Supplementary

Table S1 ELISA kits used in this study

Immune indicators	ELISA kit	Manufacturer
IFN-α	VeriKine-HS Human IFN Alpha All Subtype ELISA Kit	PBL Assay Science, Piscataway, NJ, USA
CXCL10	Human CXCL10/IP-10 ELISA Kit	Proteintech, Rosemont, IL, USA
IL-6	AuthentiKine™ Human IL-6 ELISA Kit	Proteintech, Rosemont, IL, USA
VEGF	AuthentiKine™ Human VEGF ELISA Kit	Proteintech, Rosemont, IL, USA
IFN-λ1/IL-29	IL-29 Human ELISA Kit	Invitrogen, Waltham, MA, USA
IFN-λ3/IL-28B	AuthentiKine™ Human IL-28B ELISA Kit	Proteintech, Rosemont, IL, USA

CXCL10, C-X-C motif chemokine ligand 10; ELISA, enzyme-linked immunosorbent assay; IFN, interferon; IL, interleukin; VEGF, vascular endothelial growth factor.

Table S2 Clinical symptoms other than sore throat in participants enrolled in this study

Symptoms	Delta & precedent (n=136)	Omicron	
		Vaccinated twice (n=47)	Unvaccinated (n=24)
Respiratory symptoms			
Cough	90 (66)	35 (74)	19 (79)
Sore throat	57 (42)	31 (66)	19 (79)
Nasal discharge	22 (16)	15 (32)	12 (50)
Nervous symptoms			
Headache	44 (32)	15 (32)	9 (38)
Smell or taste alteration	43 (32)	8 (17)	1 (4)
Others			
Joint or muscle pain	24 (18)	15 (32)	9 (38)
Diarrhea	18 (13)	7 (15)	3 (13)

Categorical variables are reported as numbers (percentages). The presence of each symptom was determined from daily questionnaires.

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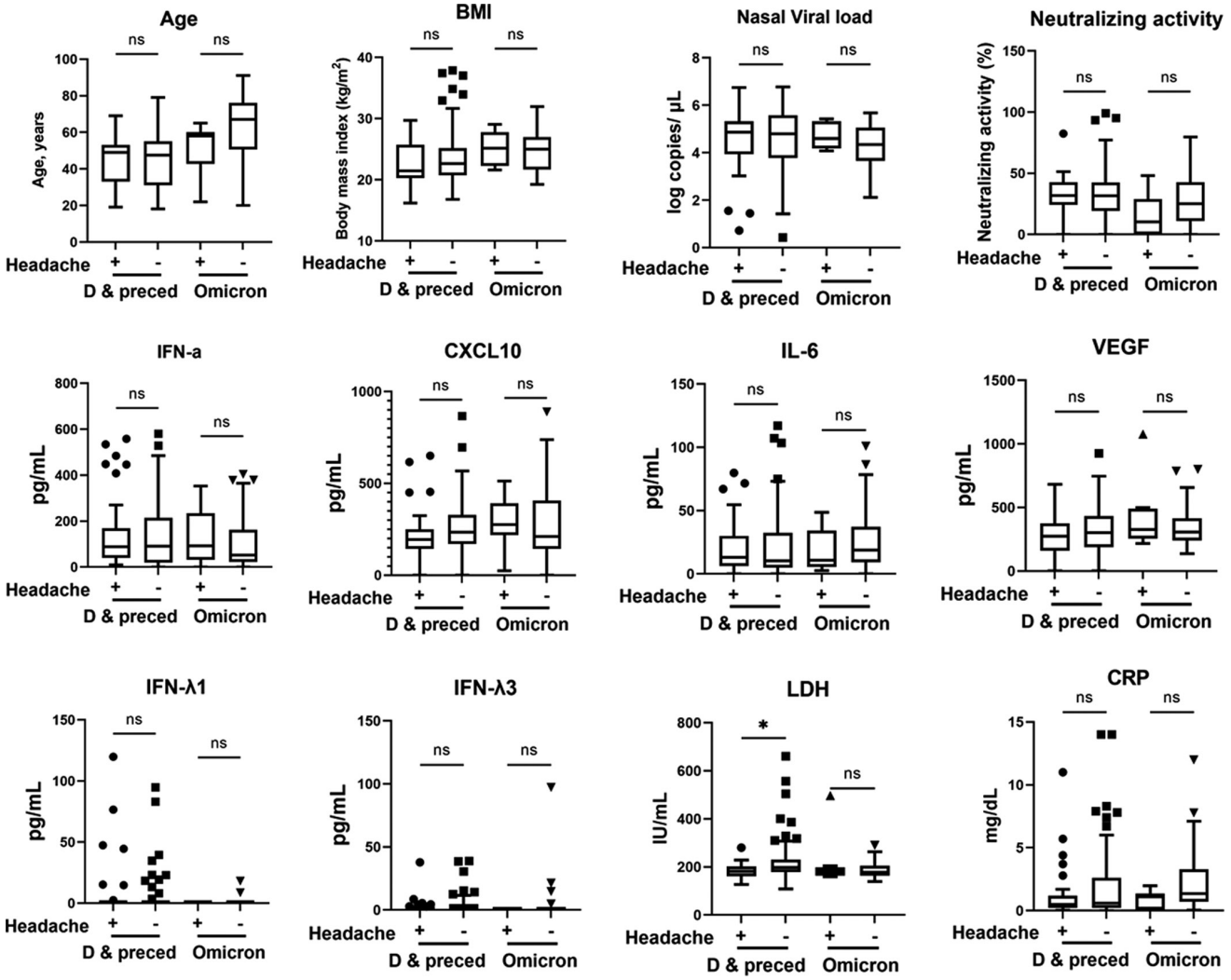

