Allergy and mental health among pregnant women in the Japan Environment and Children's Study

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Clinical Implications

- Allergy increased the risk of depression and lower quality of life among pregnant women across Japan. We should provide additional support to pregnant women with allergy, to help them maintain optimal mental health.

TO THE EDITOR:

The Japan Environment and Children's Study (JECS) is a nationwide, multicenter, prospective birth cohort study conducted by the Ministry of Environment of Japan.[1] The association of mental health with allergy in pregnant women has not been well documented. The clinical question of this study was that allergic immunological features might affect mental status among pregnant women. We aimed to investigate the association of maternal mental health, including depression, anxiety, and quality of life, with allergic features during pregnancy among JECS participants.

This is a cross-sectional study of a birth cohort. Participants in the JECS were recruited between January 2011 and March 2014. Maternal information and blood samples were obtained from women during pregnancy, using self-administered questionnaires. Lifetime prevalence of allergic disease (asthma, allergic rhinitis, eczema, food allergy, conjunctivitis, drug allergy, and contact dermatitis) was assessed on the basis of a self-reported doctor's diagnosis, obtained from the questionnaire. Serum total and allergen-specific IgE titers assayed by ImmunoCAP (Thermo Fisher Scientific, Inc, Uppsala, Sweden) were analyzed at a contract clinical laboratory. Specific titers were detected for the following allergens: *Der p* 1 (*Dermatophagoides pteronyssinus*), animal allergen mixes (cat dander, dog dander, guinea pig epithelium, rat, and mouse), Japanese cedar, birch, moth, and egg white. Positive IgE sensitization to a specific allergen was defined as allergen-specific IgE value of greater than or equal to 0.35 UA/mL. We defined high sensitization if the total IgE level was 170 IU/mL or above.[2] As for psychological assessment, Kessler's K-6 Non-Specific Psychological Distress Scale (K-6)[3] was used to evaluate maternal anxiety and depression. The K6 scale consists of 6 questions. All variables were summed to yield a total score that range from 0 to 24. Scores of 13 or higher indicate severe depression,[4] and scores of 5 or higher indicate any depression.[5] Health-related quality of life was measured using the Medical Outcomes Survey Short Form-8 questionnaire (SF-8).[6] Two summary scores of a physical component summary (PCS) and a mental component summary (MCS) are indicated as SD scores (the national standard score is 50). Higher scores mean a higher quality health status.

Figure E1 in this article's Online Repository at www.jaci-inpractice.org shows the flowchart of this study. We examined the backgrounds of participants (n = 97,058) with no missing variables for the K-6 and the SF-8 and appropriate gestational age. Among these, we performed statistical analysis for the data with no missing variables (n = 86,085). Logistic regression and linear regression were used to examine the associations of K-6 and SF-8 scores (MSC and PSC scores), respectively, with allergic features, using the same potential confounders. We considered the following factors as possible confounders in the regression analyses: maternal age, place of residence, marital status, having another child, history of abnormal pregnancy, current smoking status, employment status, and maternal education level. This study was an exploratory study to estimate the magnitude of the association between maternal allergy status and mental health. Therefore, we had not defined any statistically significant level of *P* values at the beginning of the study. In the resulting tables, we show the estimates of the coefficients adjusted or nonadjusted by the confounders and the 95% CIs. We also show the *P* values of the estimates in the tables, for reference. The JECS protocol was reviewed and approved by the Ministry of Environment's Institutional Review Board on Epidemiological Studies and by the ethics committees of all participating institutions. Written informed consent was obtained from all participants.

