Allergic disease and risk of stress in pregnant women: a PreventADALL study

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ABSTRACT

Background: Maternal stress during pregnancy may negatively affect the health of mother and child. We therefore aimed to identify the proportion of women reporting high maternal stress in mid and late pregnancy and explore whether symptoms of maternal allergic disease are associated with perceived maternal stress in late pregnancy.

Method: The population-based Preventing Atopic Dermatitis and Allergy in Children (PreventADALL) study enrolled 2697 pregnant women at their 18-week routine ultrasound examination in Norway and Sweden. Information about sociodemographic factors, symptoms and doctor-diagnosed asthma, allergic rhinitis, atopic dermatitis, food allergy, and anaphylaxis and stress using the 14-item perceived stress scale (PSS) was collected at 18 weeks (mid) and 34 weeks (late) pregnancy. High stress was defined as a PSS score $\geqslant 29$. Scores were analysed using multivariate logistic and linear regression.

Results: Among the 2164 women with complete PSS data, 17% reported asthma, 20% atopic dermatitis, 23% allergic rhinitis, 12% food allergy and 2% anaphylaxis. The proportion of women reporting high stress decreased from 15% at mid to 13% at late pregnancy ($p<0.01$). The adjusted odds ratio for high stress in late pregnancy was 2.25 (95% CI 1.41–3.58) for self-reported symptoms of asthma, 1.46 (95% CI 1.02–2.10) for allergic rhinitis and 2.25 (95% CI 1.32–3.82) for food allergy. A multivariate linear regression model confirmed that symptoms of asthma (β coefficient 2.11; 0.71–3.51), atopic dermatitis (β coefficient 1.76; 0.62–2.89) and food allergy (β coefficient 2.24; 0.63–3.84) were independently associated with increased PSS score.

Conclusion: Allergic disease symptoms in pregnancy were associated with increased stress, highlighting the importance of optimal disease control in pregnancy.

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In this population-based study, high stress was reported by 15% in mid-pregnancy and in 13% at late pregnancy. High stress in late pregnancy was associated with symptoms of asthma, allergic rhinitis and food allergy. https://bit.ly/3faKmwh

Introduction

In maternal healthcare, risk assessments are performed during pregnancy to detect factors that may negatively impact both maternal and fetal health [1]. Stress can be defined as an individual, nonspecific response of the body to various demands of the inner and outer environment [2]. Stress has been suggested to be the first step to depressive and anxiety-like symptoms [3], and the prevalence seems to be similar in pregnant and non-pregnant women [4]. However, whereas depression and anxiety can be identified using established diagnostic tools, similar assessments are lacking for stress. Cohen's perceived stress scale (PSS) is a validated method to capture maternal stress [5, 6], and cut-off for high stress levels has been used to define groups of individuals perceiving higher stress [7].

Pregnant women's perceptions of stress may be heterogeneous with respect to geographical differences and sociodemographic factors [8], and can be associated with previous and current health status [9, 10]. However, the relationship between high perceived stress, life events and chronic disease in pregnancy are to date not fully understood. Identifying prenatal risk factors and managing stress in pregnancy may reduce adverse health effects in both mother and offspring [11, 12].

Worldwide, asthma is among the most common chronic diseases in pregnant women [13]. The course of asthma in pregnancy is unpredictable and appears to fluctuate in the majority of women [14]. Atopic dermatitis is the most common skin disorder in pregnant women, and symptoms may worsen in pregnancy [15]. The links between stress and symptoms of allergic diseases like asthma, atopic dermatitis, allergic rhinitis and food allergy during pregnancy are not established. We hypothesised that symptoms of allergic diseases would increase levels of perceived maternal stress during pregnancy. The aims of this study were to estimate the prevalence of women reporting high maternal stress in mid and late pregnancy and explore whether symptoms of maternal allergic disease are associated with high perceived maternal stress in late pregnancy.

