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EAACI POSITION PAPER

Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: An ARIA-EAACI-GA^{2}LEN consensus

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Abstract

Background: Although there are many asymptomatic patients, one of the problems of COVID-19 is early recognition of the disease. COVID-19 symptoms are polymorphic and may include upper respiratory symptoms. However, COVID-19 symptoms may be mistaken with the common cold or allergic rhinitis. An ARIA-EAACI study group attempted to differentiate upper respiratory symptoms between the three diseases.

Methods: A modified Delphi process was used. The ARIA members who were seeing COVID-19 patients were asked to fill in a questionnaire on the upper airway symptoms of COVID-19, common cold and allergic rhinitis.

Results: Among the 192 ARIA members who were invited to respond to the questionnaire, 89 responded and 87 questionnaires were analysed. The consensus was then reported. A two-way ANOVA revealed significant differences in the symptom intensity between the three diseases ($p < .001$).

Conclusions: This modified Delphi approach enabled the differentiation of upper respiratory symptoms between COVID-19, the common cold and allergic rhinitis. An electronic algorithm will be devised using the questionnaire.

KEYWORDS
allergic rhinitis, common cold, cough, COVID-19, smell

1 | INTRODUCTION

Although there are many asymptomatic patients, one of the problems of COVID-19 is early recognition of the disease. Pre-medical visit screening and symptom evaluation have to be implemented quickly to minimise the risk of seeing COVID-19 patients unprepared. Furthermore, testing for coronavirus is still widely restricted due to the shortage of available PCR tests in many countries.[1] Testing capacities have improved dramatically since the beginning of the pandemic, with the recent addition of antigen-based testing. Some of these tests are home-based and have only just obtained FDA approval. However, they still represent a bottleneck,[2] with the subsequent waiting periods leading to large groups of people at risk of infection requiring quarantine. To prevent unnecessary closure of critical facilities, for example schools and public services, triage requires further improvement in terms of speed and accuracy.

COVID-19 symptoms are polymorphic. Typically, COVID-19 induces shortness of breath, cough, fever, nasal congestion and general malaise.[3] However, SARS-coronavirus-2 (SARS-CoV-2) infection has been linked to a number of other symptoms afflicting several organ systems, including muscle and joint pain, sore throat, headache, nausea, vomiting and diarrhoea, as well as coagulopathy.[4] Impaired sense of smell and taste has emerged as an alarming symptom of SARS-CoV-2 infection in the West, but not so much in Asia.[5–9] Presentation in the upper respiratory tract has also been described as extremely variable across age groups,[10] making it difficult to distinguish COVID-19 from common upper respiratory infections (e.g. croup in children[10]).

Therefore, besides the management of severe COVID-19, one of the major problems of the infection is how to screen citizens with possible COVID-19 and distinguish them from patients with similar symptoms caused by allergic rhinitis[11,12] or other common viral infections of the respiratory tract. A digital tool enabling a rapid

TABLE 1 The original survey with 15 items

		COVID−19				Common cold				Allergic rhinitis					
Question		Occurrence	Characteristics	Max VAS (mean)	SD	Occurrence	Characteristics	Max VAS (mean)	SD	Occurrence	Characteristics	Max VAS (mean)	SD	Level Agreement MEAN	SD
1	Runny nose (anterior rhinorrhea)	Very rare	If present, mild symptoms (VAS<5/10)	3.98	0.15	Always	Anterior and posterior rhinorrhea	9.93	0.54	Often	Profuse anterior rhinorrhea	5.41	1.22	8.50	1.90
2	Sneezing	Very rare	Not in bursts	3.99	0.11	Common	Not in burst	5.02	0.21	Very common	In burst	9.99	0.11	9.37	1.09
3	Stuffy nose	Not uncommon	If present, mild symptoms (VAS<5/10)	4.10	0.68	Always	Often severe	10.00	0.00	Very common	May be severe	8.07	0.36	8.86	1.51
4	Nasal pruritus	NO		0.00	0.00	NO		0.08	0.53	Very common	Variable in intensity	8.02	0.21	9.22	1.38
5	Nasal pain	Possible		2.99	0.11	Sometimes		3.00	0.00	NO		0.00	0.00	8.21	2.22
6	Ocular itch	NO		2.94	0.38	NO		3.00	0.00	Common		10.00	0.00	9.31	1.41
7	Ocular pain	Possible		3.09	0.78			3.00	0.00	NO		0.06	0.53	8.14	2.43
8	Ocular redness	Possible		3.07	0.54	NO		3.05	0.30	Common		9.98	0.21	8.36	2.29
9	≥3 nasal symptoms	NO		N/A		YES		N/A		YES		N/A		8.92	1.82
10	Smell dysfunction	Not uncommon	Usually anosmia whereas in other diseases it is hyposmia. Associated with other COVID−19 symptoms, it is likely to be a significant diagnostic criterion	10.00	0.00	Sometimes		6.98	0.21	Rare	Anosmia very seldom	6.95	0.30	8.88	1.88
11	Taste dysfunction	Not uncommon	Dysgeusia rather than loss of taste. Associated with other COVID−19 symptoms, it is likely to be a significant diagnostic criterion	10.00	0.00	Rare		3.00	0.00	Very rare		2.00	0.00	9.24	1.34
12	Dyspnea	Relatively common	May start as an isolated mild symptom but may rapidly become severe with respiratory rate>24/min	10.00	0.00	Rare		5.00	2.92	Sometimes if asthma		10.00	0.00	9.08	1.35

