).

To assess the impact of AR status on GAD-7 scores while controlling for other variables, a hierarchal multiple regression was conducted, as summarized in Table 2. Predictor variables (demographic variables and COVID-19 pandemic-specific parameters) were included in the model if they were determined to have a significant predictive effect on GAD-7 score in bivariate analyses or if they were not balanced between the AR and control groups at baseline as determined by χ^2 testing (Table 1). Predictor variables meeting this inclusion criteria included sex, age, asthma diagnosis, previous anxiety syndrome or symptom diagnosis, current access of mental health services (MHS), past access of MHS, general COVID-19-related worry, and perceived COVID-19 stress of others. Sex was coded as a binary variable—participants who did not identify with the gender binary or who preferred not to disclose their gender identity were not included owing to insufficient sample size (Table 1). The parameter of general COVID-19-related worry was assessed by asking respondents how they felt about the current situation with COVID-19 in general (not worried, somewhat worried, worried, or extremely worried). To assess the parameter of perceived COVID-19 stress of others, respondents were asked to separately rate the level of stress associated with COVID-19 they believed others around them were experiencing (family, relatives they did not live with, and close friends) on a Likert scale from 0 to 10 (10 being the most worried). The mean of these 3 values formed the composite measure of perceived COVID-19 stress of others, which had good internal consistency when tested by Cronbach's alpha (α = 0.80). After filtering for survey responses with valid responses to the included parameters, the sample size of the HMR model was n = 704.

As shown in Table 2, in Model 1a (GAD-7 as the dependent variable and the aforementioned list of predictor variables), the overall regression was statistically significant with R^2 = .39 (F (8,695) = 55.23; *P* < .001), indicating that the model provided a reasonable fit for predicting GAD-7 scores. After AR status was added as a predictor variable to Model 1a to construct Model 1b, there was no change in the predictive value of the model (ΔR^2 = .00, F (1,694) = 0.16; *P* = .69). In other words, AR status did not have a significant predictive effect on GAD-7 scores after controlling for the effect of the other predictor variables (β = .01; *P* = .69).

Subgroup Analysis

A subgroup analysis of cases (n = 599) was conducted to explore factors associated with anxiety within the AR group, including AR burden of disease and COVID-19-specific concerns.

Figure 3 shows the AR burden of disease as assessed on the RQLQ, including both the total RQLQ score and the 7 RQLQ domain scores. The mean total RQLQ score was 1.5 (SD = 0.99), and the non-nose-eye symptom domain had the highest mean score of 1.9 (SD = 1.2).

To investigate the relationship between burden of disease and anxiety in the AR subgroup, bivariate linear correlations were calculated between GAD-7 score and all RQLQ scores (n = 599 for all correlations). The results of these correlations are summarized in Table 3. There was a statistically significant positive correlation between

Table 2
Results of the Hierarchal Multiple Regression (HMR) with Generalized Anxiety Disorder Assessment-7 (GAD-7) Score as the Independent Variable (n = 704)

Predictor variables	Model 1a				Model 1b			
		95% confidence intervals				95% confidence intervals		
	β	Lower bound	Upper bound	*P* value	β	Lower bound	Upper bound	*P* value
Sex (0 = man, 1 = woman)	0.02	−0.60	1.13	.55	0.02	−0.60	1.13	.55
Age	−0.17	−0.95	−0.46	<.001	−0.18	−0.96	−0.47	<.001
Asthma status (0 = N, 1 = Y)	0.01	−0.63	0.79	.83	0.00	−0.66	0.77	.88
Previous anxiety diagnosis (0 = N, 1 = Y)	0.36	3.30	4.79	<.001	0.36	3.29	4.79	<.001
Current access of MHS (0 = N, 1 = Y)	0.06	−0.04	2.09	.06	0.06	−0.04	2.09	.06
Past access of MHS (0 = N, 1 = Y)	0.05	−0.20	1.31	.15	0.05	−0.20	1.31	.15
General COVID-19-related worry	0.16	0.60	1.36	<.001	0.16	0.60	1.36	<.001
Perceived COVID-19 stress of others	0.24	0.49	0.85	<.001	0.24	0.49	0.85	<.001
AR status (0 = N, 1 = Y)	—	—	—	—	0.01	−0.69	1.04	.69

Abbreviations: AR, allergic rhinitis; COVID-19, coronavirus disease 2019; MHS, mental health services.
NOTE. Predictor variables significant at *P* ≤ .05 are indicated in red. Allergic rhinitis status did not add to the predictive value of Model 1a when included in Model 1b (ΔR^2 = .00, F (1,694) = 0.16; *P* = .69).