Methods

Study design and recruitment

The present study is part of the Preventing Atopic Dermatitis and Allergy in Children (PreventADALL) study. PreventADALL is a Nordic multicentre, 2×2 factorial, interventional birth cohort study with two objectives: to investigate the effect of primary prevention of allergic diseases by early skin care and early complementary food introduction, as described in detail elsewhere [16]; and secondly to explore early life factors associated with non-communicable disease development. Pregnant women were enrolled in connection with the 18-week routine ultrasound scanning from December 2014–October 2016, at Oslo University Hospital and Østfold Hospital Trust in Norway and at Karolinska University Hospital and collaborating obstetrical units in Stockholm, Sweden. Women with singleton or twin pregnancies and sufficient language skills (Norwegian or Swedish) were invited to participate. Women were excluded if they were planning to move far from any of the study sites shortly after inclusion or if they had severe fetal or maternal disease.

Their newborn infants included at birth [16] are not part of the present study. The women provided informed written consent prior to enrolment. Ethical approval was granted by the regional ethics committees in Norway (2014/518) and Sweden (2014/2242-31/4). Clinical Trial Registration: ClinicalTrials.gov number: NCT02449850.

Subjects

A total of 2697 pregnant women were enrolled constituting 2701 pregnancies, with four women participating with two different pregnancies. The present study included all 2164 women who completed information on PSS in mid (18th week of gestation) and late (34th week of gestation) pregnancy (figure S1).

Data collection

The inclusion visit conducted at enrolment between 16 and 22 pregnancy weeks involved a short interview about current and previous pregnancies as well as measurements of height, weight and blood pressure.

Two electronic questionnaires were sent by e-mail, the first in mid-pregnancy, shortly after study inclusion, and the second in late pregnancy. The first questionnaire collected background information on women's socio-demographics, previous and current health status and maternal stress. Further, histories of doctor-diagnosed asthma, atopic dermatitis, allergic rhinitis and food allergy were collected. In late pregnancy a second questionnaire was sent to capture information about the father and changes from mid-pregnancy corresponding to socio-demographics, women's stress, medical history of allergic disease and symptoms. The majority of questions had been used in other birth cohort studies [17]. Maternal stress was assessed with Cohen's PSS (14 items) scored from 0 to 4 for each item with a total maximum score of 56,

as previously reported in pregnant women [18]. Higher score corresponds to higher perceived stress, as it measures how often in the past month the woman felt their life was "unpredictable, uncontrollable or overloaded" [5]. The completed questionnaires were submitted electronically and data stored at University of Oslo, University Centre for Information Technology (USIT).

Definitions and outcomes
Socio-demographics
An annual family income of 600 000 Norwegian or Swedish kroner (NOK/SEK) or less was categorised as a low income. High school as the highest achieved education was defined as low education. Unemployment was defined as being a student, on parental leave, having an internship or being unemployed. Single marital status was defined as living alone, being widowed or separated from partner. Women reporting previous pregnancy had been pregnant at least once before but had not necessarily given birth.

Maternal health
The presence of allergic disease was defined as self-reported doctor-diagnosed asthma, allergic rhinitis, atopic dermatitis and food allergy at mid and late pregnancy. Reported symptoms of and treatment for allergic disease were restricted to women who had reported doctor diagnosis for each relevant disease at mid and late pregnancy. Treatment of asthma was categorised by any use of inhaled corticosteroids (ICS), for atopic dermatitis by use of skin emollients and topical treatment with tacrolimus monohydrate, pimecrolimus and corticosteroids, and for allergic rhinitis by any use of nasal antihistamine or steroids for at least the last 2 weeks. Use of analgesics corresponded to any use of paracetamol, nonsteroidal anti-inflammatory drug or acetylsalicylic acid between mid- and late-pregnancy questionnaires.

Stress
High perceived stress was defined by a PSS score of 29/56 or more, equal to 1 SD of sample mean in the PreventADALL study.

Statistical analysis
All analyses were performed using SPSS statistics version 25 (IBM, Chicago, IL, USA). Continuous variables were presented as mean and SD, categorical variables as number and percentages (%) and recoded into binary variables when necessary. Differences between categorical variables were analysed using Chi-squared or univariate regression analysis and presented with a p-value or odds ratio with 95% confidence intervals. Statistically significant factors in univariate analysis were included in multivariate regression Models I and II, respectively. Multivariate binary regressions with adjusted odds ratio were used to compare symptoms of allergic disease between women with high stress and the reference group of women with low stress at mid and late pregnancy. Univariate and multivariate linear regression analyses were used to further study associations identified in binary regression analyses. The results of linear regression are presented as unstandardisedβ coefficient with 95% confidence intervals and p-values. The association of stress and diagnosis of allergic disease with or without symptoms was assessed in a subgroup analysis. All analyses for statistical significance were at the 5% significance level.

