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Maternal psychological problems increased the risk of childhood atopic dermatitis

I.J. Wang,^{1,2,3*} H.J. Wen,⁴ T.L. Chiang,⁵ S.J. Lin,⁶ and Y.L. Guo^{7,8*}

¹Department of Pediatrics, Taipei Hospital, Ministry of Health and Welfare, Taipei, Taiwan;

²Institute of Environmental and Occupational Health Sciences, College of Medicine, National Yang-Ming University, Taipei, Taiwan;

³ Department of Health Risk Management, China Medical University, Taichung, Taiwan;

⁴ National Institute of Environmental Health Sciences, National Health Research Institutes, Miaoli, Taiwan

⁵ Institute of Health Policy and Management, National Taiwan University College of Public Health, Taipei, Taiwan

⁶ Department of Pediatrics, National Cheng Kung University Hospital and College of Medicine, National Cheng Kung University, Tainan, Taiwan

⁷ Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, Taipei, Taiwan

⁸Department of Environmental and Occupational Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

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*equally correspondence to this article

Running title: Psychological problems and atopic dermatitis

Correspondence: Dr. I-Jen Wang and Professor Yueliang Leon Guo

E-mail: wij636@gmail.com; leonguo@ntu.edu.tw

Abstract

Background: Little is known about the effect of postnatal maternal psychological problems on the development of childhood atopic disorders.

Objectives: To assess the association between early life maternal psychological problems and atopic dermatitis (AD) in children in a national birth cohort.

Methods: We used multistage, stratified systematic sampling to recruit 24,200 mother-newborn pairs from the Taiwan national birth registration. Maternal psychological problems and potential confounders were gathered by the standard questionnaire at 6 months old. At 3 years of age, information about the development of AD was assessed by International Study of Asthma and Allergies in Childhood (ISAAC) via home interviews. Multiple logistic regression analysis was performed to estimate the association of postnatal maternal psychological problems (postpartum depression and maternal mental health index) and AD.

Results: The prevalence of physician-diagnosed AD was 10.5%. Postpartum depression increased the risk of subsequent physician-diagnosed AD in children after adjusting for potential confounders and other maternal mental health index (aOR=1.42, 95%CI=1.21-1.66). We observed that the risk of AD associated with postpartum depression was not confounded by other social demographic factors such as maternal AD, maternal education, family income, breastfeeding, day care, and number of siblings.

Conclusions: Postpartum depression increased the risk of childhood AD even when other maternal mental health index and social demographic factors are considered. Early intervention of postpartum depression might be helpful for AD prevention.

Keywords: atopic dermatitis, mental health, postpartum depression, birth cohort, children

Introduction

It is increasingly clear that traditional environmental risk factors do not fully explain the origins of childhood asthma and atopy. Growth in chronic stress of women has paralleled the rising prevalence of asthma (1). The children of mothers who had experienced maternal stressful life events during pregnancy were at an increased risk of having wheezing, asthma, eczema and allergic rhinitis during their childhood (2). A study from Danish National Birth Cohort reported that maternal exposure to high strain and active jobs during pregnancy was associated with asthma and AD among 7-year-old children (3). However, there are no human studies to date that have investigated the association of postnatal maternal depression with subsequent AD in children.

Postpartum depression (PPD) is one of the most common complications in the postpartum period and has potentially significant negative consequences for mothers and their families (4). Estimates of prevalence range from 13% to 19%. The first six months after delivery may represent a high-risk time for depression (5). Meta-analysis evidence shows that postpartum depression has a large effect on mother–infant interactions and disrupts bonding between mother and child (6). Depressed mothers demonstrate less affection and fewer responses to infant cues. Their infants spend more time fussing and crying, and exhibit more stress behaviors compared with infants of mothers who are not depressed (7). Essex and colleagues demonstrated that elevated cortisol levels and behavioral problems were more common in children whose mothers had postpartum and later-life depression (8). In a Pakistani population, postpartum anxiety and depression was reported to have detrimental effects on the mental development of children (9). Children whose mothers had persistent depressive symptoms in the preschool period had the greatest levels of emotional and behavioral difficulties at age 5 years (10). However, whether postpartum anxiety and depression may increase the risk of allergic diseases remains unclear.