Figure S1 Serum biomarker levels during the early phase of SARS-CoV-2 infection and their association with the occurrence of headache. Serum biomarker levels during the early phase of SARS-CoV-2 infection and their associations with the occurrence of headache: age, BMI, nasal viral load, neutralizing activity, IFN-α, CXCL10, IL-6, VEGF, IFN-λ1, IFN-λ3, LDH, and CRP. The level of each biomarker was evaluated upon hospital admission (within five days of symptom onset). Data are presented as Tukey box-plots and individual values. *, P<0.05; ns, not significant. BMI, body mass index; CRP, C-reactive protein; CXCL10, C-X-C motif chemokine ligand 10; IFN, interferon; IL, interleukin; LDH, lactate dehydrogenase; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VEGF, vascular endothelial growth factor.

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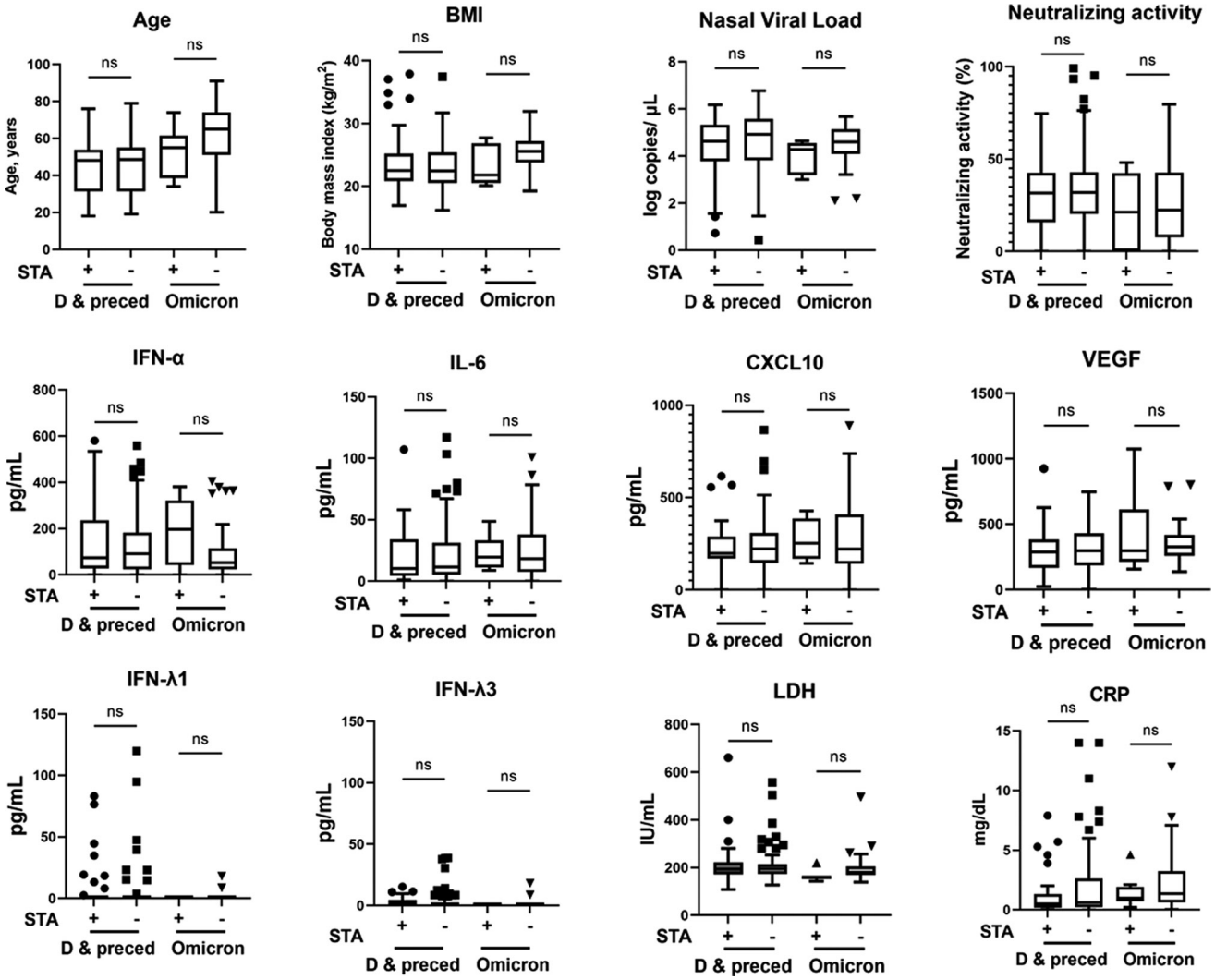

Figure S2 Serum biomarker levels during the early phase of SARS-CoV-2 infection and their association with smell or taste alteration. Serum biomarker levels during the early phase of SARS-CoV-2 infection and their association with smell/taste alteration: age, BMI, nasal viral load, neutralizing activity, IFN-α, IL-6, CXCL10, VEGF, IFN-λ1, IFN-λ3, LDH, and CRP. The level of each biomarker was evaluated upon hospital admission (within five days of symptom onset). Data are presented as Tukey box-plots and individual values. ns, not significant. BMI, body mass index; CRP, C-reactive protein; CXCL10, C-X-C motif chemokine ligand 10; IFN, interferon; IL, interleukin; LDH, lactate dehydrogenase; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STA, smell or taste alteration; VEGF, vascular endothelial growth factor.