Results
The characteristics of the 2164 women at inclusion are presented in table 1. The mean age was 32 years, the majority were employed (91%) and 55% had undergone a previous pregnancy.

Doctor-diagnosed asthma ever in life was self-reported in mid pregnancy by 365 women (17%) 63 of whom reported use of ICS, one had used oral corticosteroids for asthma in the last 2 weeks and none reported use of biologics, including anti-IgE. Atopic dermatitis was reported by 20%, allergic rhinitis by 23% and food allergy by 14% of the women. For food allergy, most reported reactions to nuts other than peanut (6.7%) followed by fruits and vegetables (5.5%), while 3% reported having an anaphylactic reaction to any allergen some time in their life.

The mean (SD) PSS score was 21.1 (7.2) in mid pregnancy and 20.3 (7.3) in late pregnancy. The proportion of women with high stress according to definition decreased from 15% to 13% between mid and late pregnancy (p<0.01), while 7% had high stress at both time points and 20% at any time point.

Univariate analysis of maternal factors associated with high stress in mid and late pregnancy are presented in table 2. High stress at any time point was significantly associated with low income, with an OR 1.92 (95% CI 1.40–2.64) in late pregnancy and with at least one previous pregnancy with an OR 1.64 (95% CI 1.27–2.12). Possible risk factors for onset of high stress after mid-pregnancy were doctor's diagnosis of allergic rhinitis (OR 1.54, 95% CI 1.14–2.07), use of analgesics (OR 1.57, 95% CI 1.22–2.01), moving to a

TABLE 1 Background characteristics of enrolled pregnant women with self-reported low and high stress

	Total	Low PSS (<29) mid pregnancy	High PSS (⩾29) mid pregnancy	p-value
Subjects n	2164	1836	328	
Age years	32.4±4.1	32.5±4.1	32.0±4.3	0.05
Nordic country of birth	1954 (90)	1664 (91)	290 (88)	
Other country of birth	210 (9.7)	172 (9.4)	38 (12)	0.21
Lower academic education[+]	223 (10)	181 (9.9)	42 (13)	0.11
High income ⩾600 001 kroner[+]	1836 (86)	1580 (87)	256 (80)	<0.01
Employed[+]	1934 (91)	1649 (91)	285 (89)	
Unemployed[#]	192 (9.0)	156 (8.6)	36 (11)	0.14
Married or cohabitant	2104 (97)	1789 (97)	315 (96)	
Single marital status	60 (2.8)	47 (2.6)	13 (4.0)	0.15
Previously pregnant[¶]	1187 (55)	990 (54)	197 (60)	0.04
Previous early miscarriages[+]	540 (25)	466 (26)	74 (23)	0.26
Assisted conception[+]	172 (8.0)	151 (8.3)	21 (6.4)	0.25
Self-reported doctor's diagnosis, ever				
Asthma	375 (17)	307 (17)	68 (21)	0.08
ICS intake in the last 2 weeks	63 (2.9)	50 (2.7)	13 (4.0)	0.95
Atopic dermatitis	426 (20)	365 (20)	61 (19)	0.59
Atopic dermatitis treatment in last 2 weeks	80 (29.4)	68 (3.7)	12 (3.7)	0.77
Allergic rhinitis[+]	440 (23)	370 (22)	70 (25)	0.34
Nasal spray in last 2 weeks	20 (7.8)	14 (0.8)	6 (1.9)	0.06
Food allergy[+]	281 (14)	243 (14)	38 (13)	0.52
Anaphylaxis	70 (3.4)	59 (3.4)	11 (3.6)	0.85
Peanuts	74 (3.7)	68 (4.0)	6 (2.0)	0.1
Other nuts	133 (6.7)	113 (6.7)	20 (6.8)	0.93
Milk	63 (3.2)	57 (3.4)	6 (2.0)	0.23
Egg	23 (1.2)	21 (1.2)	2 (0.7)	0.41
Wheat	35 (1.8)	32 (1.9)	3 (1.0)	0.30
Fruits/vegetables	109 (5.5)	92 (5.4)	17 (5.8)	0.80
Fish	18 (0.9)	13 (0.8)	5 (1.7)	0.12
Other	81 (4.1)	67 (4.0)	14 (4.8)	0.52
Report of medication in the last 2 weeks				
ICS	109 (5.0)	90		
Atopic dermatitis treatment	119 (5.5)			
Nasal spray	169 (7.8)			
Any tobacco use up until inclusion	9 (0.4)	5 (0.3)	4 (1.2)	0.01
Any alcohol use up until inclusion	50 (2.3)	39 (2.1)	11 (3.4)	0.17
PSS late pregnancy				
Low stress <29	1877 (87)	1694 (92)	183 (56)	
High stress ⩾29	287 (13)	142 (7.7)	145 (44)	<0.01
PSS mid pregnancy	21.05±7.2	18.94±5.5	32.89±3.7	
PSS late pregnancy	20.26±7.3	18.94±6.6	27.61±6.4	

