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The Effect of Psychological Factors on COVID-19 Vaccination Side Effects: A Cross-Sectional Survey in South Korea

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Objective Side effects from the coronavirus disease-2019 (COVID-19) vaccine, such as pain, headache, nausea, and fatigue, have caused vaccine hesitancy. Research on the effects of psychological factors on COVID-19 vaccine side effects is insufficient. This study aims to investigate the effect of psychological factors on COVID-19 vaccination side effects.

Methods We recruited a total of 226 individuals registered for the COVID-19 vaccine in Seoul, South Korea, for this study. Participants completed a pre-vaccination questionnaire, including the 5C antecedents of vaccination, and a survey of psychological factors (Patient Health Questionnaire–9 [PHQ-9], Generalized Anxiety Disorder–7, Somatic symptom amplification scale [SSAS], and Illness Attitude Scale [IAS]). After vaccination, participants completed an online questionnaire regarding vaccine side effects at 20 minutes, three days, and seven days after vaccination. We added a discrete set of hierarchical variables with vaccine side effects as the dependent variable to the hierarchical regression analysis: demographics for Model 1, 5C antecedents of vaccination for Model 2, and psychological factors for Model 3.

Results Our results indicated that the risk factors for side effects 20 minutes after vaccination were young age, high PHQ, and SSAS scores. Risk factors for side effects three days after vaccination were young age, high constraints, and calculation, and the risk factor for side effects at seven days was a high IAS score.

Conclusion Our study confirmed that there is a significant relationship between psychological factors and COVID-19 vaccine side effects in chronological order. Psychosocial factors should be examined when assessing side-effect reactions to the COVID-19 vaccine.

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Keywords COVID-19; Depression; Illness anxiety; Psychological factors; Somatic symptoms; Vaccination.

INTRODUCTION

Coronavirus disease-2019 (COVID-19) quickly caused a global pandemic, overwhelming the medical field and threatening the general population's health.[1] The pandemic started at the end of December 2019 in Wuhan, China, spreading to the rest of the world within months.[2] According to World Health Organization, COVID-19 has undergone multiple variants and numerous series of epidemic waves. As of March 2022, 5,960,972 deaths and 437,333,859 confirmed cases of COVID-19 have been reported worldwide. COVID-19 has imposed enormous morbidity and mortality burdens and economic strain on the health and governmental systems.[3] Acquired immunity by vaccination in a sufficient proportion of the population is essential to overcoming the COVID-19 pandemic.

However, the current public attitude concerning the effectiveness and safety of the COVID-19 vaccine threatens vaccine uptake.[4] Recent studies revealed that aversion to the vaccines' potential side effects was the most frequent cause of vaccine hesitancy.[5,6] A South Korean study showed that 77.9% of COVID-19 vaccination refusers were reluctant due to a lack of confidence in the vaccine, including safety concerns and side effects.[7] Several reports of fatal mRNA vaccine side effects including myocarditis, pericarditis, and thrombocytopenia may cause public concern.[8-11]

More commonly reported side effects of the COVID-19 vaccine include fatigue, myalgia, soreness, headache, chills, fever, joint pain, nausea, muscle spasm, sweating, dizziness, decreased sleep quality, and palpitations.[12] While nonfatal, these can make vaccination unpleasant.[13] The causes of less fatal and nonspe-

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cific side effects often remain unexplained even after a complete medical evaluation. In such cases, it is difficult to determine if there is a psychological or a medical cause, and patients are often referred to psychiatrists for examination.[14,15]

Several sociodemographic factors, such as younger age, female sex, and higher subjective social status, influence nonspecific vaccine side effects.[16,17] Although studies have evaluated the demographic, health, and vaccine-related factors that influence COVID-19 vaccine reactions,[16,17] little is known about the role of psychological factors involved in these adverse reactions.

Geers et al.[18] reported that factors such as the expectation of vaccine side effects, worry about COVID-19, and depressive symptoms predicted vaccine side effects more than demographical and clinical variables such as age, vaccine type, and prior COVID-19 infection. The addition of psychosocial variables significantly improved the prediction of vaccine side effects compared to clinical and demographical variables alone. Gold et al.[19] suggested that physical symptoms following immunization, including vasovagal-mediated reactions, hyperventilation-mediated reactions, and stress-related psychiatric reactions, may be related to anxiety, not the vaccine itself. Higher stress levels and anxiety, more prevalent during the pandemic, worsen side effects experienced immediately after vaccination.[20] Moreover, one's expectations and selective attention toward potential vaccine side effects can amplify somatic symptoms.[18] Somatic amplification is a tendency for patients with somatic symptom disorder to excessively focus on their bodily sensations and then amplify and misinterpret them to be indicative of a pathological process.[21]