Question	COVID-19 Occurrence	COVID-19 Characteristics	COVID-19 Max VAS (mean)	COVID-19 SD	Common cold Occurrence	Common cold Characteristics	Common cold Max VAS (mean)	Common cold SD	Allergic rhinitis Occurrence	Allergic rhinitis Characteristics	Allergic rhinitis Max VAS (mean)	Allergic rhinitis SD	Level Agreement MEAN	SD
13 Cough	Relatively common	May start as an isolated mild symptom (2–4 episodes of dry cough per hour) but rapidly becomes severe	10.00	0.00	Common	Follows the nasal symptoms	7.60	2.06	Sometimes if asthma		10.00	0.00	9.22	1.22
14 Wheezing	Not uncommon	Rarely isolated, not severe in contradistinction to asthma	4.99	0.11	Rare		3.50	1.12	Sometimes if asthma		10.00	0.00	8.77	1.73
15 Sore throat	Not uncommon		5.09	0.62	Common		8.25	1.09	Rare		4.33	2.87	8.84	1.66

distinction is needed for this approach and may be of great importance during the winter with the co-existence of COVID-19, flu, common cold or other respiratory viral infections and house dust mite-induced rhinitis.

Systematic reviews and meta-analyses have been produced for many COVID-19 symptoms including differentiation between flu and COVID-19.[13] However, there is insufficient knowledge on consensus across the international medical community regarding nasal symptoms that may enable differentiation between COVID-19, common cold and allergic rhinitis. An ARIA (Allergic Rhinitis and its Impact on Asthma)-EAACI (European Academy of Allergy and Clinical Immunology)-GA^{2}LEN (Global Allergy and Asthma European Network) initiative was carried out to establish consensus on a set of questions aimed at distinguishing these diseases. From this consensus, an algorithm will be proposed and digitalised using a method already validated in MASK.[14–16] The current paper presents the results of the consensus.

This is a new paper of the series of ARIA-EAACI papers on COVID-19.[17–21]

2 | METHODS

A modified Delphi was carried out.[22] A questionnaire developed by JB, WC, LK and JM was sent to all ARIA members by GLO. Those seeing COVID-19 patients were requested to answer within a week.

The questionnaire included items related to upper and lower airway symptoms for COVID-19, common cold and allergic rhinitis (Table 1). In the questionnaire, the respondents were asked to assess five nasal symptoms, three ocular symptoms, taste, smell, cough, wheezing and sore throat. For each question, there was a statement on frequency and severity. For this, participants were asked to grade the severity from 0 to 10. Then, they gave a global assessment from 0 to 10 according to whether they agreed on the suggested severity grading for the three diseases. A level of 6 or higher was considered as agreement. Suggestions for questions/statements were able to be added to the questionnaire.

A total of 87 answer sheets were included in this analysis. Any written comments were transformed into numeric changes where possible. To determine whether the participants agreed that the symptom/item was to be included in the tool, we collected the total number of participants agreeing as well as the total percentages. The same procedure was used for disagreement and missing/invalid data, respectively.

3 | RESULTS

Among the 192 questionnaires sent out, 89 (46.3%) were returned within 7 days. The average monthly number of COVID-19 consultations among the participants was 16.8 ± 20. The participants were from 37 different countries (Figure 1).