Data are presented as mean±SD or n (%), unless otherwise stated. p-values for high *versus* low stress. PSS: perceived stress scale; ICS: inhaled corticosteroids. [#]: student, internship, housewife or unemployed; [¶]: previously pregnant was defined as been pregnant once or more before current pregnancy; [+]: due to missing data, sample numbers are not identical between groups: education n=2158, income n=2130, employment n=2127, miscarriages n=2154, assisted conception n=2154, allergic rhinitis n=1953, food allergy n=1990.

new residence (OR 1.72, 95% CI 1.20–2.45), changes in employment (OR 1.75, 95% CI 1.08–2.85), high school only (OR 1.9, 95% CI 1.34–2.69) and unemployment (OR 2.10, 95% CI 1.46–3.02).

Symptoms from mid to late pregnancy was reported by 108 women with asthma, 170 with atopic dermatitis, 244 with allergic rhinitis and 82 with food allergy. Five women reported incident asthma symptoms in late pregnancy, *i.e.* without previous diagnosis or symptoms reported at mid pregnancy, while 11 reported first-time atopic dermatitis symptoms and eight women first-time allergic rhinitis symptoms. In late pregnancy, 48 of 108 women had used ICS. The use of ICS in the last 2 weeks was significantly associated with high stress in late pregnancy but not in mid pregnancy, in univariate analyses (table 2). Reporting symptoms of both asthma and allergic rhinitis, as well as of both asthma and food allergy, were significantly associated with high stress (Models: I and II, table 3). Further, symptoms of asthma as well as food allergy after mid trimester were significantly associated with high stress in late pregnancy as shown in table 3. Model

TABLE 2 Univariate analysis of factors associated with women perceiving high stress compared to low stress at study inclusion and late pregnancy[#]

