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LETTER

Presentation of airway and general symptoms in COVID-19 caused by dominant SARS-CoV-2 variants: A follow-up on ARIA consensus

Dear Editor,

Several SARS-CoV-2 variants have occurred since the beginning of the COVID-19 pandemic. Mutated *variants of concern*s (VOC; World Health Organization nomenclature) have a variable contamination rate and virulence. COVID-19 symptoms are polymorphic and vary according to VOC.[1] A consensus effort from the ARIA group (*Allergic Rhinitis and its Impact on Asthma*) has been shown that symptoms from common cold, allergic rhinitis, and COVID-19 are likely to be differentiated in a panel of 15 items.[2]

Although papers have described major clinical manifestations in these new variants,[3,4] there is no consensus on important symptom changes caused by VOC Delta and Omicron. Following the methods of the first EAACI-ARIA-GA[1]LEN paper,[2] we assessed globally how physicians seeing COVID-19 patients are rating various symptoms induced by different VOC.

2 | METHODS

A bibliographic survey identified common symptoms induced by VOC Delta and Omicron. Then, a Delphi questionnaire regarding key symptoms associated with SARS-CoV-2 infection was developed based on the items from ARIA-EAACI-GA2LEN consensus[2] and from literature. Symptoms included common cold (upper airway), chemosensory, bronchial, and pulmonary as well as systemic illness symptoms (Table 1).

Participants (not involved in the study design process) were asked to estimate frequency (none, very rare, possible, common, always) and expected symptom intensity (visual analogue scale/VAS, 0 to 10) according to their experience as of March 2022 when seeing VOC Delta and Omicron COVID-19 patients. Wild-type symptom rating was performed in 2020 during the first waves of the pandemic by the same participants. Participants are ARIA airway specialists working in hospitals (in- and outpatient, ICU, and specialty clinic) and/or smaller offices.

Statistical analysis (ANOVA/*t*-test for multiple/two groups) and data analysis were performed through GraphPad Prism (USA).

3 | RESULTS

Among 47 questionnaires sent out, 40 were received within 7-day notice. Physicians saw an average of 43.5 COVID-19 patients per month. Responses originated in 26 countries.

Symptom intensity differed significantly between wild type and VOC (Figure 1). ANOVA test analyses revealed several significant differences of the symptom intensity between the three variants (Figure 1, left). Nasal symptoms (anterior rhinorrhea, nasal congestion, and pruritus) ($p < .001$) and sore throat ($p < .001$) were more pronounced in VOC Omicron, compared to wild type. Olfactory function loss was significantly less marked in VOC Delta and Omicron ($p < .001$). The same patterns occurred for pulmonary symptoms and signs of severe disease (Figure 1). Symptom intensity also differed significantly between VOC Delta and Omicron for all symptoms mentioned above ($p < .01$).

Significantly differing symptoms were grouped concerning common cold and sore throat, chemosensory, bronchial and pulmonary,

TABLE 1 Tasks of the questionnaire

Symptom	Occurence	Expected VAS
Runny nose, sneezing, stuffy nose, nasal pruritus, facial/nasal pain, ocular itch, ocular pain, Ocular redness, >3 nasal symptoms, smell dysfunction, taste dysfunction, dyspnea, cough, wheezing, sore throat, headache, fatigue, fever, duration of illness >1 week, undulating symptoms, gastrointestinal symptoms, skin symptoms, body/muscle ache, arthralgia, altered consciousness	Choice between: (none, very rare, possible, common, always) or (yes, no)	(grade from 0–10)