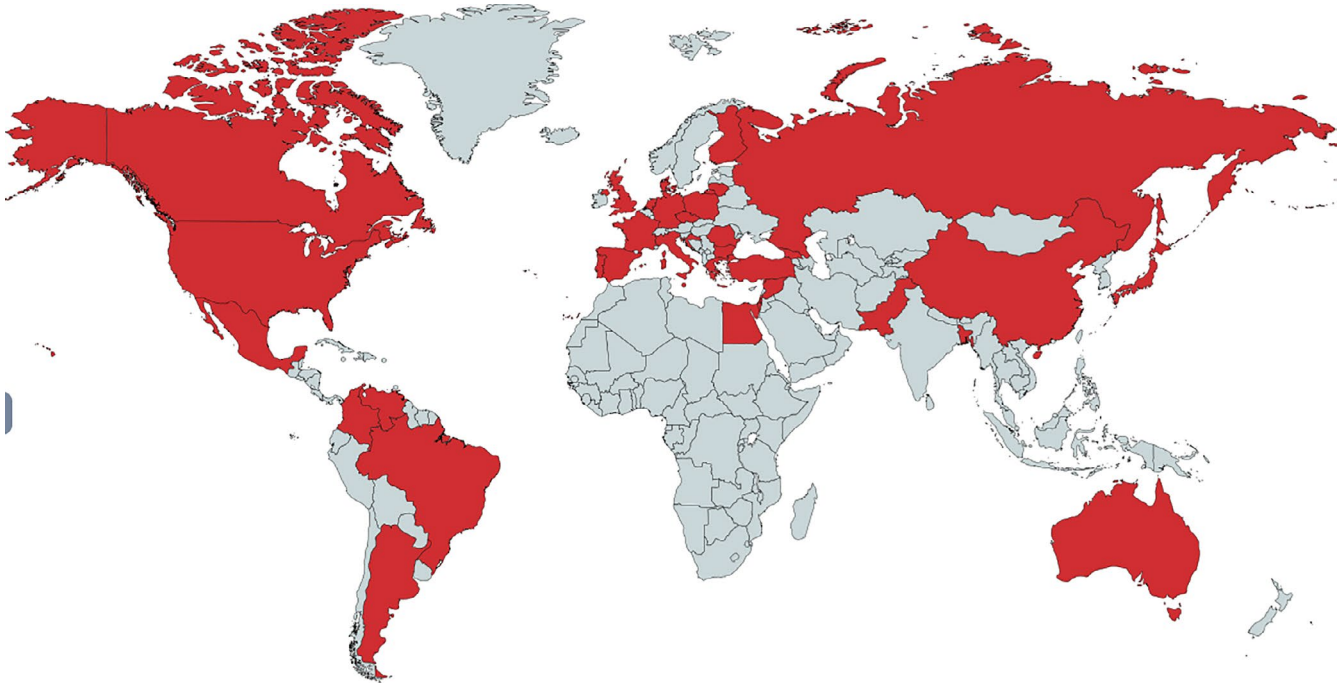

FIGURE 1 Countries involved in the questionnaire

TABLE 2 Participants' agreement to the questionnaire items

		Disagree (≤6)		Agree (>6)		Missing/invalid answer	
		n = 87					
No.	Symptom	*n*	%	*n*	%	*n*	%
1	Runny nose (anterior rhinorrhea)	12	13.8	62	71.3	13	14.9
2	Sneezing	3	3.4	72	82.8	12	13.8
3	Stuffy nose	8	9.2	68	78.2	11	12.6
4	Nasal pruritus	7	8.0	69	79.3	11	12.6
5	Nasal pain	14	16.1	61	70.1	12	13.8
6	Ocular itch	5	5.7	70	80.5	12	13.8
7	Ocular pain	16	18.4	60	69.0	11	12.6
8	Ocular redness	13	14.9	62	71.3	12	13.8
9	≥3 Nasal symptoms	7	8.0	65	74.7	15	17.2
10	Smell dysfunction	8	9.2	67	77.0	12	13.8
11	Taste dysfunction	2	2.3	73	83.9	12	13.8
12	Dyspnea	5	5.7	67	77.0	15	17.2
13	Cough	4	4.6	69	79.3	14	16.1
14	Wheezing	7	8.0	64	73.6	16	18.4
15	Sore throat	8	9.2	67	77.0	12	13.8
	Mean		9.1		76.3		14.6

There was a high proportion of agreeing participants, with an average of 76.3% (range 69–83). The overall data quality was acceptable, and missing values for some of the questions were below 20% (Table 2).