	High PSS (⩾29) mid-pregnancy[¶]			High PSS (⩾29) late pregnancy[+]		
	n (%)	OR	95% CI	n (%)	OR	95% CI
Other country of birth	38 (12)	1.27	(0.87–1.84)	31 (11)	1.15	(0.77–1.72)
High school only	42 (13)	1.34	(0.94–1.92)	47 (16)	1.90	(1.34–2.69)
Low income	65 (20)	1.76	(1.30–2.39)	61 (22)	1.92	(1.40–2.64)
Unemployed [§]	36 (11)	1.34	(0.91–1.96)	44 (16)	2.10	(1.46–3.02)
Single marital status	13 (4.0)	1.57	(0.84–2.94)	14 (4.9)	2.04	(1.11–3.77)
Previously pregnant [f]	197 (60)	1.29	(1.01–1.63)	187 (65)	1.64	(1.27–2.12)
Early miscarriages	77 (23)	1.12	(0.84–1.48)	77 (27)	1.12	(0.84–1.48)
Late miscarriages	10 (3.0)	1.61	(0.79–3.28)	10 (3.5)	1.90	(0.93–3.87)
Assisted conception	21 (6.4)	0.78	(0.52–1.19)	19 (6.6)	0.78	(0.49–1.31)
Self-reported doctor's diagnosis ever						
Asthma	68 (21)	1.30	(0.97–1.75)	60 (21)	1.31	(0.96–1.79)
ICS last two weeks	13 (4.0)	1.47	(0.79–2.75)	17 (6.0)	3.08	(1.77–5.34)
Atopic dermatitis	61 (19)	0.92	(0.68–1.25)	58 (20)	1.04	(0.76–1.42)
AD treatment last 2 weeks	12 (4.0)	0.99	(0.53–1.85)	5 (2.0)	1.13	(0.43–2.94)
Allergic rhinitis	70 (25)	1.16	(0.86–1.55)	73 (30)	1.54	(1.14–2.07)
Nasal spray last 2 weeks	6 (2.0)	1.87	(0.66–5.29)	6 (2.0)	2.01	(0.86–4.73)
Food allergy	38 (13)	0.89	(0.62–1.28)	39 (15)	1.09	(0.75–1.57)
Events in pregnancy						
Use of analgesic				152 (54)	1.57	(1.22–2.01)
Moved to new residence				44 (16)	1.72	(1.20–2.45)
Changes in employment				22 (7.7)	1.75	(1.08–2.85)

PSS: perceived stress scale; ICS: inhaled corticosteroids. [#]: n=2164; [¶]: n=328; [+]: n=287; [§]: student, internship, housewife or unemployed; [f]: previously pregnant was defined as been pregnant once or more before current pregnancy.

I adjusted for factors at inclusion of lower income and previous pregnancy and Model II for factors at late pregnancy of moving to new residence, changes in employment and use of analgesics.

Using PSS score as a continuous variable, high stress was associated with symptoms of asthma, atopic dermatitis and food allergy in model I (adjusted for factors at inclusion). In Model II (adjusting for factors at late pregnancy), the PSS score was significantly associated with symptoms of asthma, atopic dermatitis and food allergy on their own, but only with the symptoms of atopic dermatitis when combined with asthma (table 4).

The risk of high stress increased among women with doctor-diagnosed asthma who had asthma symptoms compared to no symptoms in pregnancy (OR 2.97, 95% CI 1.30–6.74) (table 5). Neither symptoms nor doctor diagnosis of atopic dermatitis and allergic rhinitis, nor food allergy were significantly associated with high stress compared to women with no symptoms and relevant allergic disease.

Discussion

In this population-based study including pregnant women, high stress was reported by 15% in mid pregnancy, in 13% in late pregnancy and in 7% in both mid and late pregnancy. High stress in late pregnancy was associated with symptoms of asthma, atopic dermatitis, allergic rhinitis and food allergy.

The finding that 15% reported high perceived stress in mid pregnancy and 13% in late pregnancy is, to our knowledge, the first report from a large population-based study using the validated Cohen's PSS in pregnant women within the Nordic countries. Our findings are in line with high perceived stress in 17% of pregnant women in Canada [19], but lower than the median PSS-10 score of 26/40 in the Swedish Born into Life study including 92 pregnant at gestational age 26–28 weeks [20] and high stress in 33% of pregnant women in Saudi Arabia [21]. The operational cut-off value for high stress in our study has been used elsewhere [22, 23]. We found that low education, low income and unemployed status increased the risk of high stress in late pregnancy (suggesting that a poor financial situation during pregnancy is a stressor [24]), as did moving to a new residence and changes in employment. Further, use of analgesics increased the risk of incident high stress, suggesting that pain rather than use of analgesics may be the stressor. Although maternal smoking and alcohol use have been associated with increased stress [21, 25, 26], in our study very few individuals reported such exposure.