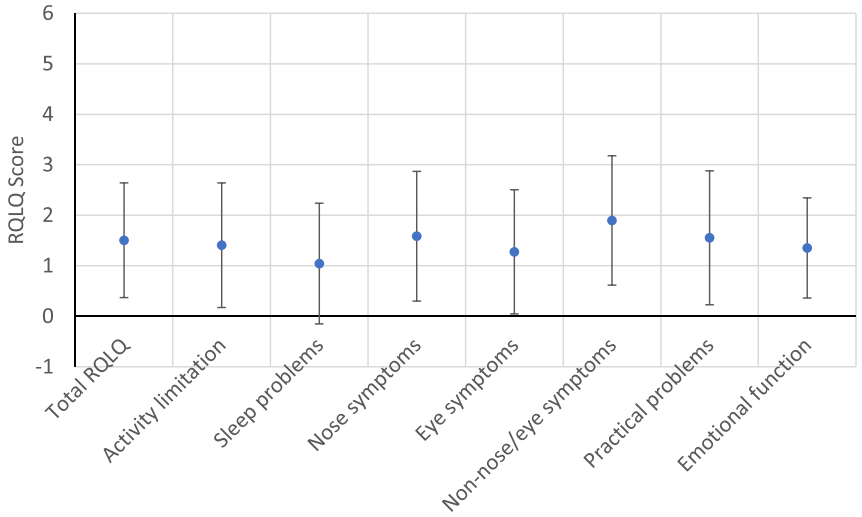

Figure 3. Mean scores for the total RQLQ and all 7 domains in the AR subgroup (n = 599). Error bars represent ± 1 standard deviations from the mean. AR, allergic rhinitis; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire.

GAD-7 score and total RQLQ score (r (597) = .46; $P < .001$). There were statistically significant positive correlations between GAD-7 score and all 7 RQLQ domain scores, with the non-nose or eye symptom domain having the strongest correlation with GAD-7 scores (r (597) = .63; $P < .001$).

To assess the impact of AR burden of disease on anxiety while controlling for the effect of other variables, a second hierarchal multiple regression was conducted within the AR subgroup—a summary of the subgroup HMR is reported in Table 4. Predictor variables again were included if they were determined to have a significant predictive effect on GAD-7 scores within the AR subgroup in bivariate analyses. These predictor variables were sex, age, previous anxiety syndrome or symptom diagnosis, current access of MHS, past access of MHS, general COVID-19-related worry, perceived COVID-19 stress of others, being treated differently by others, worry about the AR-COVID-19 symptom overlap, and worry about increased COVID-19 risk. The parameter of being treated differently by others was assessed by a dichotomous yes or no question asking respondents if their friends or family treated them differently when they showed AR symptoms. The parameter of worry about the AR-COVID-19 symptom overlap was assessed by asking participants how worried they were that they would mistake their normal allergy symptoms for symptoms of COVID-19 (not worried, somewhat worried, worried, or extremely worried). Finally, the parameter of worry about increased COVID-19 risk was assessed by asking participants how worried they were that having AR would increase their risk of developing serious symptoms from COVID-19 (not worried, somewhat worried, worried, or extremely worried). After the exclusion of survey responses without valid responses to the included parameters, the sample size of the subgroup HMR was n = 571.