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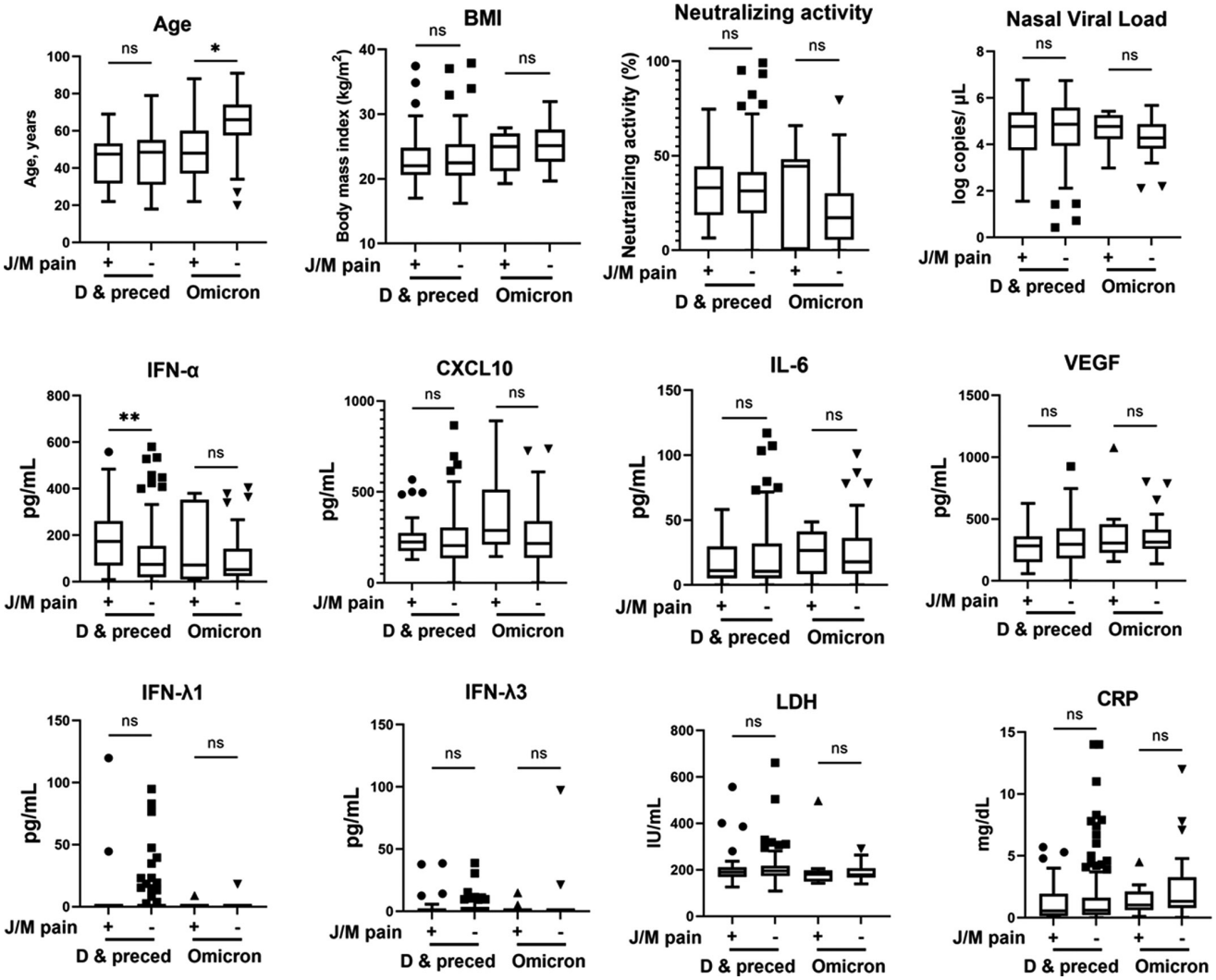

Figure S3 Serum biomarker levels during the early phase of SARS-CoV-2 infection and their association with the occurrence of joint or muscle pain. Serum biomarker levels during the early phase of SARS-CoV-2 infection and their association with the occurrence of joint/muscle pain: age, BMI, neutralizing activity, nasal viral load, IFN-α, CXCL10, IL-6, VEGF, IFN-λ1, IFN-λ3, LDH, and CRP. The level of each biomarker was evaluated upon hospital admission (within five days of symptom onset). Data are presented as Tukey box-plots and individual values. *, P<0.05; **, P<0.01; ns, not significant. BMI, body mass index; CRP, C-reactive protein; CXCL10, C-X-C motif chemokine ligand 10; IFN, interferon; IL, interleukin; J/M, joint or muscle; LDH, lactate dehydrogenase; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VEGF, vascular endothelial growth factor.