Vaccine hesitancy and antecedents could also be considered risk factors for vaccine side effects. However, data supporting the effect of vaccine hesitancy in causing side effects after vaccination is scarce. Several studies report the influence of vaccine side effects that generate fear regarding COVID-19 vaccination.[22,23] Expectations, emotions, and attitudes may modulate vaccine responses. As such, vaccine hesitancy or certain antecedents of vaccination must be investigated as risk factors for vaccine adverse events. The 5C psychological antecedents of vaccination is a well-established theoretical model that explains the fundamentals of vaccine hesitancy, including confidence, complacency, constraints, calculation, and collective responsibility.[24] This study aimed to evaluate potential risk factors of vaccine adverse events, with a special interest in an individual's psychological state and vaccination intention. This could assist mental health professionals in determining appropriate assessments and interventions for patients suffering from vaccination side effects without an evident medical cause.

Previous studies report adverse events appear mostly from the day of to three days after vaccination, with symptoms such as tiredness persisting for longer than seven days.[25] Therefore, in this study, vaccine side effects were recorded per the time of vaccination—20 minutes, three days, and seven days post-vaccination. We aimed to identify the effect of psychological factors on symptoms following the COVID-19 vaccination, in chronological order.

We hypothesized that sociodemographic, 5C antecedents of vaccination, and emotional factors would be related to COVID-19 vaccine side effects.

METHODS

Participants

We conducted this study between August 23 and October 7, 2021, during priority vaccinations for health professionals and the elderly (those aged 65 years or older). During this period, the South Korean government implemented large-scale vaccinations for those aged 18 years or older. We recruited study participants from the general population through advertisements. The study consisted of a pre-vaccination survey and a post-vaccination survey. Eligibility criteria for the pre-vaccination survey were individuals 1) at least 18 years of age; 2) currently non-vaccinated, but registered for vaccination; and 3) with no current psychiatric diseases (e.g., major depressive disorder, bipolar disorder, or schizophrenia). Eligibility for the post-vaccination survey included both completion of the pre-vaccination survey and the first dose of the COVID-19 vaccination. This study was approved by the Institutional Review Board of the Chung-Ang University Hospital (approval number: 2107-044-472).

We enrolled all 267 participants meeting the eligibility criteria for the pre-vaccination survey after they provided written informed consent. Before vaccination, we asked participants to complete a pre-vaccination questionnaire regarding demographic and emotional factors. After vaccination, we asked participants to complete online questionnaires regarding vaccine side effects at 20 minutes, three days, and seven days post-vaccination. Of the 267 people enrolled, 238 (89.1%) completed the pre-vaccination questionnaire, and 226 (84.6%) completed all three post-vaccination questionnaires. Participants received monetary compensation of 20 USD upon completion of the post-vaccination survey.

Assessment scales

We collected demographic data, including age, sex, education, marital status, income, and job status, from all participants. Participants also completed the Patient Health Questionnaire−9 (PHQ-9), Generalized Anxiety Disorder−7 (GAD-7), Somatic Symptom Amplification Scale (SSAS), and Illness Attitude Scale (IAS) to assess their emotional states.

5C scale

The 5C scale is a validated measure based on the 5C model of the drivers of vaccine hesitancy that assesses the psychological antecedents of vaccination. The 5C scale assesses five main individual determinants of vaccine hesitancy: confidence (lack of trust in the safety and effectiveness of vaccines), complacency (not perceiving diseases as being a risk and vaccination as necessary), constraints (practical barriers to vaccination), calculation (preference for deliberation), and collective responsibility (communal orientation). The short version of the 5C scale is suitable for field settings and regular global monitoring of relevant vaccination antecedents.[24]

PHQ-9

The PHQ-9 measures the severity of depression by assessing 9 symptoms from the Diagnostic and Statistical Manual for Mental Disorders, 4th edition depressive episode criteria.[26] Each item of the PHQ-9 is scored from 0 to 3, and total PHQ-9 scores of 5, 10, 15, and 20 indicate mild, moderate, moderately severe, and severe depression, respectively.[26] PHQ-9 is a valid and reliable measure to screen for the presence and severity of depression in a primary-care setting.[26]

GAD-7

The GAD-7 is a 7-item scale for screening and assessing the severity of generalized anxiety disorder, one of the most common mental disorders in clinical practice.[27] Similar to the previous PHQ-9, each item is rated on a 4-point scale from 0 to 3. Total GAD-7 scores of 5, 10, and 15 represent mild, moderate, and severe anxiety, respectively. GAD-7 is a brief, efficient measure with good reliability and validity.[27]