In Model 2a, with GAD-7 score as the dependent variable and the aforementioned predictor variables, the overall regression was statistically significant with $R^2 = .42$ (F (10,560) = 39.84; $P < .001$), indicating that the model provided a reasonable fit for predicting GAD-7 scores in the AR subgroup. After RQLQ was added as a predictor variable in Model 2b, there was a significant improvement in the fit of the model ($\Delta R^2 = .049$, F (1,559) = 51.66; $P < .001$). This indicates that after accounting for the effects of the other predictor variables, RQLQ had a significant predictive effect on GAD-7 score in the subgroup HMR ($\beta = 0.26$; $P < .001$).

Two COVID-19-specific parameters were identified as significant predictors of anxiety in AR participants in Model 2b of the subgroup HMR, general COVID-19-related worry and perceived COVID-19 stress of others. To further investigate the impact of these COVID-19-specific parameters on the relationship between RQLQ score and

Table 3
Correlation Matrix Between GAD-7 score and RQLQ scores (total and all 7 domains) of AR group (n = 604)

	1	2	3	4	5	6	7	8	9
1. GAD-7	—								
2. Total RQLQ	0.457	—							
3. RQLQ (activity limitations)	0.276	0.810	—						
4. RQLQ (sleep problems)	0.241	0.776	0.655	—					
5. RQLQ (nose symptoms)	0.280	0.846	0.676	0.632	—				
6. RQLQ (eye symptoms)	0.232	0.790	0.594	0.588	0.609	—			
7. RQLQ (non-nose or eye symptoms)	0.626	0.719	0.456	0.442	0.424	0.429	—		
8. RQLQ (practical problems)	0.280	0.840	0.697	0.608	0.836	0.623	0.407	—	
9. RQLQ (emotional function)	0.372	0.880	0.711	0.653	0.759	0.685	0.484	0.778	—

Abbreviations: GAD-7, Generalized Anxiety Disorder Assessment-7; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire.
NOTE. All correlations were significant at $P < .001$ (2-tailed).

Table 4
Results of a Hierarchal Multiple Regression (HMR) Model Within the AR Subgroup, With Generalized Anxiety Disorder Assessment-7 (GAD-7) Score as the Independent Variable (n = 571)

Predictor variables	Model 2a				Model 2b			
		95% confidence intervals				95% confidence intervals		
	β	Lower bound	Upper bound	*P* value	β	Lower bound	Upper bound	*P* value
Sex (0 = man, 1 = woman)	−0.01	−1.09	0.82	.78	−0.02	−1.26	0.56	.45
Age	−0.17	−1.00	−0.43	<.001	−0.17	−1.00	−0.46	<.001
Previous anxiety diagnosis (0 = N, 1 = Y)	0.34	3.03	4.68	<.001	0.3	2.63	4.23	<.001
Current access of MHS (0 = N, 1 = Y)	0.05	−0.33	2.01	.16	0.03	−0.52	1.72	.3
Past access of MHS (0 = N, 1 = Y)	0.06	−0.12	1.53	.1	0.06	−0.08	1.51	.08
General COVID-19-related worry	0.10	0.18	1.03	.005	0.1	0.23	1.05	.002
Perceived COVID-19 stress of others	0.22	0.43	0.82	<.001	0.19	0.35	0.73	<.001
Being treated differently when showing AR symptoms (0 = N, 1 = Y)	0.02	−0.69	1.34	.53	−0.01	−1.09	0.88	.83
Worry about symptom overlap	0.08	0.01	0.87	.04	0.02	−0.29	0.54	.56
Worry about increased COVID-19 risk	0.10	0.15	1.01	.009	0.05	−0.11	0.72	.15
RQLQ	—	—	—	—	0.26	1.06	1.86	<.001

Abbreviations: AR, allergic rhinitis; COVID-19, coronavirus disease 2019; MHS, mental health services; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire.
NOTE. Red indicates predictor variables significant at $P \leq .05$. The RQLQ significantly improved the predictive value of Model 2a after added in Model 2b ($\Delta R^2 = .049$, $F(1,559) = 51.66$; $P < .001$).

GAD-7 score, a parallel multiple mediator (PMM) model was tested using Hayes's PROCESS with 95% confidence intervals (CIs), 10,000 bootstrap samples, and standardized regression coefficients.[21] Age and previous anxiety syndrome or symptom diagnosis were included as covariates in the PMM model because they had significant predictive effects in Model 2b. After the exclusion of survey responses without valid responses to the included parameters, the sample size of the subgroup PMM was n = 577.