K-6 scores of 13 or more and 5 or more were seen in 3.5% and 31.9% of participants, respectively (see Table E1); IgE sensitization was found in 73.9%. The prevalence of asthma, allergic rhinitis, eczema, food allergy, and drug allergy was 10.9%, 36.1%, 15.8%, 4.8%, and 2.6%, respectively. Among the confounding factors, marital status and smoking status may have strongly affected the K-6 and SF-8 scores (PCS) (data not shown). Table I presents the associations of K-6 with allergic features. *Der p* 1 (adjusted odds ratio [aOR], 1.05; 95% CI, 1.02-1.08), animal allergen mixes (aOR, 1.05; 95% CI, 1.01-1.09), and moth (aOR, 1.05; 95% CI, 1.01-1.08) sensitizations increased the risk of any depression (K-6 scores $\geq$ 5). Allergic diseases increased the risk of any depression even more. The aOR for contact dermatitis (aOR, 1.55; 95% CI, 1.40-1.72) was the highest among all allergic diseases, including asthma (aOR, 1.28; 95% CI, 1.22-1.34), rhinitis (aOR, 1.20; 95% CI, 1.17-1.24), eczema (aOR, 1.17; 95% CI, 1.12-1.22), and food allergy (aOR, 1.33; 95% CI, 1.24-1.42). Severe depression (K-6 score $\geq$ 13) was statistically associated with allergic diseases (aOR, 1.25; 95% CI, 1.15-1.35), including asthma (aOR, 1.49; 95% CI, 1.34-1.66), rhinitis (aOR, 1.11; 95% CI, 1.02-1.20), eczema (aOR, 1.22; 95% CI, 1.10-1.35), food allergy (aOR, 1.40; 95% CI, 1.20-1.64), and contact dermatitis (aOR, 1.53; 95% CI, 1.19-1.96). For PSC and MCS scores of the SF-8, allergic diseases were negatively associated with PCS and MCS (see Table II). With regard to sensitization, only *Der p* 1 sensitization showed a

TABLE I. Univariate and multivariate logistic regression results for allergic features associated with depression (K-6) in pregnant women across Japan (n = 78,705)