SSAS

The SSAS is a 5-point Likert scale consisting of 10 items to assess the level of somatosensory amplification or the tendency to experience bodily sensations as intense, noxious, and disturbing.[21] Higher total SSAS scores indicate greater somatic symptom amplification.[28] The SSAS has good internal consistency and validity.[21,29]

IAS

The IAS is a highly reliable 9-item scale designed to evaluate fears, attitudes, and beliefs associated with hypochondriacal concerns and abnormal illness behaviors.[30,31]

Vaccine side effects

We evaluated vaccine side effects using a questionnaire requiring participants to complete a checklist of symptoms at 20 minutes, three days, and seven days after vaccination. We included side effects such as pain, fatigue, fever, chills, and nausea based on literature reviews.[32-35] Each symptom severity was scored from 1 (none) to 4 (very severe) based on Food and Drug Administration's guidance on vaccine trials (Toxicity Grading Scale for Preventative Vaccine Clinical Trials).[36] Those who scored at least 3 (severe) or 4 (very severe) were more susceptible to side effects (Supplementary Tables 1 and 2 in the online-only Data Supplement).

Statistical analysis

We analyzed the sociodemographic factors, 5C antecedents of vaccination, and participants' psychological states using t-test, chi-square tests, and the Bonferroni posthoc test with a significance level of $p<0.05$. In a multiple hierarchical regression analysis of all factors, we added a discrete set of hierarchical variables with vaccine side effects as the dependent variable: demographic factors for Model 1, Model 1+5C scale for Model 2, and Model 2+psychological states for Model 3.

RESULTS

Demographic factors and psychological states

At 20 minutes after vaccination, there were no significant differences in sex, marital status, occupation, chronic illness, all 5C subscales, or GAD-7 and IAS scores between the susceptible and non-susceptible groups. The susceptible group was younger and had higher PHQ-9 and SSAS scores compared to the non-susceptible group (Table 1).

At three days after vaccination, there were no significant differences in sex, marital status, occupation, presence of chronic illness, confidence, complacency, constraints, and collective responsibility between the susceptible and non-susceptible groups. The susceptible group was younger and had higher calculation, PHQ-9, GAD-7, SSAS, and IAS scores compared to the non-susceptible group (Table 2).

At seven days after vaccination, there were no significant differences in sex, occupation, presence of chronic illness, complacency, constraints, calculation, collective responsibility, or PHQ-9 and SSAS scores. The susceptible group was younger, had a higher proportion of single individuals, lower confidence, and higher GAD-7 and IAS scores compared to the non-susceptible group (Table 3).

Hierarchical logistic regression analysis

Of the three models employed in this study, Models 1 and 3 were significantly associated with vaccine side effects 20 minutes after vaccination (Table 4). At three days after vaccination, Models 1, 2, and 3 predicted vaccine side effects (Table 5). At seven days after vaccination, Model 3 could predict vaccine side effects (Table 6).

In Model 1 at 20 minutes after vaccination, model χ^2 (11.158,

Table 1. Demographic and psychological characteristics of participants (20 minutes after vaccination)

Variables	Susceptible (N=43)	Non-susceptible (N=183)	Statistics
Age (yr)	30.21±7.00	35.40±12.06	t=-3.74, p<0.01**
Sex, male/female	22/21	92/91	χ^2=0.01, p=0.92
Marital status, married/single	11/32	70/113	χ^2=2.43, p=0.12
Occupation†, yes/no	27/16	109/73	χ^2=0.12, p=0.73
Chronic illness†, yes/no	4/39	34/148	χ^2=2.18, p=0.14
Confidence†	3.14±0.94	3.07±1.08	t=-0.41, p=0.68
Complacency†	1.56±0.77	1.70±0.92	t=1.03, p=0.31
Constraints†	1.35±0.57	1.58±0.85	t=1.67, p=0.10
Calculation†	4.09±0.78	3.90±1.08	t=-1.13, p=0.26
Collective responsibility†	4.30±0.96	4.18±1.04	t=-0.76, p=0.45
PHQ-9	7.09±6.49	4.62±4.84	t=2.35, p=0.02*
GAD-7	4.91±5.71	3.80±4.62	t=1.18, p=0.24
SSAS	12.14±7.09	9.73±5.57	t=2.08, p=0.04*
IAS	37.12±17.85	35.72±13.66	t=0.48, p=0.63

Values are presented as mean±standard deviation or number. *p<0.05; **p<0.01; †one value missing on non-susceptible. PHQ-9, Patient Health Questionnaire–9; GAD-7, Generalized Anxiety Disorder–7; SSAS, Somatic Symptom Amplification Scale; IAS, Illness Anxiety Scale