TABLE 3 The associations between allergic disease with symptoms and high stress (n=287) in late pregnancy are shown as crude odds ratios, as well as adjusted odds ratios compared to low stress (n=1877)[#]

	Subjects n	High PSS (⩾29) late pregnancy		Model I high PSS (⩾29) late pregnancy		Model II high PSS (⩾29) late pregnancy	
		crude OR	95% CI	aOR[¶]	95% CI	aOR[+]	95% CI
Asthma with symptoms	26	2.18	1.38–3.46	2.25	1.41–3.58	2.07	1.29–3.30
Atopic dermatitis with symptoms	30	1.45	0.96–2.19	1.49	0.98–2.27	1.42	0.93–2.15
Allergic rhinitis with symptoms	42	1.43	1.00–2.05	1.46	1.02–2.10	1.42	0.98–2.03
Food allergy with symptoms	20	2.19	1.30–3.69	2.25	1.32–3.82	2.06	1.22–3.49
Symptoms of asthma and atopic dermatitis	30	1.45	0.96–2.20	1.49	0.98–2.27	1.41	0.93–2.15
Symptoms of asthma and allergic rhinitis	42	1.48	1.03–2.12	1.52	1.06–2.19	1.47	1.02–2.11
Symptoms of asthma and food allergy	16	1.96	1.11–3.46	2.05	1.14–3.66	1.85	1.04–3.30

PSS: perceived stress scale. [#]: n=2164; [¶]: adjusted for factors at inclusion: low income, previously pregnant; [+]: adjusted for factors at late pregnancy: moved to new residence, changes in employment and use of analgesics.

Our results indicate that having asthma symptoms between mid and late pregnancy increased the risk of high stress in the general population and among symptomatic *versus* asymptomatic women with doctor-diagnosed asthma. The association of stress with symptoms of asthma remains insufficiently understood. Environmental stressors may act on a pathway of endogenous mechanisms *via* the release glucocorticoids and pro-inflammatory cytokines [27], thereby potentially promoting symptoms of underlying allergic disease. Among our participating women with asthma symptoms from mid to late pregnancy, five women reported first-time symptoms and only 48 out of 108 (44%) women used ICS by late pregnancy. Although we are unaware of the exact prescribed doses before and during pregnancy, our results indicate that pregnant women with asthma may be undertreated. Pregnant women with poor asthma control in pregnancy risk adverse outcomes in both themselves and their fetuses [28]. Guidelines highlight continued medication and symptom control in pregnancy. This is considered to be both

TABLE 4 Simple and adjusted linear regression of stress and symptoms of allergic disease in late pregnancy with unstandardised β coefficient[#]

	Simple linear PSS late pregnancy			Model I adjusted linear PSS[¶] late pregnancy			Model II adjusted linear PSS[+] late pregnancy		
	β coeff	95% CI	p-value	β coeff	95% CI	p-value	β coeff[¶]	95% CI	p-value
Asthma with symptoms, n=26	1.97	0.57–3.38	0.006	2.11	0.71–3.51	0.003	1.68	0.27–3.09	0.02
Atopic dermatitis with symptoms, n=30	1.62	0.48–2.76	0.005	1.76	0.62–2.89	0.002	1.51	0.38–2.65	0.009
Allergic rhinitis with symptoms, n=42	0.84	−0.13–1.81	0.090	0.95	−0.02–1.92	0.054	0.73	−0.24–1.69	0.14
Food allergy with symptoms, n=20	2.03	0.43–3.64	0.013	2.24	0.63–3.84	0.006	1.82	0.22–3.41	0.03
Symptoms of asthma and atopic dermatitis, n=30	1.62	0.48–2.76	0.005	1.76	0.62–2.89	0.002	1.51	0.38–2.65	0.009
Symptoms of asthma and allergic rhinitis, n=42	0.79	−0.19–1.78	0.11	0.93	−0.05–1.91	0.06	0.69	−0.30–1.66	0.17
Symptoms of asthma and food allergy, n=16	1.61	−0.11–3.34	0.07	1.90	0.17–3.62	0.03	1.44	−0.28–3.15	0.10

PSS: perceived stress scale. [#]: n=2164; [¶]: adjusted for factors at inclusion: income, previously pregnant; [+]: adjusted for factors at late pregnancy: moved to new residence, changes in employment and use of analgesics.