Figure 4 shows the PMM model with RQLQ score as the independent variable, GAD-7 score as the dependent variable, and the 2 COVID-19-specific parameters as mediators. In terms of total effects, the PMM model significantly predicted GAD-7 scores with a reasonable fit ($R^2 = .40$, $F(3,573) = 125.80$; $P < .001$). In terms of indirect effects, the parameter of general COVID-19-related worry was a significant mediator in the PMM model (β = .015; 95% CI, [.0035-.031]). The RQLQ score positively affected general COVID-19-related worry (β = .13, $t = 3.00$; $P = .003$), which, in turn, positively affected the GAD-7 score (β = .12, $t = 3.72$; $P < .001$), as shown in Path A of Figure 4. Perceived COVID-19 stress of others also was identified as a significant mediator of the relationship between RQLQ and GAD-7—the indirect effect of Path B of Figure 4 was β = .043 (95% CI, [.023-.066]). The RQLQ score positively affected perceived COVID-19 stress of others (β = .22, $t = 5.26$; $P < .001$), which, in turn, positively affected the GAD-7 score (β = .20, $t = 5.89$; $P < .001$). However, even after accounting for the mediating role of these 2 COVID-19-specific parameters, the RQLQ score still had an independent predictive effect on the GAD-7 scores as shown in Path C of Figure 4 (β = .283, $t = 8.64$; $P < .001$).

Discussion

Summary of Results and Comparison With Existing Literature

In summary, high levels of pandemic-time anxiety were found among all participants, regardless of AR status. Within the control group, 27.5% of participants met the diagnostic criteria for GAD, which is markedly higher than prepandemic estimates of a 2.5% GAD prevalence among Canadians.[22] In the AR group, 28.0% of participants met the diagnostic criteria for GAD, compared with a prepandemic report of a 9.3% incidence of anxiety disorders among patients with AR.[23]

These high levels of anxiety are in keeping with elevated pandemic-time anxiety reported in recent literature.[12,13] However, the finding that anxiety levels were not significantly different between participants with AR and those without is novel, compared with both prepandemic and pandemic-time studies.[5-8,17] The study by Wang et

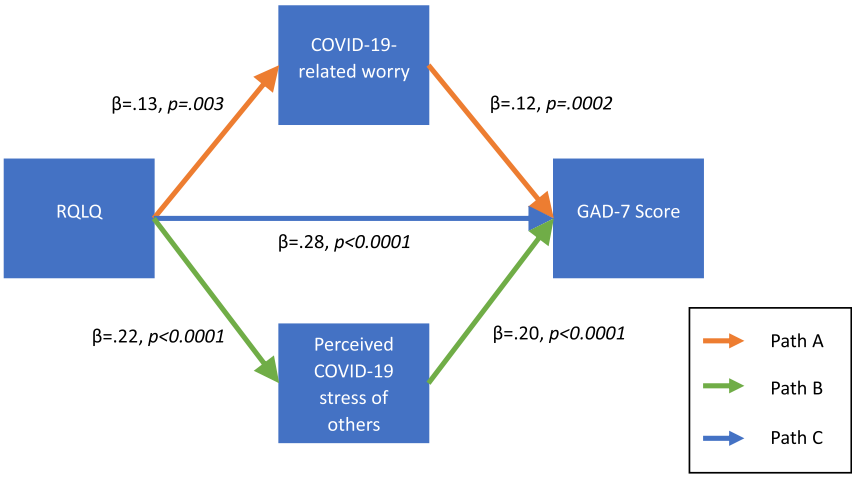

Figure 4. Parallel multiple mediator (PMM) model with RQLQ score as the independent variable, GAD-7 score as the dependent variable, and 2 COVID-19-specific worry parameters as mediators. Covariates included age, previous anxiety syndrome or symptom diagnosis. COVID-19, coronavirus disease 2019; GAD-7, Generalized Anxiety Disorder Assessment-7; RQLQ, Rhinoconjunctivitis Quality of Life Questionnaire.