Table 2. Demographic and psychological characteristics of participants (three days after vaccination)

Variables	Susceptible (N=56)	Non-susceptible (N=170)	Statistics
Age (yr)	30.61±7.86	35.67±12.16	t=-3.61, p<0.01**
Sex, male/female	30/26	84/86	χ^2=0.29, p=0.59
Marital status, married/single	15/41	66/104	χ^2=2.66, p=0.10
Occupation†, yes/no	31/25	105/64	χ^2=0.81, p=0.37
Chronic illness†, yes/no	12/44	26/143	χ^2=1.10, p=0.30
Confidence†	3.04±1.11	3.10±1.03	t=0.39, p=0.70
Complacency†	1.73±0.92	1.65±0.89	t=-0.58, p=0.57
Constraints†	1.70±0.87	1.48±0.78	t=-1.66, p=0.10
Calculation†	4.23±0.95	3.83±1.04	t=-2.64, p=0.01*
Collective responsibility†	4.07±1.09	4.24±1.00	t=1.04, p=0.30
PHQ-9	6.71±5.65	4.55±5.05	t=2.70, p=0.01*
GAD-7	5.82±5.68	3.42±4.40	t=2.89, p<0.01**
SSAS	11.86±6.95	9.64±5.49	t=2.17, p=0.03*
IAS	40.54±18.73	34.48±12.54	t=2.26, p=0.03*

Values are presented as mean±standard deviation or number. *p<0.05; **p<0.01; †one value missing on non-susceptible. PHQ-9, Patient Health Questionnaire–9; GAD-7, Generalized Anxiety Disorder–7; SSAS, Somatic Symptom Amplification Scale; IAS, Illness Anxiety Scale

p=0.048), and Nagelkerke's R^2 (0.078, explaining about 7.8% of the variance) indicated that it adequately predicted vaccine side effects, with an accuracy of 80.8%. In Model 2 (Model 1+ 5C scale) at 20 minutes after vaccination, model χ^2 (15.115, p=0.128), and Nagelkerke's R^2 (0.105, explaining about 10.5% of the variance) indicated that it inadequately predicted vaccine side effects. In Model 3 (Model 2+psychologic states) at 20 minutes after vaccination, model χ^2 (31.125, p=0.005), and Nagelkerke's R^2 (0.208, explaining about 20.8% of the variance) indicated that it best predicted vaccine side effects, with an accuracy of 83.9% (Table 4).

In Model 1 at three days after vaccination, model χ^2 (13.751, p=0.017), and Nagelkerke's R^2 (0.088, explaining about 8.8% of the variance) indicated that it adequately predicted vaccine side effects, with an accuracy of 75.0%. In Model 2 (Model 1+ 5C scale) three days after vaccination, model χ^2 (27.898, p= 0.002), and Nagelkerke's R^2 (0.136, explaining about 13.6% of the variance) indicated that it best predicted vaccine side ef-

Table 3. Demographic and psychological characteristics of participants (seven days after vaccination)

	Susceptible (N=27)	Non-susceptible (N=199)	Statistics
Age (yr)	30.67±8.01	34.92±11.76	t=-2.43, p=0.02*
Sex, male/female	9/18	105/94	χ^2=3.60, p=0.06
Marital status, married/single	4/23	77/122	χ^2=5.90, p=0.02*
Occupation†, yes/no	14/13	122/76	χ^2=0.95, p=0.33
Chronic illness†, yes/no	5/22	33/165	χ^2=0.06, p=0.81
Confidence†	2.63±1.15	3.15±1.02	t=2.22, p=0.03*
Complacency†	1.81±0.68	1.65±0.90	t=-0.90, p=0.37
Constraints†	1.67±0.68	1.52±0.82	t=-1.06, p=0.30
Calculation†	4.15±0.82	3.90±1.06	t=-1.40, p=0.17
Collective responsibility†	3.89±1.22	4.24±0.99	t=1.69, p=0.09
PHQ-9	6.67±6.51	4.87±5.06	t=1.66, p=0.10
GAD-7	6.04±6.09	3.74±4.61	t=2.33, p=0.02*
SSAS	11.44±5.96	10.02±5.94	t=1.17, p=0.24
IAS	43.44±15.97	34.97±14.05	t=2.89, p<0.01**

Values are presented as mean±standard deviation or number. *p<0.05; **p<0.01; †one value missing on non-susceptible. PHQ-9, Patient Health Questionnaire–9; GAD–7, Generalized Anxiety Disorder-7; SSAS, Somatic Symptom Amplification Scale; IAS, Illness Anxiety Scale

Table 4. Hierarchical logistic regression analysis model, dependent factor: COVID-19 vaccine side effects (20 minutes after vaccination)