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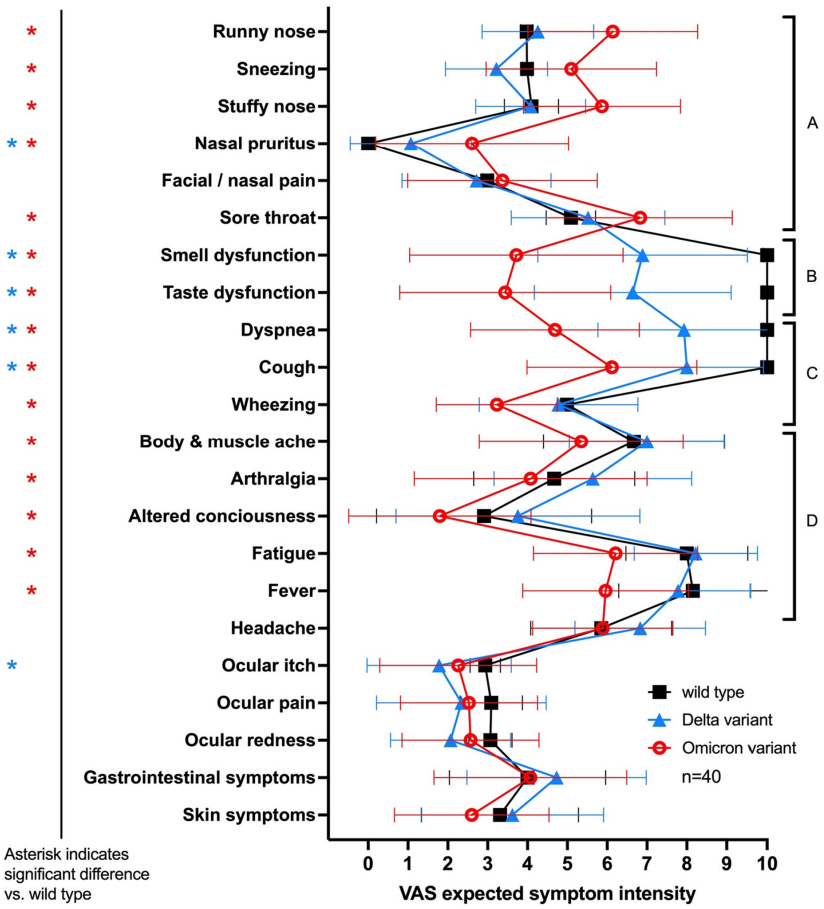

FIGURE 1 Expected symptom intensity on analogue scale (0: no symptom and 10: strongest symptoms) for wild-type and virus variants of SARS-CoV-2, rated by ARIA specialists. Asterisk (left) indicates significant difference ($p < .01$) for Delta (blue) and Omicron (red), compared to wild type. Symptom groups A/B/C/D are explained in the main text and referred to Figure 2