Caregiver stress has been associated with increased cord IgE levels and been shown to increase the frequency of wheeze in infants (11). In addition, parenting difficulties in the first year of life have been associated with asthma at ages 6–8 (12). Wright et al reported an increase in early childhood wheezing in association with caregiver stress in a high-risk cohort of infants (13). Caregiver stress in the first 6 months after birth was also reported to be associated with an atopic immune profile in infants predisposed to asthma: increased production of TNF- α , reduced IFN- γ production, and an increased proliferative response to Der f 1 (14). However, whether the increasing postpartum depression linked to the unfavorable trend of AD prevalence in recent decades is not clear. Moreover, data obtained from women are scanty, because psychoneuroimmunologic research has

traditionally included more men than women. Since AD is the first step of atopic march, we wanted to explore the effects of postnatal maternal psychological problems (postpartum depression and maternal mental health index) on the development of AD in their offspring based on a national birth cohort.

Methods

Study population

The Taiwan Birth Cohort Study is a national prospective longitudinal cohort study. In the study, we used a multistage stratified systematic sampling design to obtain representative samples from the Taiwan national birth registration data in 2005. We categorized a total of 369 towns in Taiwan into 12 strata according to the administrative division (four strata) and the total fertility rate (three strata). Using the principle of probability proportional to size, we randomly sampled 90 out of 369 towns in Taiwan. A total of 24,200 pairs of parents and newborns from these 90 towns were recruited. All study participants provided written informed consents. The study protocol was approved by the institutional review board from National Taiwan University and complied with the principles outlined in the Helsinki Declaration.

We conducted a home interview with the 24,200 postpartum women 6 and 36 months after their deliveries in 2005 by using a structured questionnaire as previously described (15). There were 2,952 cases of loss to follow-up because of refusal to participate, relocation, incorrect addresses, infant deaths, and others. A total of 21,248 postpartum women were interviewed on children at the age of 6 months old, and the completed interview rate was thus 87.8%. We then excluded multiple gestations (N = 561) (twins, triples, etc) and 856 cases of loss to follow-up in 36-month-old phone interview. To avoid reverse causation (maternal distress appearing after AD was diagnosed in the child), 1,357 children with AD before 6 months old were excluded. A final number of 18,024 participants (74.5%) were included in this study (Figure 1)

Exposures

The self-report questionnaire was collected 6 months after delivery to assess the psychological problems. Postpartum depression was defined through the questions “Have you ever been informed by a doctor that you have postpartum depression?” The vitality (VT) and mental health (MH) subscales of the Taiwanese version of the short-form 36 (SF-36) were measured as self-reported psychological stress. The SF-36 developed by Ware *et al.* is one of the most commonly used health-related quality of life questionnaire and has high construct validity, internal consistency and reliability (16). In the current study, the Taiwanese version of the SF-36, translated in 1996 and with good psychometric properties, reliability and validity was used (17). The 36 items tap eight subscales, including VT, MH, physical functioning, role limitations because of physical health

problems, bodily pain, general health perceptions, social functioning and role limitations because of emotional problems. The questionnaires used a six-point Likert scale (from 'never', 'seldom', 'occasionally', 'often', 'mostly', to 'regularly'). Summing the Likert-scaled items, each scale is standardized and ranges from 0 to 100, and a higher score for a subscale indicates better health.

The self-perceived VT, part of SF-36, contains questions: 'How much of the time during the last month: (1) Did you feel full of life? (2) Did you have a lot of energy? (3) Did you feel worn out? (4) Did you feel tired?' The Mental Health Index, part of SF-36, to assess self-perceived MH has been shown to have adequate psychometric properties to identify depression and psychosocial diseases (18, 19). It contains five questions: 'How much of the time during the last month have you: (1) been a very nervous person? (2) felt downhearted and blue? (3) felt calm and peaceful? (4) felt so down in the dumps that nothing could cheer you up? and (5) been a happy person?'

Outcomes

Cases of AD were defined as physician-diagnosed AD through the questions "Have you ever been informed by a doctor that your child has eczema?". Questionnaire-diagnosed AD was defined as "Has your child ever had recurrent itchy rash for at least 6 consecutive half-months periods over elbows, knees, face, wrists, neck, periauricular and eyebrow areas during his/her lifetime?" by International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (20).