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Table S3 Clinical features of unvaccinated patients infected with the Omicron variant (during sixth wave) in this study

Features	Total (n=24)	Sore throat	
		G0 (n=7)	G1–3 (n=17)
Age, years	56 [45–69]	62 [53–71]	54 [43–61]
Sex, male (%)	14 (58)	6 (86)	8 (47)
Underlying disease			
None	6 (25)	1 (14)	5 (29)
Hypertension	8 (33)	3 (43)	5 (29)
Diabetes mellitus	3 (13)	1 (14)	2 (12)
Body mass index (kg/m^2)	24.4 [21–26]	23.9 [19–25]	24.7 [22–26]
Presence of sore throat	17 (71)	–	–
Nasal viral load (log)	3.9 [3.4–4.8]	4.3 [4.0–4.4]	3.8 [3.1–4.5]
Viremia	4 (17)	1 (14)	3 (18)
Severity			
Mild	12 (50)	4 (57)	8 (47)
Moderate-to-severe (developed SARS-CoV-2 pneumonia)	12 (50)	3 (43)	9 (53)
Development of respiratory failure	3 (13)	2 (29)	1 (6)

Continuous variables are reported as median [interquartile range (IQR): 25–75]. Categorical variables are reported as numbers (percentages). SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

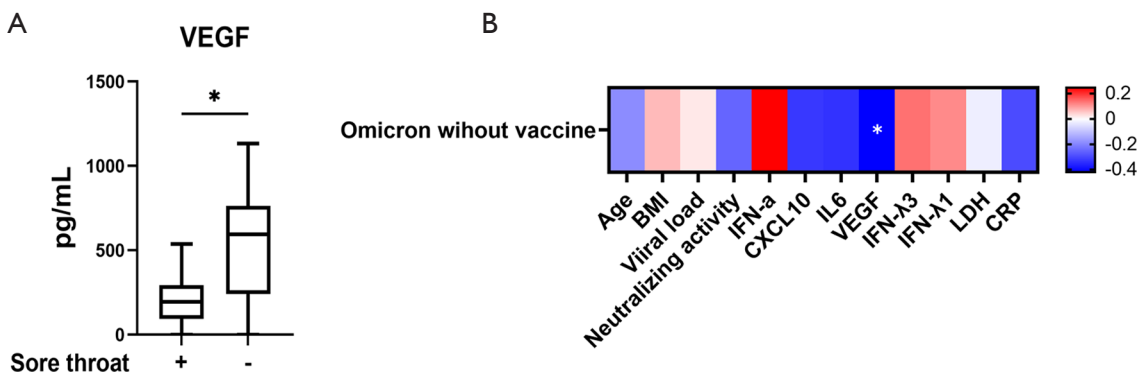

Figure S4 Association between serum immune indicators and grade of sore throat in unvaccinated participants infected with the Omicron variant (during the sixth wave). (A) Serum VEGF levels in unvaccinated participants infected with Omicron infection and their association with the occurrence of sore throat. (B) Correlation between serum biomarker levels and the grade of sore throat in unvaccinated participants with Omicron infection. Results are presented as a heat map. Spearman's correlation coefficients with grade of sore throat are plotted in each cell. Cells are colored based on the strength and trend of correlations; shades of red represent positive correlations, and blue represent negative correlations. *, P<0.05. BMI, body mass index; CRP, C-reactive protein; CXCL10, C-X-C motif chemokine ligand 10; IFN, interferon; IL, interleukin; LDH, lactate dehydrogenase; VEGF, vascular endothelial growth factor.

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