Independent variables	Model 1				Model 2				Model 3			
	B	Wald	Sig.	OR	B	Wald	Sig.	OR	B	Wald	Sig.	OR
Sociodemographic factors												
Age	-0.061	5.215	0.022*	0.941	-0.061	4.976	0.026*	0.941	-0.062	4.853	0.028*	0.940
Sex	-0.248	0.500	0.479	0.780	-0.220	0.359	0.549	0.803	-0.331	0.731	0.392	0.718
Marital status	-0.128	0.068	0.794	0.880	-0.002	0.000	0.997	0.998	-0.180	0.115	0.734	0.835
Occupation	0.463	1.466	0.226	1.589	0.474	1.417	0.234	1.606	0.355	0.730	0.393	1.426
Chronic illness	0.494	0.728	0.393	1.638	0.518	0.769	0.380	1.679	0.999	2.307	0.129	2.714
5C scale												
Confidence					0.089	0.211	0.646	1.094	0.236	1.273	0.259	1.266
Complacency					0.008	0.001	0.976	1.008	-0.162	0.313	0.576	0.850
Constraints					-0.311	0.948	0.330	0.732	-0.305	0.852	0.356	0.737
Calculation					0.153	0.642	0.423	1.166	0.166	0.644	0.422	1.181
Collective responsibility					0.093	0.187	0.666	1.098	-0.012	0.003	0.956	0.988
Psychologic state												
PHQ-9									0.148	6.215	0.013*	1.159
GAD-7									-0.099	1.777	0.183	0.906
SSAS									0.084	4.739	0.029*	1.088
IAS									-0.003	0.030	0.862	0.997
Statistics of the model												
-2LL	207.940				203.984				187.973			
Model χ^2	11.158, p=0.048*				15.115, p=0.128				31.125, p=0.005**			
Step χ^2	11.158, p=0.048*				3.956, p=0.128				16.001, p=0.003**			
Nagelkerke's R^2	0.078				0.105				0.208			
Class accur (%)	80.8				80.8				83.9			

Model 1: Sociodemographic factors. Model 2: Model 1+5C antecedents of vaccination. Model 3: Model 2+psychological factors. *p<0.05; **p<0.01. COVID-19, coronavirus disease-2019; Sig., significance; OR, odd ratio; PHQ-9, Patient Health Questionnaire–9; GAD-7, Generalized Anxiety Disorder–7; SSAS, Somatic Symptom Amplification Scale; IAS, Illness Anxiety Scale; -2LL, -2 log likelihood; Class accur, classification accuracy

fects, with an accuracy of 87.9%. In Model 3 (Model 2+psychologic states) three days after vaccination, model χ^2 (37.245, p=0.001), and Nagelkerke's R^2 (0.227, explaining about 22.7% of the variance) indicated that it adequately predicted vaccine side effects, with an accuracy of 76.8%. However, in Model 3 at three days after vaccination, step χ^2 (9.347, p=0.053) indicated that psychologic states cannot predict vaccine-related side effects (Table 5).

In Model 1 at seven days after vaccination, model χ^2 (9.840, p=0.080), and Nagelkerke's R^2 (0.082, explaining about 8.2% of the variance) indicated that it inadequately predicted vaccine side effects. In Model 2 (Model 1+5C scale) seven days after vaccination, model χ^2 (16.420, p=0.088), and Nagelkerke's R^2 (0.136, explaining about 13.6% of the variance) indicated it was inadequate to predict vaccine side effects. In Model 3 (Model 2+psychologic states) seven days after vaccination, model χ^2 (24.213, p=0.043), and Nagelkerke's R^2 (0.197, explaining about 19.7% of the variance) indicated it predicted vaccine side effects with an accuracy of 88.4% (Table 6).

We used Wald statistics to confirm whether each variable had a significant individual relationship with vaccine hesitancy. Among all independent variables, younger age, high PHQ-9, and SSAS scores were statistically significant predictors of vaccine side effects 20 minutes after vaccination (Table 4). Younger age, high constraints, and calculations were significant predictors of vaccine side effects three days after vaccination (Table 5). A high IAS score was the only predictor of vaccine side effects seven days after vaccination (Table 6).