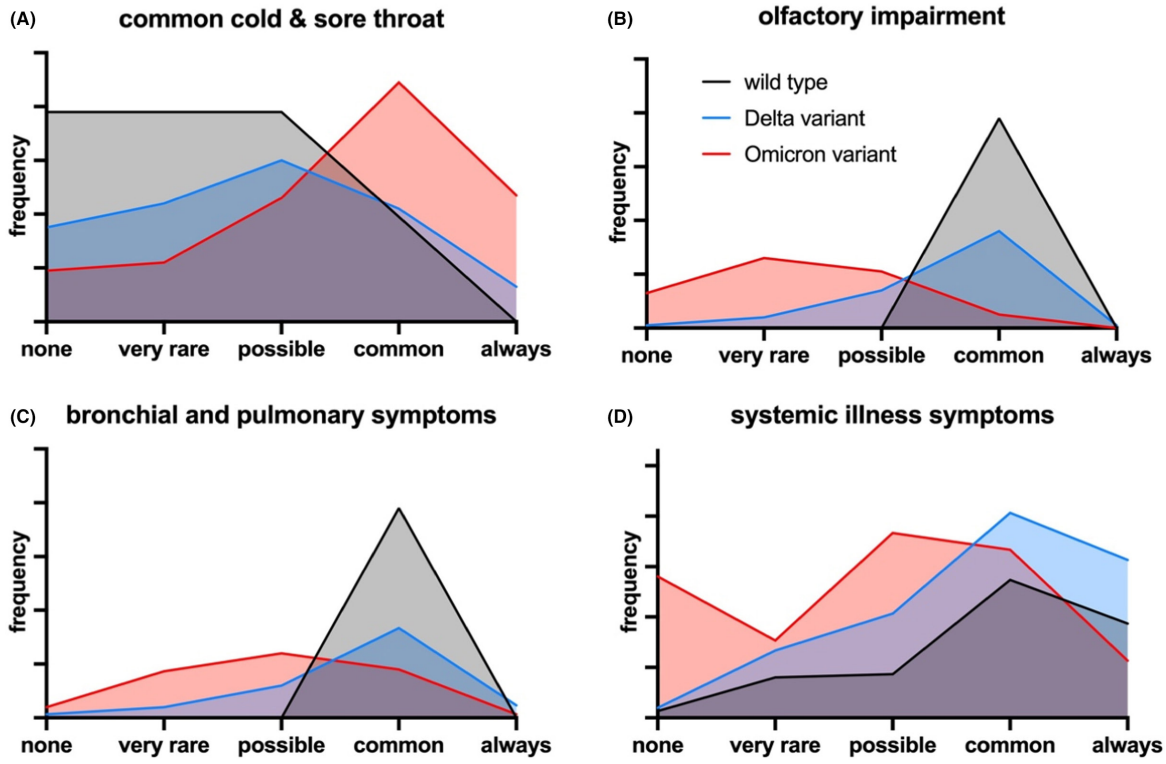

FIGURE 2 Expected frequency of symptoms with regard to wild-type and virus variants. The sum of mentions in the questionnaire responses are plotted. (A) common cold/sore throat (rhinorrhea, nasal obstruction, sneezing, facial pain, sore throat, multiple nasal symptoms); (B) chemosensory symptoms (smell and taste dysfunction); (C) bronchial and pulmonary symptoms (wheezing, cough, dyspnea); (D) signs of systemic illness (body ache, arthralgia, fever, fatigue, illness duration, vigilance)