		Univariate				Multivariate			
Outcome	**Allergy features**	**OR**	**Lower 95% CI**	**Upper 95% CI**	***P* value**	**aOR**	**Lower 95% CI**	**Upper 95% CI**	***P* value**
K-6 (≥13) Severe depression	None (reference)								
	log_IgE. nonspecific (continuous)	**1.03**	**1.01**	**1.06**	**.0172**	1.01	0.98	1.04	.4935
	IgE (nonspecific) ≥170 UA/mL	**1.16**	**1.06**	**1.27**	**.0015**	1.08	0.98	1.18	.1124
	IgE_sensitization to any specific allergen	0.96	0.88	1.05	.3217	0.94	0.86	1.03	.1855
	IgE_*Der p 1*	1.04	0.96	1.12	.3514	1.01	0.93	1.09	.8083
	IgE_Japanese cedar	0.93	0.86	1.01	.0892	0.90	0.83	0.98	.0134
	IgE_egg white	**1.57**	**1.14**	**2.16**	**.0059**	**1.53**	**1.11**	**2.11**	**.0010**
	IgE_animal allergen mixes	1.08	0.98	1.19	.1052	1.03	0.93	1.13	.6135
	IgE_moth	**1.11**	**1.02**	**1.21**	.0180	1.08	0.99	1.17	.1023
	Any allergic disease	**1.20**	**1.11**	**1.30**	**<.0001**	**1.25**	**1.15**	**1.35**	**<.0001**
	Asthma	**1.57**	**1.41**	**1.75**	**<.0001**	**1.49**	**1.34**	**1.66**	**<.0001**
	Allergic rhinitis	1.05	0.97	1.14	.2025	**1.11**	**1.02**	**1.20**	**.0132**
	Eczema	**1.22**	**1.11**	**1.35**	**<.0001**	**1.22**	**1.10**	**1.35**	**.0002**
	Allergic conjunctivitis	**1.18**	**1.05**	**1.34**	**.0073**	**1.26**	**1.12**	**1.43**	**.0002**
	Food allergy	**1.44**	**1.23**	**1.69**	**<.0001**	**1.40**	**1.20**	**1.64**	**<.0001**
	Drug allergy	**1.38**	**1.11**	**1.71**	**.0032**	**1.54**	**1.24**	**1.91**	**<.0001**
	Contact dermatitis	**1.35**	**1.06**	**1.73**	**.0163**	**1.53**	**1.19**	**1.96**	**.0008**
K-6 (≥5) Any depression	None (reference)								
	log_IgE. nonspecific (continuous)	**1.02**	**1.01**	**1.03**	**.0001**	1.01	1.00	1.02	.0511
	IgE (nonspecific) ≥170 UA/mL	**1.05**	**1.01**	**1.09**	**.0112**	1.05	0.98	1.05	.4299
	IgE_sensitization to any specific allergen	1.02	0.98	1.05	.2901	1.01	0.97	1.05	.6236
	IgE_*Der p 1*	**1.06**	**1.03**	**1.10**	**<.0001**	**1.05**	**1.02**	**1.08**	**.0014**
	IgE_Japanese cedar	1.00	0.97	1.04	.7775	0.98	0.95	1.02	.2798
	IgE_egg white	1.04	0.89	1.21	.6205	1.02	0.88	1.19	.7962
	IgE_animal allergen mixes	**1.08**	**1.04**	**1.12**	**.0001**	**1.05**	**1.01**	**1.09**	**.0212**
	IgE_moth	**1.06**	**1.02**	**1.09**	**.0012**	**1.05**	**1.01**	**1.08**	**.0093**
	Any allergic diseases	**1.23**	**1.19**	**1.27**	**<.0001**	**1.25**	**1.21**	**1.29**	**<.0001**
	Asthma	**1.31**	**1.25**	**1.37**	**<.0001**	**1.28**	**1.22**	**1.34**	**<.0001**
	Allergic rhinitis	**1.18**	**1.14**	**1.21**	**<.0001**	**1.20**	**1.17**	**1.24**	**<.0001**
	Eczema	**1.18**	**1.14**	**1.23**	**<.0001**	**1.17**	**1.12**	**1.22**	**<.0001**
	Allergic conjunctivitis	**1.28**	**1.22**	**1.35**	**<.0001**	**1.32**	**1.26**	**1.39**	**<.0001**
	Food allergy	**1.35**	**1.26**	**1.44**	**<.0001**	**1.33**	**1.24**	**1.42**	**<.0001**
	Drug allergy	**1.28**	**1.17**	**1.40**	**<.0001**	**1.35**	**1.23**	**1.48**	**<.0001**
	Contact dermatitis	**1.45**	**1.31**	**1.61**	**<.0001**	**1.55**	**1.40**	**1.72**	**<.0001**

Adjustors for multivariate analysis: maternal age, place of residence, marital status, having another child, history of abnormal pregnancy, current smoking status, employment status, and maternal education level. Statistically significant results shown in bold font.

significant negative association with PCS (regression coefficient of −0.145). Drug allergy and contact dermatitis were more significantly associated with MCS than were asthma and eczema (regression coefficients of −0.799, −0.933, −0.513, and −0.375, respectively).

To our knowledge, this is the first report to evaluate the associations of mental health with allergic features among Japanese pregnant women from a nationwide population-based birth cohort study. Compared with allergic sensitization, allergic diseases seemed to be related to a higher risk of depressive symptoms and deterioration in quality of life from the multiple regression analysis. A population-based study of adults in China demonstrated that IgE sensitization was not associated with depression but that depression was associated with asthma and eczema[7]; our study findings coincide with these results. The reason why more than 70% pregnant women had IgE sensitization to any allergens in our study is considered to be that allergy to Japanese cedar and/or house dust mites is very common among Japanese populations.[8]

A case series study of 695 patients with asthma, aged 20 to 44 years, from 29 medical centers in Japan reported a weak correlation between the severity of asthma and PCS of the SF-8 ($r = -0.144$; $P = .003$).[9] The data from an international survey by the World Health Organization found that diagnosed depression and 30-day anxiety were associated with adult asthma in 65% and 40% of countries, respectively.[10] Taken together, the association between asthma and depression or anxiety appears to exist at a global level. A systematic review and meta-analysis reported that IL-4, IL-6, and IL-10, produced by T_H2 cells, were significantly higher among patients