Statistical Analysis

Principal component analysis was used to identify the major responses of psychological problems. For the association between maternal psychological problems and AD in 3-year-old children, odds ratios (ORs) with 95% confidence intervals (95% CIs) were calculated by logistic regression models. Analyses were performed in both univariate and multivariate models. P values for interaction between postpartum depression and other social demographic factors on AD were further calculated to see if there was any interaction effect of other social demographic factors. Variables were included in the model if they changed the univariate point estimate by at least 10%. All hypothesis testing was two-sided at the significance level of 0.05 and was performed using statistical software JMP version 5.0.1 (SAS Institute Inc., Cary, NC, U.S.A.).

Results

The prevalence of questionnaire- and physician-diagnosed AD was 959 (5.3%) and 1,339 (7.4%). There were 3,024 (16.8%) mothers with postpartum depression and 3,459 (19.2%) mothers with postnatal high maternal stress (Table 1). To further test this association, principal component analysis was applied to identify the major responses. Two factors (I and II) were found for psychosocial stress (Table 2). Factor I was strongly associated with vitality, vigour, and happiness. Factor II was positively associated with nervousness, anxiety, and tiredness.

Children with maternal AD, family history of atopy, higher maternal education, high family income, with breast feeding may increase the risk of questionnaire-diagnosed AD with adjusted OR (95% CI) of 2.47 (1.84-3.24), 1.95 (1.71-2.22), 1.67 (1.47-1.91), 1.54 (1.34-1.77), and 1.38 (1.15-1.68), and physician-diagnosis AD with adjusted OR (95% CI) of 2.31 (1.79-2.96), 2.02 (1.81-2.27), 1.91 (1.70-2.14), 1.77 (1.57-1.99), and 1.69 (1.43-2.01) (Table 3).

Independent of prenatal maternal stress, postpartum depression increased the risk of subsequent physician-diagnosed AD in children (aOR=1.42, 95%CI=1.21-1.66) (Table 4). So was children with questionnaire-diagnosed AD. Maternal stress increased the risk of subsequent physician-diagnosed AD in children. However, the association of maternal stress and AD failed to reach statistical significance after adjusting for potential confounders and postpartum depression (Table 4). Family history of atopy and maternal AD were significantly associated with postpartum depression (aOR [95% CI] =1.26 [1.14-1.40] and 1.39 [1.06-1.81]) (Table S2). We adjusted family history of atopy and found that family history of atopy did not confound our result (Table 4).

For fear of any interaction effect of other social demographic factors, p value for interaction between postpartum depression and social demographic factors on questionnaire- and physician-diagnosed AD was calculated. There was no significant interaction effect for postpartum depression and other social demographic factors, except family history of atopy (Table S1). After stratification by family history of atopy, the effect of postpartum depression on AD at age 3 still existed (aOR=1.55, 95%CI=1.25-1.91) for those without family history of atopy (Table 5).

Discussion

Associations between mothers with postpartum depression and AD among their offspring in a non-high-risk cohort have not been previously reported, and thus merit further investigation.

Independent of prenatal maternal stress, significant associations between childhood AD at age 3 and postpartum depression during the first 6 months of life were found. In addition, postnatal maternal stress may increase the risk of AD in children with a dose response relationship. This study adds important knowledge to the fact that postpartum depression has significant effects on the development of AD in their offspring.

In our study, significant associations between childhood AD at age 3 and postpartum depression during the first 6 months of life were found. Maternal stress in early life may promote an enhanced allergy-specific proliferative response in infants and maternal depression during the postnatal period may increase cortisol levels in offspring in later life (14). The increase in cortisol levels can disrupt the skin's barrier function, leaving it vulnerable to inflammatory disorders like AD (21). Another

possible mechanism for a postnatal effect is through epigenetic regulation via DNA methylation or histone deacetylation of the glucocorticoid receptor (GR) gene. Emerging evidence suggests that maternal stress could operate through direct epigenetic effects and indirect effects mediated through neuroendocrine dysregulation (13).

A cohort demonstrated an increased risk of childhood asthma among children exposed to continued maternal distress from birth until age 7. However, exposure to maternal depression and anxiety limited to the first year of life did not have a demonstrable association with subsequent asthma (22). Therefore, there exists a difference between the duration of maternal distress exposure and disease outcome. This might be because the disease features of AD is different from asthma. The development AD is usually earlier than asthma. Moreover, mothers with postpartum depression at 6 months old may have persistent maternal distress thereafter. Maternal stress can persistently affect the mother, which can alter maternal behavior after birth (23).