Participants were able to grade the maximum expected severity for each disease, and the average final VAS severity data are shown in Figure 2. A two-way ANOVA revealed significant differences in symptom intensity between the three diseases ($p < .001$).

Eye symptoms (7, 8) were among the most discussed statements, and the corresponding statements had relatively low levels of approval (Figure 1). Nasal pain (5) was regarded as impractical by six participants, which was also reflected by a relatively low level of

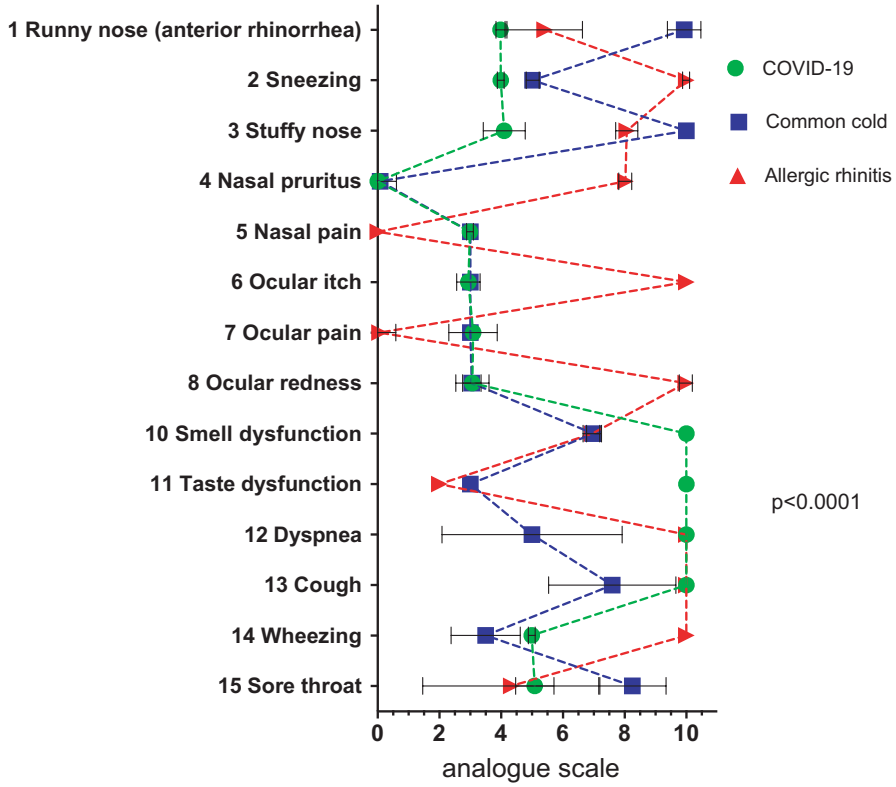

FIGURE 2 Maximum expected symptom severity. Analogue scale from 0 (not present) to 10 (maximum severity). Means ± SD are shown. A two-way ANOVA revealed significant differences in VAS between diseases ($p < .001$)