al[17] of anxiety among patients with AR in Wuhan, China during the COVID-19 pandemic reported a significantly higher prevalence of pooled anxiety and depression of 24.8% among patients with AR than the prevalence of 19.4% in healthy controls ($P < .001$). Given the high levels of anxiety found in both the AR and control groups in the present study, the lack of a significant difference in anxiety between groups suggests that the COVID-19 pandemic carried enough of an anxiety burden to overwhelm the effect of any AR-specific anxiety on top of baseline pandemic-time anxiety.

This novel finding that AR status did not contribute to increased anxiety may, also, be partially explained by the fact that patients with AR believe they can clearly distinguish between AR and COVID-19 symptoms. This idea is supported by findings from the AR subgroup analysis, in which the parameter of worry about the AR-COVID-19 symptom overlap was not found to be a significant predictor for increased anxiety (Table 4). Previous research has also found that patients with AR were able to easily differentiate between AR symptoms and those of COVID-19 owing to familiarity with their own AR symptom history, lack of fever and malaise, and response to AR medications.[24]

Furthermore, the lack of an AR-anxiety relationship within this study population may be attributed to decreased symptom burden within the AR subgroup during the COVID-19 pandemic. The mean total RQLQ score among the AR subgroup in this study was 1.52 (SD = 1.00), which is lower than the prepandemic estimate of 2.43 (SD = 1.23) within patients with AR.[25] The lower AR disease burden may be partially explained by the widespread adoption of face masks over the COVID-19 pandemic—Dror et al[26] found that use of both N95 and surgical face masks was linked to reduced AR symptom burden, which, the authors hypothesized, was because of decreased allergen exposure. There also has been a report of decreased AR disease burden in relation to altered behaviors during the pandemic (eg, working from home, spending less time outdoors)—Sözener et al[27] found that patients with AR who spent less time outdoors during the 2020 pollen season reported a reduction in AR symptoms.

An ancillary finding within the case-control HMR was that increasing age was found to be associated with decreased anxiety after controlling for the effect of the other predictor variables—$\beta = -.17$, $P < .001$ and $\beta = -.18$, $P < .001$ in Model 1a and in Model 1b, respectively (Table 2). This finding contradicts the thought that higher anxiety would be seen with increasing age because older adults are at greater risk of serious illness after COVID-19 infection—a systematic review with meta-analysis of 70 pandemic-time studies found a continuous increase in COVID-19 disease severity with increasing age.[28] Furthermore, this finding also somewhat contradicts the prepandemic literature—the prevalence of anxiety disorders is expected to increase from early adulthood, peaking at middle age and decreasing afterward.[29] However, the decreasing anxiety with increasing age seen within the CAAARES study population is consistent with the existing literature published in the context of the COVID-19 pandemic—studies examining mental health during the COVID-19 pandemic conducted in various countries (China, Spain, Iran, and Poland) consistently found that young adults experienced higher pandemic-time anxiety than other age groups.[30–33] The difference in the age-anxiety relationship between prepandemic and pandemic-time literature may be attributed to young people being disproportionately affected by the psychological impact of the COVID-19 pandemic—a study by Gambin et al[33] conducted in Poland found difficulty coping with COVID-19 restrictions to be 1 of the most significant predictors of anxiety and depressive symptoms, but only within the youngest group of participants (18-29 years).

The key finding of the AR subgroup analyses was that AR disease burden was associated with increased anxiety, with non-nose or eye symptoms having the strongest correlation. The non-nose or eye symptom domain of the RQLQ assesses the degree to which individuals with AR are impacted by fatigue, thirst, reduced productivity, tiredness, poor concentration, headache, and feeling worn out.[20] The correlation between RQLQ scores and anxiety is consistent with existing literature; Yu et al[34] reported that anxiety symptoms were significantly associated with total RQLQ score and all 7 domain scores. However, the finding that non-nose or eye symptoms are most strongly correlated with anxiety is novel. In the existing literature, nasal and ocular symptoms (eg, severity of nasal obstruction, congestion, pruritis) have been reported to be the strongest predictor of anxiety and poor quality of life in patients with AR.[9]

Lastly, the PMM model identified general COVID-19-related worry and perceived COVID-19 stress of others as mediators of the relationship between RQLQ score and GAD-7 score in the AR subgroup. In other words, greater AR disease burden is linked to increased COVID-19-related worry, which, in turn, is linked to increased anxiety levels. This novel finding provides insight into how the RQLQ-anxiety relationship in patients with AR is influenced by factors specific to the context of the COVID-19 pandemic.