Early literature reported that the risk of asthma associated with continued maternal distress was increased in children living in high- versus low-income households (22). Evidence also supports an inverse relationship between AD and endotoxin, early day care, farm animal and dog exposure in early life (24). However, we observed that the risk of AD associated with postpartum depression was not confounded by other social demographic factors such as maternal AD, maternal education, family income, breastfeeding, day care, and number of siblings (Table S1). The strength of the associations after adjusting for various potential confounders support the effect of postpartum depression on subsequent AD. Therefore, we are fairly confident about our results.

A potential weakness of this study was the reliance on maternal self-report to define depression symptoms and stress severity. Also, we had no maternal biomarker data to measure the biological effect of stress. However, the scales used have been validated previously (25). There is currently no standard methods to quantify stress and it is difficult to determine differences in the resistance of the individuals to human stress. Furthermore, our study was limited by the use of questionnaire for ascertaining AD, which might not be accurate as the standard diagnostic criteria by a dermatologist. Nevertheless, maternal report of doctor-diagnosed AD with typical morphology and atopic distribution has been previously validated versus clinical examination in the studies performed in the United States and Denmark and has been used by many epidemiological studies (15, 26, 27).

The strengths of our study included the well-powered sample size and the population based prospective cohort design. Because of the large sample size, we were able to control for numerous potential confounders by the statistical analysis. It was not limited to high risk cohort but in a national representative population, which could provide the un-biased estimation. Moreover, the multistage stratified systematic sampling including urban, suburban, and rural population could enhance generality. We assess previous studies was the use of principal component analysis to identify the major responses of psychosocial stress factors. It can be used to compress the data by reducing the number of dimensions without much loss of information. The consistency across different outcome measures (questionnaire-diagnosed AD, physician-diagnosed AD) in this prospective cohort raise the possibility that this association may be causal. Therefore, we are fairly

confident about our results. In addition, this is the first contribution to the literature to link the association between postpartum depression and subsequent AD development during childhood. In addition, we focus on singleton child, which increased the validity and generality of the results and decreased misclassification and confounding from multi-afterbirth. Since the follow-up rate was high, selection bias could not be a major problem in our study. Finally, the prevalence of most variables in those lost in the follow-up and in those completed the followed-up was not significantly different from each other.

Conclusion

Postpartum depression increased the risk of AD even when other maternal mental health index and social demographic factors are considered. Early intervention of postpartum depression might be helpful for AD prevention. It is important to evaluate the psychological problems of pregnant women and provide them with possible ways of preventing and reducing stress during postnatal care. Action must also be taken by governments to integrate mental health screening into routine primary care for pregnant and postpartum women and to follow up this screening with psychotherapy and antidepressant medications.

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Conflicts of interest: None declared.

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Table 1. Characteristics of parents and children (n = 18,024)

Factors	n (%)
Sex	
Boys	9,352 (51.9)
Girls	8,672 (48.1)
Gestation length (weeks) ^a	38.5 ± 1.5
Birth weight (g) ^f	3124.0 ± 426.5
Number of siblings	
≤ 1	15,491 (85.9)
> 1	2,527 (14.0)
Delivery method	
Natural delivery	12,147 (67.4)
Caesarean section	5,868 (32.6)
Maternal age at baby birth (year) ^a	28.8 ± 4.9
Maternal education	
≤ 12 years	10,009 (55.5)
> 12 years	7,984 (44.3)
Maternal smoking	
Yes	1,150 (6.4)
No	16,855 (93.5)
Family income	
Low	7,685 (42.6)
High	10,281 (57.0)
Maternal nationality	
Taiwan	14,433 (80.1)
Foreign	3,589 (19.9)
Residential area	
Urban	10,127 (56.2)

Rural	7,897 (43.8)
Questionnaire-diagnosed AD	
Yes	959 (5.3)
No	17,065 (94.7)
Physician-diagnosed AD	
Yes	1,339 (7.4)
No	16,685 (92.6)

Some numbers do not add up to total n because of missing values.

^a mean $\pm$ SD

Table 2. Maternal mental health rotated factors of 6-month-old children by principle component analysis.