DISCUSSION

This study demonstrated a significant association between psychological factors and COVID-19 vaccine side effects. Our findings are in line with previous studies, which revealed sev-

Table 5. Hierarchical logistic regression analysis model, dependent factor: COVID-19 vaccine side effects (three days after vaccination)

Independent variables	Model 1				Model 2				Model 3			
	B	Wald	Sig.	OR	B	Wald	Sig.	OR	B	Wald	Sig.	OR
Sociodemographic factors												
Age	-0.065	7.630	0.006*	0.937	-0.074	8.608	0.003*	0.928	-0.074	8.129	0.004*	0.929
Sex	-0.324	1.009	0.315	0.723	-0.375	1.152	0.283	0.687	-0.431	1.447	0.229	0.650
Marital status	-0.217	0.230	0.631	0.805	-0.167	0.125	0.723	0.846	-0.225	0.214	0.643	0.798
Occupation	0.070	0.042	0.838	1.073	0.245	0.457	0.499	1.277	0.285	0.578	0.447	1.329
Chronic illness	-0.787	3.374	0.066	0.455	-0.897	3.716	0.054	0.408	-0.328	0.401	0.526	0.720
5C scale												
Confidence					0.108	0.373	0.541	1.114	0.258	1.854	0.173	1.294
Complacency					-0.047	0.036	0.849	0.954	-0.188	0.531	0.466	0.829
Constraints					0.560	5.026	0.025*	1.750	0.558	4.575	0.032*	1.747
Calculation					0.586	8.498	0.004*	1.796	0.642	8.803	0.003*	1.900
Collective responsibility					-0.071	0.131	0.717	0.931	-0.162	0.624	0.430	0.850
Psychologic state												
PHQ-9									0.015	0.075	0.785	1.015
GAD-7									0.061	0.895	0.344	1.063
SSAS									0.016	0.224	0.636	1.017
IAS									0.014	0.927	0.336	1.014
Statistics of the model												
-2LL	238.175				224.028				214.681			
Model χ^2	13.751, p=0.017*				27.898, p=0.002**				37.245, p=0.001**			
Step χ^2	13.751, p=0.017*				14.147, p=0.015*				9.347, p=0.053			
Nagelkerke's R^2	0.088				0.136				0.227			
Class accur (%)	75.0				87.9				76.8			

Model 1: Sociodemographic factors. Model 2: Model 1+5C antecedents of vaccination. Model 3: Model 2+psychological factors. *p<0.05; **p<0.01. COVID-19, coronavirus disease-2019; Sig., significance; OR, odd ratio; PHQ-9, Patient Health Questionnaire–9; GAD-7, Generalized Anxiety Disorder–7; SSAS, Somatic Symptom Amplification Scale; IAS, Illness Anxiety Scale; -2LL, -2 log likelihood; Class accur, classification accuracy

Table 6. Hierarchical logistic regression analysis model, dependent factor: COVID-19 vaccine side effects (seven days after vaccination)

Independent variables	Model 1				Model 2				Model 3			
	B	Wald	Sig.	OR	B	Wald	Sig.	OR	B	Wald	Sig.	OR
Sociodemographic factors												
Age	-0.008	0.076	0.783	0.992	-0.001	0.000	0.984	0.999	0.007	0.041	0.840	1.007
Sex	0.699	2.517	0.113	2.012	0.523	1.284	0.257	1.687	0.610	1.611	0.204	1.840
Marital status	1.099	2.447	0.118	3.002	1.309	3.252	0.071	3.704	1.436	3.692	0.055	4.203
Occupation	-0.131	0.091	0.763	0.877	-0.116	0.066	0.798	0.890	-0.055	0.013	0.908	0.946
Chronic illness	-0.426	0.568	0.451	0.653	-0.640	1.154	0.283	0.527	0.014	0.000	0.984	1.014
5C scale												
Confidence					-0.314	2.033	0.154	0.730	-0.261	1.189	0.275	0.770
Complacency					-0.050	0.029	0.865	0.951	-0.135	0.181	0.671	0.873
Constraints					0.057	0.036	0.849	1.059	-0.012	0.001	0.971	0.988
Calculation					0.305	1.495	0.221	1.357	0.307	1.267	0.260	1.359
Collective responsibility					-0.252	1.198	0.274	0.777	-0.323	1.723	0.189	0.724
Psychologic state												
PHQ-9									0.007	0.011	0.917	1.007
GAD-7									0.034	0.172	0.679	1.035
SSAS									-0.058	1.550	0.213	0.944
IAS									0.042	4.986	0.026*	1.043
Statistics of the model												
-2LL	155.020				148.440				140.647			
Model χ^2	9.840, p=0.080				16.420, p=0.088				24.213, p=0.043*			
Step χ^2	9.840, p=0.080				6.580, p=0.254				7.794, p=0.099			
Nagelkerke's R^2	0.082				0.136				0.197			
Class accur (%)	87.9				87.9				88.4			