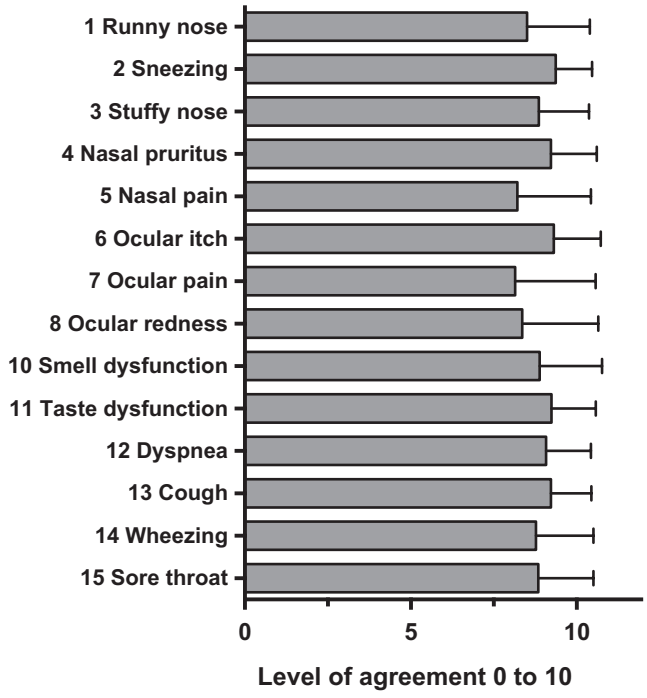

FIGURE 3 Mean level of agreement to suggested symptom severity. Analogue scale rating with range from 0 (disagreement) to 10 (complete agreement). A level of 6 or higher was considered as 'agreement'. Means ± SD are shown

agreement (8.21 ± 2.2; Figure 3). This was possibly caused by different interpretations of the item's description, and this issue needs to be addressed in further developments of the algorithm.

Additional common COVID-19 symptoms will be considered for integration in the future algorithm development process (Table 3).

TABLE 3 Additional items to be integrated in the algorithm

Strenuous fatigue
Fever
COVID–19 comorbidities
Contact with COVID patient
Travel to 'high-risk' region
Gastrointestinal symptoms
Muscle/body ache
Profound sweating

4 | DISCUSSION

This paper presents the results of a consensus initiative across the ARIA network of health professionals. The aim was to develop a set of questions on symptoms and their intensity in order to discriminate between classical rhinologic disorders and COVID-19. The presentation of COVID-19 is highly variable, ranging from a complete absence of symptoms to severe illness and critical organ dysfunction. The underlying mechanisms for this polymorphic behaviour are yet to be defined.

Within the ARIA network of specialists in upper and lower respiratory diseases, we asked 193 to respond to our consensus initiative, of whom 89 did. The response rate was under 50%, but many physicians were not seeing COVID-19 patients. The strength of this paper is that the involved participants represented different medical specialties and many different countries, suggesting a generalisation of the study.

We found high levels of consensus among this community, with over 76% of participants agreeing to the symptoms presented in our

questionnaire. VAS was found to be a useful and simple tool for discussing questions of symptom intensity in this large group of health professionals. Statistical analysis revealed a significantly different expected maximum VAS of the three diseases (two-way ANOVA, $p < .001$). Hence, there are potential symptom constellations that allow discrimination between the three diseases.

The triage of patients with newly developed symptoms – any individual under suspicion of being at risk of SARS-CoV-2 infection – remains a challenge during this pandemic. Digital application-based symptom reporting and triage have been evaluated in prospective trials in the UK, China and the US.[23–25] The improvement of triage will also (i) enhance pre-test probability for SARS-CoV-2 PCR swabs or alternative test methods; (ii) increase the availability of tests in general to make current infection numbers more accurate; (iii) ease unnecessary quarantine; and (iv) reduce the closure of schools, child day care and public services.

ARIA-MASK includes a decision-making tool for allergic rhinitis.[14] With a broad user base of 39,670, there is an opportunity to provide newly developed tools for a large group of patients. The questionnaire, along with the participants' comments, has to be transferred to a validation process. This process can be enhanced by already-developed artificial intelligence (AI) in order to fine-tune and improve symptom VAS thresholds. A final questionnaire and algorithm are open for use across the medical community, focussing on specialists treating upper and lower airway diseases and allergy, hence confronted with similar rhinologic, pneumologic and ophthalmologic symptoms. For allergy and respiratory tract specialists, undoubtedly at high risk of infection during examinations, recommendations for treatment and handling of the field of allergic diseases have been suggested by the European Academy of Allergy and Clinical Immunology (EAACI) in alliance with the global initiative 'Allergic Rhinitis and its Impact on Asthma' (ARIA).[17,19–21,26] It has been shown that digital decision-making tools and app-based algorithms can improve patient–doctor communication and therapy adherence for both patients and physicians.[27,28]

In summary, our future COVID-19 symptom tool may be a helpful device for improving active patient reporting and triage of patients when integrated in the ARIA MASK-air App. We have asked the networks to circulate the tool to their members for testing, and we hope to be able to present the results and create more robust evidence in its practicality. This article presents a substantial consensus effort in COVID-19-treating physicians across the globe. Limitations arise from missing or inappropriate data in the returned questionnaires. However, the development process is followed by AI-supported validation, and future studies have to show the power of such questionnaires.

CONFLICTS OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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APPENDIX 1

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