	Factor 1	Factor 2
Eigenvalue (% variance explained)	2.78 (37.0%)	1.09 (27.6%)
Self-reported vitality	0.85	-0.12
Self-reported nervousness	-0.04	0.82
Self-reported vigour	0.87	-0.14
Self-reported anxiety	-0.32	0.68
Self-reported happiness	0.73	-0.27
Self-reported tiredness	-0.31	0.64
Conceived indicators	Energy and happiness	Stress

Factors 1 and 2 account for 64.5% of variance.

Factor 1 was conceived to be energetic and happy indicator. Factor 2 was conceived to be stress indicator.

Table 3. Associations between potential risk factors and questionnaire/ physician-diagnosis AD in 3-year-old children (n = 18,024)

Factors (n)	Questionnaire-diagnosed AD		Physician-diagnosis AD	
	n (%)	OR (95%CI) ^a	n (%)	OR (95%CI) ^a
Sex				
Boys (9,352)	487 (5.2)	0.95 (0.84-1.09)	719 (7.7)	1.08 (0.97-1.21)
Girls (8,672)	472 (5.4)	Reference	620 (7.2)	Reference
Maternal AD				
Yes (492)	58 (11.8)	2.47 (1.84-3.24)***	75 (15.2)	2.31 (1.79-2.96)***
No (17,532)	901 (5.1)	Reference	1,264 (7.2)	Reference
Family history of atopy				
Yes (5,455)	430 (7.9)	1.95 (1.71-2.22)***	607 (11.1)	2.02 (1.81-2.27)***
No (12,569)	529 (4.2)	Reference	732 (5.8)	Reference
Maternal education				
> 12 years (7,984)	541 (6.8)	1.67 (1.47-1.91)***	792 (9.9)	1.91 (1.70-2.14)***
≤ 12 years (10,009)	417 (4.2)	Reference	546 (5.5)	Reference
Family income				
High (10,281)	640 (6.2)	1.54 (1.34-1.77)***	927 (9.0)	1.77 (1.57-1.99)***
Low (7,685)	317 (4.1)	Reference	408 (5.3)	Reference
Breastfeeding				
Yes (14,826)	828 (5.6)	1.38 (1.15-1.68)***	1,183 (8.0)	1.69 (1.43-2.01)***
No (3,198)	131 (4.1)	Reference	156 (4.9)	Reference
Number of siblings				

≤ 1 (15,491)	831 (5.4)	1.06 (0.88-1.29)	1,196 (7.7)	1.39 (1.17-1.67)***
> 1 (2,527)	128 (5.1)	Reference	143 (5.7)	Reference
Residential area				
Urban (10,127)	568 (5.6)	1.14 (1.00-1.30) ^b	870 (8.6)	1.49 (1.33-1.67)***
Rural (7,897)	391 (5.0)	Reference	469 (5.9)	Reference

^aOR (95% CI) = Odds Ratio (95% confident interval).

*p < 0.05, ** p < 0.01, ***
p < 0.001

^bp = 0.0512.

Some numbers do not add up to total n because of missing values.

Table 4. The effect of postpartum depression and maternal mental health on child atopic dermatitis at age 3 by multiple logistic regression analysis (n = 18,024)

Factors (n)	Questionnaire-diagnosed AD			Physician-diagnosis AD		
	n (%)	OR (95%CI) ^a	AOR (95%CI) ^b	n (%)	OR (95%CI) ^a	AOR (95%CI) ^b
Postpartum depression						
Yes (3,024)	200 (6.6)	1.33 (1.13-1.56)***	1.17 (0.97-1.41) ^c	323 (10.7)	1.65 (1.44-1.88)***	1.42 (1.21-1.66)***
No (15,000)	759 (5.1)	Reference	Reference	1,016 (6.8)	Reference	Reference
Maternal mental health index						
Factor 1 (energy and happiness)						
High (3,975)	218 (5.5)	0.88 (0.73-1.07)	0.87 (0.72-1.06)	345 (8.9)	1.11 (0.94-1.30)	1.10 (0.94-1.30)
Median (3,976)	228 (5.7)	0.93 (0.77-1.14)	0.93 (0.77-1.12)	312 (7.9)	0.99 (0.84-1.17)	1.01 (0.85-1.19)
Low (3,976)	245 (6.2)	Reference	Reference	314 (7.9)	Reference	Reference
Factor 2 (stress)						
High (3,975)	248 (6.2)	1.17 (0.97-1.41)	1.07 (0.88-1.30)	357 (9.0)	1.22 (1.04-1.43)*	1.08 (0.92-1.28)