Model 1: Sociodemographic factors. Model 2: Model 1+5C antecedents of vaccination. Model 3: Model 2+psychological factors. *p<0.05. COVID-19, coronavirus disease-2019; Sig., significance; OR, odd ratio; PHQ-9, Patient Health Questionnaire–9; GAD-7, Generalized Anxiety Disorder–7; SSAS, Somatic Symptom Amplification Scale; IAS, Illness Anxiety Scale; -2LL, -2 log likelihood; Class accur, classification accuracy

eral sociodemographic risk factors that influence non-specific vaccine side effects. These include demographic factors, knowledge regarding COVID-19, and psychological factors.[17,37,38] In this study, age, depression, and somatic symptoms were significant factors affecting vaccine side effects 20 minutes after vaccination. On day three, age, constraints, and calculation were significant, and on day seven, illness anxiety was important. To our knowledge, this is the first study to examine the influence of psychological factors and 5C antecedents of vaccination on vaccine side effects.

We categorized our results in chronological order, based on the time passed after vaccination. Our findings that younger individuals experience post-vaccination side-effects 20 minutes after vaccination concurs with previous studies, such as Riad et al.,[39] who reported that those aged younger than 43 years were more frequently affected by injection site pain, fatigue, headache, and muscle pain. High scores on the PHQ-9 and SSAS suggesting depressive and somatic symptoms were significantly associated with vaccine side effects 20 minutes after vaccination, indicating that those with depressive and somatic symptoms were more likely to have immediate reactions to the vaccine. This is in line with a previous study conducted by Geers et al.[18] in which vaccine side effect expectations, concerns about COVID-19, and depressive symptoms predicted vaccine side effects.

Moreover, patients with depression or anxiety are likely to react to their emotional distress with a low threshold of somatic pain due to sensitive perception.[21,40,41] Somatic symptoms are characterized by an extreme focus on physical symptoms, such as pain or fatigue, causing emotional distress and difficulties with daily functioning.[21] Pain, shortness of breath, fatigue, or weakness may have no pathological or organic causes.[40] These sensations are also possible symptoms experienced after vaccination due to vaccine side effects.[41] SSAS measures the tendency to experience psychological distress in the form of somatic and visceral sensations.[21] While the etiology of somatic

symptoms remains unclear, it may be a mechanism through which patients with depression or anxiety react to their emotional distress.[40] Although they experience the same physical symptoms after vaccination, those with a high tendency to experience somatization are more likely to have heightened awareness of certain body sensations, suggesting an amplification of perceived visceral sensations resulting in vaccine side effects.[21,40] Our results indicate that people with high SSAS scores are more likely to be sensitive to vaccine side effects, implying somatization.

Age was also an important factor three days after vaccination, as the younger group was more susceptible to side effects. On day three, psychological antecedents of vaccination, including constraints (practical barriers for vaccination) and calculation (one's engagement in an extensive information search) were significantly associated with vaccine side effects. Calculation is related to one's engagement in an extensive information search. When coupled with accessibility to anti-vaccination content in the media, individuals with high calculation are skeptical of vaccine safety and effectiveness, increasing their fear of side effects.[24,42] High calculation characteristics could lead to misleading information from various sources,[42] exacerbating the excessive fear and anxiety of COVID-19 vaccination.[22] Such fear and anxiety can amplify and even induce side effects,[43] contributing to systemic vaccine side effects.

Younger individuals are more likely to use social media, a platform with abundant content regarding vaccination.[44] Data from these networks may be inaccurate,[45] contributing to anxiety regarding side effects post-vaccination.[46] Constraints represent psychological and physical barriers, such as geographical accessibility, comprehension (language and health literacy), and affordability, which could hinder vaccination.[24] Low health literacy skills affect communication. Social media can be a useful source of information to address vaccine hesitancy, but it is limited by conflicting information and the exclusion of individuals without internet access or with low literacy levels.[47] Such conflicting information and misconceptions may lead to vaccine-hesitant attitudes,[47] forming anxiety that overestimates the vaccination threat.[48] Individuals exposed to this conflicting information may be more hesitant to become vaccinated and have a heightened immune response to side effects after vaccination.[41]

Treatment costs for vaccine side-effects are economic barriers and psychological concerns.[22] Economic barriers could lead to a pessimistic outlook before vaccination, increasing anxiety and the expectation of adverse events.[49] A randomized COVID-19 vaccine meta-analysis found that 76% of systemic and 24% of local reactogenicity were attributed to anxiety and nocebo effects,[50] implying that heightened anxiety due to vaccine hesitancy modulates physical responses to the COVID-19 vaccine. Further studies are needed to explore the complicated associations between such barriers and vaccine side effects.