Limitations of Present Study

The limitations of the present study include the potential of self-report bias owing to the nature of self-reported data collection. In addition, this was a cross-sectional survey with no data collected about prepandemic levels of anxiety or AR disease burden. It was therefore not possible to compare pandemic-time GAD-7 and RQLQ scores with a baseline. Furthermore, although the 2 main measures of interest in this study (GAD-7 and RQLQ) have been validated, these measures have not been validated within the context of the CAAARES questionnaire. The CAAARES questionnaire itself has not been validated, introducing the potential for measurement bias because the reliability and validity of the questions assessing COVID-19 specific parameters have not been formally tested. These include the following 5 parameters: (1) general COVID-19-related worry, (2) perceived COVID-19 stress of others, (3) worry about AR-COVID-19 symptom overlap, (4) being treated differently when showing AR symptoms, and (5) worry about increased COVID-19 risk owing to AR status.

Conclusions, Impact, and Future Directions

The findings from this study have notable implications for AR and anxiety management during and after the pandemic. The high prevalence of anxiety highlights the importance of screening for anxiety in all patients during the COVID-19 pandemic, regardless of AR status, and indicates the large psychological burden of the COVID-19 pandemic in Canada.

Moreover, the results of the AR subgroup analyses point to the importance of addressing non-nose or eye symptoms in AR management. This consideration has broad implications extending beyond the context of the COVID-19 pandemic, highlighting the value of a holistic approach to AR management that considers functional impairment and impacts on quality of life. In the past, AR control was traditionally dictated by the severity of nose and eye symptoms, with clinical trials using subjective patient ratings of these symptoms as outcome measures for AR control.[35] Since that time, there has been a paradigm shift to acknowledge the overall AR disease burden with the development and validation of AR quality of life measures, including the RQLQ.[20] Now, there are a number of measures of AR control available to clinicians and researchers, including quality-of-life scores, visual analog scale scores, and symptom scores like the Total Nasal Symptom Score and the Sino-Nasal Outcome Test-22.[20,36-38] The findings of the CAAARES survey indicate that the severity of non-nose or eye symptoms in individuals with AR is more closely tied to anxiety than the traditional nose or eye symptoms—patients may be more concerned about symptoms that represent greater functional limitations in their daily lives, like fatigue, reduced

productivity, and poor concentration. Given this novel finding, the RQLQ non-nose or eye domain score in particular may hold clinical utility as a treatment target and marker to assess AR control. To explore the potential application of the RQLQ non-nose or eye domain score as a proxy for AR control, it may be of interest to design a large-scale cross-sectional study of patients with AR, comparing their RQLQ non-nose or eye domain scores with other typically used measures of AR control (eg, visual analog scale, Total Nasal Symptom Score, Sino-Nasal Outcome Test-22). This further research can also be extended into a longitudinal study, examining how these scores may change with fluctuating AR control and in different allergy seasons.

In terms of future research directions, it may also be of interest to explore quality of life and anxiety in patients with asthma in the context of the COVID-19 pandemic, specifically examining whether this relationship differs between the different domains of the asthma quality-of-life scale chosen (ie, asthma symptoms vs other functional symptoms). Further work can also interrogate whether there are any COVID-19 specific parameters that may serve as moderators of this relationship.

Finally, a longitudinal study of anxiety levels and AR disease burden throughout the COVID-19 pandemic may be of interest to explore the effect of time-dependent trends (eg, different allergy seasons, changing COVID-19 case incidence, policy changes to mask mandates, vaccine rollout).

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