Median (3,976)	229 (5.8)	1.07 (0.89-1.30)	1.00 (0.83-1.22)	316 (8.0)	1.07 (0.90-1.26)	0.98 (0.83-1.16)
Low (3,976)	214 (5.4)	Reference	Reference	298 (7.5)	Reference	Reference

^aOR (95%CI) = odds ratio (95% confident interval).

^b AOR (95% CI) = Adjusted OR (95% CI). AOR was adjusted by gender, birth weight, family history of atopy,maternal education, prenatal maternal stress, breastfeeding, family income, number of siblings, help for children care, residence location, postpartum depression, and maternal mental health index.

^c p = 0.0936

[#]P<0.1, *p< 0.05, ** p < 0.01, *** p< 0.001.

Some numbers do not add up to total n because of missing values.

Table 5. The effect of postpartum depression on child atopic dermatitis (AD) at age 3 across family atopy (n = 18,024)

Factors	Without family history of atopy (n = 12,569)				With family history of atopy (n = 5,455)			
	Questionnaire-diagnosed AD		Physician-diagnosis AD		Questionnaire-diagnosed AD		Physician-diagnosis AD	
	n (%)	AOR (95% CI) ^a	n (%)	AOR (95% CI) ^a	n (%)	AOR (95% CI) ^a	n (%)	AOR (95% CI) ^a
Postpartum depression								
Yes	106 (5.6)	1.31 (1.01-1.69)*	175 (9.2)	1.55 (1.25-1.91)***	94 (8.4)	1.04 (0.78-1.35)	148 (13.2)	1.26 (1.00-1.58)*
No	423 (4.0)	Reference	557 (5.2)	Reference	336 (7.8)	Reference	459 (10.6)	Reference

**Maternal mental health
index**

Factor 1 (energy and
happiness)

High (3,975)	120 (4.4)	0.86 (0.67-1.12)	191 (7.0)	1.12 (0.90-1.40)	98 (7.8)	0.88 (0.66-1.17)	154 (12.2)	1.07 (0.84-1.37)
Median (3,976)	118 (4.3)	0.86 (0.66-1.11)	167 (6.1)	0.99 (0.79-1.24)	110 (8.8)	1.02 (0.78-1.35)	145 (11.6)	1.03 (0.80-1.31)
Low (3,976)	130 (4.9)	Reference	162 (6.1)	Reference	115 (8.7)	Reference	152 (11.4)	Reference

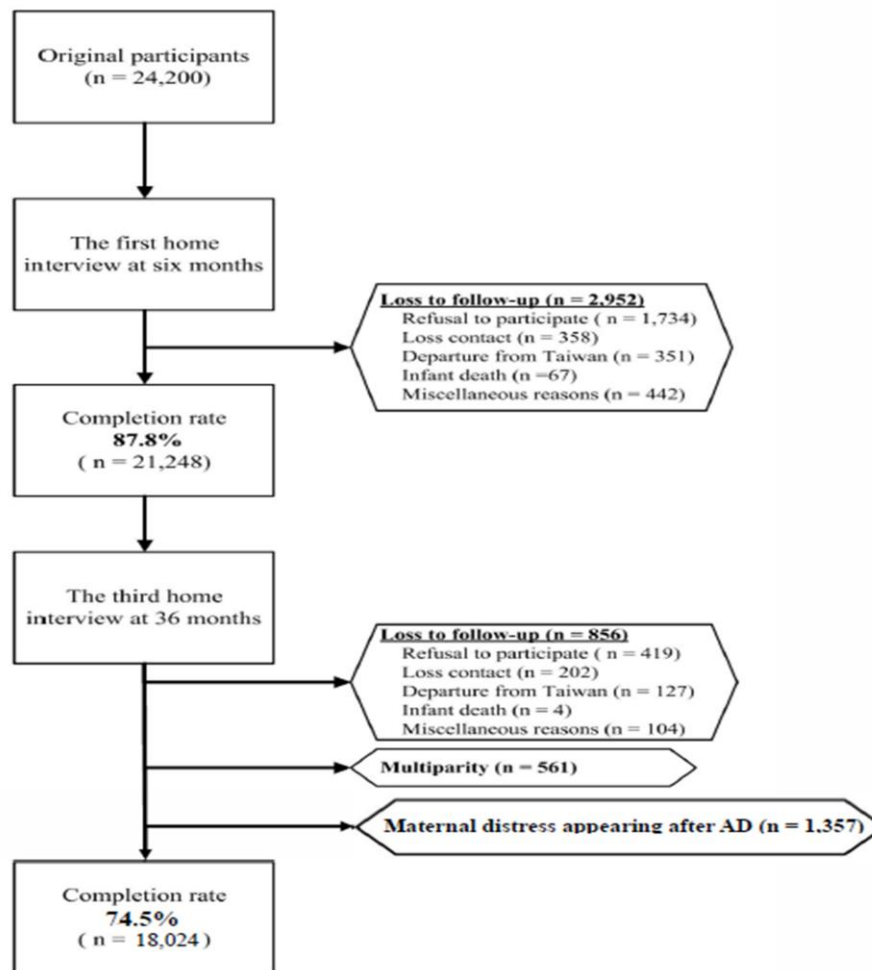
Factor 2 (stress)