Seven days after vaccination, Model 3 (demographics, psychological antecedents of vaccination, and psychological status) significantly explained vaccine side effects. The only determining psychological status factor was the IAS score, which evaluates fears, attitudes, and beliefs associated with hypochondriacal concerns.[31] This suggests that vaccination side effects at seven days would be affected by the interaction between demographic data, psychological antecedents of vaccination, and psychological status, including illness anxiety.

Previous studies showed that psychosocial factors, such as expectations and attitudes, modulate responses to COVID-19 vaccines.[18] Psychosocial factors, such as emotions and attitudes, may modulate these responses as well.[18] Our research reveals a novel, significant relationship between psychological factors and side effects 20 minutes after vaccination. Depression and somatization were risk factors for side effects 20 minutes after vaccination, and illness-anxiety was a risk factor for side effects seven days after vaccination. These risk factors are modifiable and may serve as critical intervention points to reduce vaccine side effects. Side effects from the influenza vaccine were more likely to be reported by people who knew of another person who had experienced side effects and those who believed that vaccines cause short-term side effects.[51] Screening processes to provide psychological education to people with such risk factors should be implemented to increase vaccine acceptance and reduce vaccine hesitancy.

The current study had several strengths. First, we observed vaccination's adverse effects in chronological order from 20 minutes to seven days. Second, we investigated the correlations between vaccination adverse effects and psychological factors using well-established clinical scales to assess psychological state and antecedents of vaccination. This study allows the general population to further understand vaccine side effects and recognize possible psychological factors underlying vaccine responses.

This study also had several limitations. First, we included only 267 participants. Such a small sample size may not be representative of the general population. Furthermore, all participants were South Korean, which may limit the generalizability of our findings. Second, people who are more interested in COVID-19 vaccination were more likely to volunteer to participate. Third, people with prior COVID-19 exposure were excluded from the study, so vaccine side effects were not evaluated in this population. However, previous studies report that prior COVID-19 infection is a risk factor for more vaccine side effects.[52]

The population may have concerns about the COVID-19 vaccine as it is a novel mRNA vaccine with no available long-

term data. Further research on the psychological impact of different vaccination types is warranted to generalize our findings. Future comparative studies should examine the different psychological responses between inactivated vaccines and mRNA vaccines.

In conclusion, sociodemographic factors and psychosocial factors influence side-effect responses to COVID-19 vaccines. Age, depressive symptoms, and somatic amplification tendency were significant determinants of reactions reported 20 minutes after vaccination. Age and psychological status regarding vaccination, especially constraints and calculation, were key factors three days after vaccination. At seven days, illness anxiety factors were relevant. Psychosocial factors must be included when assessing reactions to the COVID-19 vaccine.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.30773/pi.2023.0116.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: all authors. Data curation: Eun Kim, Hee Jin Kim. Formal analysis: Doug Hyun Han. Investigation: Eun Kim, Hee Jin Kim. Methodology: Hee Jin Kim, Doug Hyun Han. Project administration: Doug Hyun Han. Resources: Eun Kim, Hee Jin Kim. Software: Hee Jin Kim. Supervision: Doug Hyun Han. Validation: Doug Hyun Han. Visualization: Eun Kim, Hee Jin Kim. Writing—original draft: Eun Kim. Writing—review and editing: Hee Jin Kim, Doug Hyun Han.

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Supplementary Table 1. Questionnaires for post-vaccination symptoms (20 minutes after vaccination)

	Symptom severity			
	None	Moderate	Severe	Very severe
Pain at injection site	1	2	3	4
Swelling	1	2	3	4
Redness	1	2	3	4
Itchiness	1	2	3	4
Fatigue	1	2	3	4
Headache	1	2	3	4
Myalgia (muscle pain)	1	2	3	4
Earache	1	2	3	4
Febrile sense	1	2	3	4
Chilling sense	1	2	3	4
Nausea	1	2	3	4
Abdominal pain	1	2	3	4
Diarrhea	1	2	3	4
Dizziness	1	2	3	4
Skin rash	1	2	3	4
Paresthesia	1	2	3	4

Supplementary Table 2. Questionnaires for post-vaccination symptoms (days three and seven after vaccination)

	Symptom severity			
	None	Moderate	Severe	Very severe
Pain at injection site	1	2	3	4
Swelling	1	2	3	4
Redness	1	2	3	4
Itchiness	1	2	3	4
Fatigue	1	2	3	4
Headache	1	2	3	4
Myalgia (muscle pain)	1	2	3	4
Earache	1	2	3	4
Febrile sense	1	2	3	4
Chilling sense	1	2	3	4
Nausea	1	2	3	4
Abdominal pain	1	2	3	4
Diarrhea	1	2	3	4
Dizziness	1	2	3	4
Skin rash	1	2	3	4
Insomnia	1	2	3	4
Paresthesia	1	2	3	4