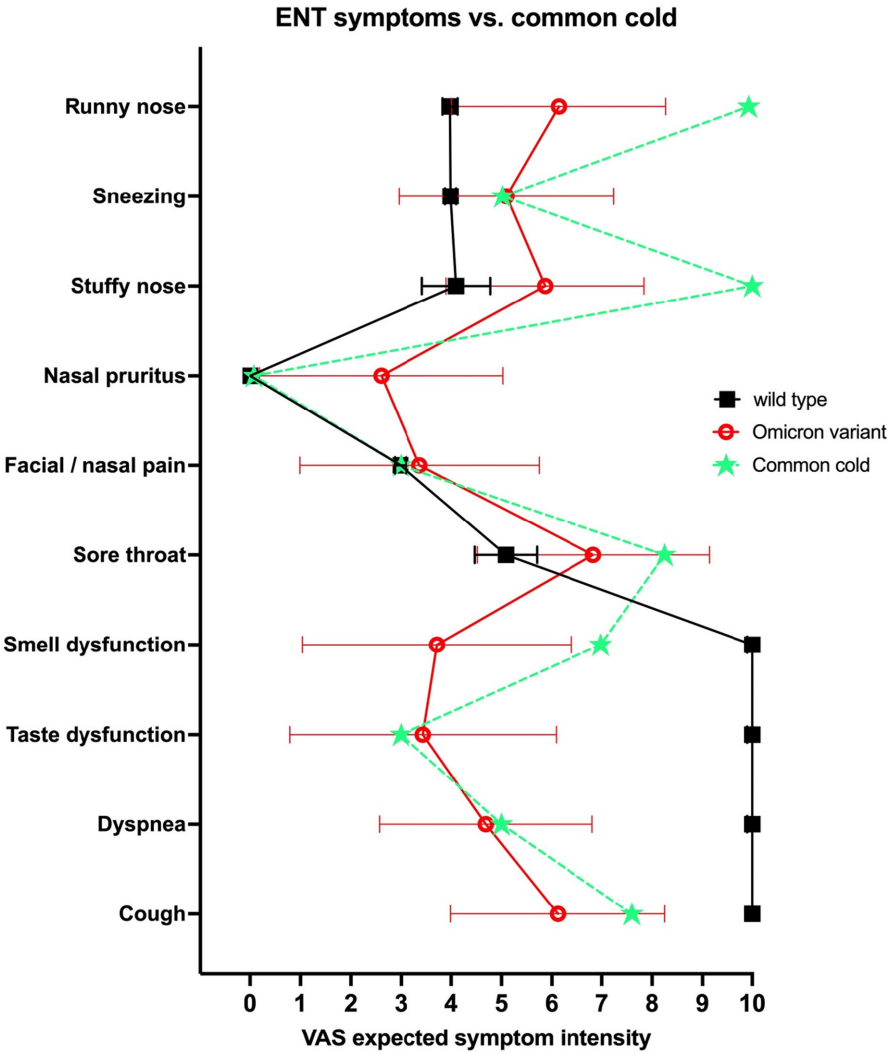

FIGURE 3 Expected symptom intensity on analogue scale (0: no symptom and 10: strongest symptoms) for wild-type and Omicron virus variant of SARS-CoV-2, rated by ARIA specialists

as well as systemic (Figure 2). VOC Omicron induce "common cold symptoms" and sore throat more often than wild-type and VOC Delta infections (Figures 2 and 3).

4 | DISCUSSION

Our data from ARIA airway specialists across the globe indicate that VOC Delta and Omicron cause various airway symptoms that significantly differ in terms of intensity and composition to those of wild-type SARS-CoV-2. A recent human challenge study to wild-type virus confirmed none to mild rhinitis symptoms with high proportion of olfactory loss.[5] Few studies mostly carried out in the UK showed that sore throat is common with VOC Omicron, whereas chemosensory symptoms were less common.[6] A UK-based COVID symptom tracker app "Zoe's Covid Symptom Study" collected millions of symptom samples and showed sore throat, runny nose, sneezing, headache, fever, and persistent cough were the most symptoms in symptoms in VOC Delta.[7] The role of vaccination on upper airway symptoms is unclear. Smith et al. found only one symptom alteration over the course of two doses of vaccine, possibly also influenced by alteration of virus strain.[8] Initial reports on mRNA vaccines entirely preventing infections are challenged by recent observations by Yochay et al. of high-viral load infections with VOC Omicron, despite multiple previous vaccinations. There are several limitations for our study. Our study is a consensus based on expert opinions. Recall bias due to long intervals between presentations and our study is possible, although small variation in answers supports reliability. These results, for the first time, provide a more global view of the problem. Ultimately, we cannot differentiate here what triggers the effects we have described (vaccination, infections previously experienced by part of the population, other virus properties, etc.), but we do want to provide physicians with a decision-making aid for the current situation.

Patients are likely to present variable airway and other symptoms in future that can be misinterpreted as common cold. Thus, the prevention of severe outcomes remains the main goal of current vaccination efforts.

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CONFLICT OF INTEREST

There are no conflicts of interest to declare with regard to this project.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. He J, Guo Y, Mao R, Zhang J. Proportion of asymptomatic coronavirus disease 2019: a systematic review and meta-analysis. *J Med Virol*. 2021;93(2):820-830.
2. Hagemann J, Onorato GL, Jutel M, et al. Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: an ARIA-EAACI-GA(2) LEN consensus. *Allergy*. 2021;76(8):2354-2366.
3. Meo SA, Meo AS, Al-Jassir FF, Klonoff DC. Omicron SARS-CoV-2 new variant: global prevalence and biological and clinical characteristics. *Eur Rev Med Pharmacol Sci*. 2021;25(24):8012-8018.
4. Iacobucci G. Covid-19: runny nose, headache, and fatigue are commonest symptoms of omicron, early data show. *BMJ*. 2021;375:n3103.
5. Killingley B, Mann AJ, Kalinova M, et al. Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adults. *Nat Med*. 2022;28:1031-1041.
6. United Kingdom Government. Technical briefing. 34–14. 2022. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050236/technical-briefing-34-14-january-2022.pdf
7. ZOE Symptom Study. https://www.ej-med.org/index.php/ejmed/article/view/1120. 2022.
8. Smith P. Correspondence to "Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: An ARIA-EAACI-GA2LEN consensus". *Allergy*. 2022;in press.

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