High (3,975)	117 (4.6)	1.01 (0.78-1.32)	172 (6.7)	1.05 (0.83-1.31)	131 (9.2)	1.12 (0.84-1.49)	185 (13.0)	1.11 (0.87-1.42)
Median (3,976)	130 (4.8)	1.07 (0.83-1.38)	181 (6.7)	1.06 (0.85-1.32)	99 (7.7)	0.92 (0.68-1.23)	135 (10.6)	0.88 (0.68-1.14)
Low (3,976)	121 (4.3)	Reference	167 (5.9)	Reference	93 (8.2)	Reference	131 (11.5)	Reference

^a AOR (95% CI) = Adjusted OR (95% CI). AOR was adjusted by gender, birth weight, maternal education, prenatal maternal stress, breastfeeding, family income, number of siblings, help for children care, residence location, postpartum depression, and maternal mental health index.

*p< 0.05, ** p < 0.01, *** p< 0.001.

FIGURE 1. Flow chart of data collection.



Supplement

Table S1. P value for interaction effect between postpartum depression and covariables on questionnaire-/ physician-diagnosis AD in 3-year-old children (n = 18,024)

Factors	P value	
	Questionnaire-diagnosed AD	Physician-diagnosis AD
Sex	0.9238	0.2099
Birth weight	0.6413	0.4296
Maternal AD	0.51	0.4048
Family atopy	0.0960 [#]	0.0075**
Maternal AD	0.607	0.7127
Maternal RAD	0.1622	<0.0001***
Paternal AD	0.5061	0.1213
Paternal RAD	0.0158*	0.2308
Maternal education	0.132	0.0643 [#]
Family income	0.1568	0.0993 [#]
Breastfeeding	0.6806	0.6597
Help for children care	0.3268	0.8022
Number of siblings	0.9984	0.7781
Residential area	0.7488	0.4747

^a Calculated by regression model analysis in using cross multiplied variable formed by postpartum depression multiplied by each variable as shown in this Table.

[#]p<0.1, *p < 0.05, ** p < 0.01, *** p< 0.001

Table S2. Associations between postpartum depression and family atopy (n = 18,024)

Factor	n (%)	OR (95%CI) ^a	AOR (95%CI) ^b
Family atopy			
Yes (5,455)	1,123 (20.6)	1.45 (1.34-1.58)***	1.26 (1.14-1.40)***
No (12,569)	1,901 (15.1)	Reference	Reference
Maternal AD			
Yes (492)	129 (26.2)	1.80 (1.46-2.21)***	1.39 (1.06-1.81)*
No (17,532)	2,895 (16.5)	Reference	Reference

^aOR (95% CI) = Odds Ratio (95% confident interval).

^b AOR (95% CI) = Adjusted OR (95% CI). AOR was adjusted by child gender, maternal education, prenatal maternal stress, breastfeeding, family income, number of children, help for children care, residence location, working stress, and smoking.

*p < 0.05, ** p < 0.01, *** p< 0.001