TABLE 5 Crude odds ratio for high stress in late pregnancy comparing pregnant women with symptoms of allergic disease with those reporting doctor-diagnosed allergic disease without symptoms

	Low PSS (<29) late pregnancy	High PSS (⩾29) late pregnancy	OR (95% CI)
Asthma without symptoms	78 (51)	9 (26)	
Asthma with symptoms	76 (49)	26 (74)	2.97 (1.30–6.74)
Atopic dermatitis without symptoms	43 (23)	9 (24)	
Atopic dermatitis with symptoms	145 (77)	29 (76)	0.96 (0.42–2.17)
Allergic rhinitis without symptoms	35 (19)	11 (26)	
Allergic rhinitis with symptoms	148 (81)	32 (74)	0.69 (0.32–1.50)
Food allergy without symptoms	59 (50)	7 (29)	
Food allergy with symptoms	58 (50)	17 (71)	2.47 (0.95–6.40)

Data are presented as n (%), unless otherwise stated. PSS: perceived stress scale. Allergic disease with symptoms was self-reported at the 34 weeks questionnaire, requiring both self-reported doctors' diagnosis and symptoms after enrolment (mid pregnancy) of each relevant disease.

important and safe [29, 30], even if poor adherence and changes in medical prescriptions during pregnancy occur [31]. A French study investigating asthma medication in pregnancy showed a decrease in fixed combination drugs and an increase in use of ICS [31].

To our knowledge, the association between symptoms of atopic dermatitis and food allergy and high stress in late pregnancy are novel findings. Our finding that high stress was significantly associated with atopic dermatitis is supported by an observational study emphasising that ~52% of women may report worsening atopic dermatitis symptoms during pregnancy [32]. Likewise, our finding that symptomatic food allergy was associated with high stress in pregnant women is supported by the reported reduced quality of life in patients with food allergy [33]. During pregnancy, women are often advised to eat a healthy diet [34], but specific individual support on food allergy and diets can be hard to provide [35, 36]. Food allergies may further restrict the diet and possibly explain our findings of high stress in late pregnancy in these women. Collectively, our findings suggest that symptoms of asthma and other allergic diseases, rather than the diagnosis *per se*, increase the risk of high stress and point to the importance of optimal disease management throughout pregnancy [29].

In PreventADALL, we found several socioeconomic factors associated with high perceived stress in late pregnancy that were not present in mid pregnancy. These included lower educational attainment level, lower income and unemployment. Our findings are in line with previous studies, suggesting that a poor financial situation during pregnancy is a stressor [24]. One theory gaining attention is the theory of allostatic load or the cumulative psychological and physiological impact of stress over a life course [37]. This theory provides a biological mechanism linking psychological stress with promotion of immune dysregulation. Further, greater and more extended inflammatory responses to acute stress have been reported among groups with lower socioeconomic status [38], which can link to our study results and explain the association between troublesome asthma/allergy and stress.

A strength of the present study is a relatively large study population recruited from the general population and the prospective design where women reported perceived stress and detailed information about previous and current health twice during their pregnancy. We also applied a previously used definition of perceived stress to define high stress in the pregnant women [13, 29], together with linear analysis of the PSS variable. High perceived stress is likely to be associated with symptoms of allergic disease in similar populations. However, PSS is a validated measurement but not a diagnostic instrument [27], so the generalizability of our results should be done with caution. The following limitations should be noted. The proportion of participants with a history of allergic diseases indicates some bias towards allergy in our population. Limited information about symptoms or asthma control score makes it difficult to assess the severity of the allergic response to stress. Pregnancy complications have been suggested to elevate stress in pregnancy [39]. In our study, pregnancy complications both in mid and late pregnancy were not included in the analysis since self-reported complications were low, and these need to be further investigated based on complementary information from medical records.

Implications of our findings suggest that high perceived stress is common, and several modifiable factors associated with high stress should be addressed during pregnancy. Stress-reducing strategies appear relevant for maternal healthcare programmes.

Conclusion

Perceived high stress was reported by 15% in mid pregnancy and 13% in late pregnancy, and was associated with lower socioeconomic status and previous pregnancies. In late pregnancy, symptomatic doctor-diagnosed asthma, allergic rhinitis and food allergy were independently and in combination associated with high stress. Our findings highlight the importance of identifying stress in pregnant women and employing strategies for stress reduction and controlling allergic symptoms in maternal healthcare.

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