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Mothers' Dietary Patterns during Pregnancy and Risk of Asthma Symptoms in Children at 3 Years

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Abstract

There is increasing evidence that dietary factors in early life play a role in the aetiology of childhood asthma. Our objective in this analysis was to assess whether maternal dietary patterns during pregnancy, as measured by a validated food frequency questionnaire, influenced general practitioner diagnosis of asthma by the age of 3 years in the Life-ways cohort of children. General Practice follow-up records were available for 631 of 1001 singleton children, twins having been excluded (63% follow-up rate). Overall 10.4% of children had diagnosed asthma, a prevalence rate comparable with other studies. In logistic regression models, based on quartiles of intake, which adjusted for maternal lifestyle and socio-economic circumstances, relatively higher maternal fruit and vegetable intake and oily fish consumption were associated with lower risk of children developing asthma, whilst those with relatively higher spreadable fat intake had a higher risk of asthma. These findings warrant further investigation as they imply an important role for maternal diet in childhood asthma, though the confounding effect of other social and lifestyle factors should be assessed as the children get older.

Introduction

Diagnosed rates of Asthma are increasing in Western populations, though the reason is unclear. It is possible that some of this is explicable by higher levels of ascertainment, in that more children are presenting for investigation than previously. However there may be a true underlying increase in propensity and incidence. Several candidate environmental allergens have been proposed besides the traditional sources such as house dust mites and domestic pets¹ and food sources in particular have received attention. It has been hypothesized in an expanding scientific literature that increasing rates of asthma are due to significant dietary shifts at population level. People arguably consume fewer vegetables and oily fish and more plant-based fats than previously and it has been suggested that antioxidants found in fruit and vegetables might have a protective effect.

The role of the mother's diet during pregnancy has been a focus of considerable recent attention, in line with the evidence of the developmental origins of disease²⁻¹⁰. This may be supported by the fact that the majority (70%) of asthma cases occur before 3 years of age³. Specific foods, nutrients and micronutrients have been investigated. Omega-3 fats found in sources such as oily fish have been proposed as protective, while the opposite is true of omega-6 fats found in plant-based oils^{2,4,5,6}. Anti-oxidant, vitamin and trace metal intakes during pregnancy have also been implicated^{7,8}. In addition, there is evidence that parity has an effect on the risk of asthma as cord blood immunoglobulin E concentration is significantly

decreased as birth order increases¹⁰. More research is required, both from a mechanistic perspective on allergenic pathways mediated at cellular or micro-nutrient level as well as demonstrable clinical or epidemiological information that links a firm diagnosis of asthma with food and nutrient consumption patterns.

The aims of the Life-ways Cross-Generation Cohort Study have been described previously. Our objective in this analysis was to identify factors associated with asthma in the Life-ways Cohort children followed up from birth through general practice records, and specifically to assess the influence of aspects of the mothers' diets during pregnancy, controlling for socio-demographic, lifestyle and environmental factors.

Methods

Data

All general practitioners were contacted, with prior consent of the mother, during summer 2005, when the children were on average three years old, and asked to review their clinical records for the proband child. The outcome measure for this analysis was a record of diagnosed asthma in the GP notes for each child by age three. The data available are summarised in Figure 1, which shows the explanatory variables considered as potentially associated with asthma. At baseline, there were hospital records for the mothers and babies, and the mothers were asked to complete a questionnaire on health, lifestyle and nutrition during pregnancy.

The self-administered questionnaire included a semi-quantitative food frequency questionnaire (SQFFQ). This was adapted for the Survey of Lifestyle, Attitudes and Nutrition (SLAN) from the SQFFQ used in the UK arm of the European Prospective Investigation of Cancer (EPIC) study. The EPIC SQFFQ has been validated in several populations. The Irish version was developed for SLAN and was validated at NUI Galway using 7-day weighed inventory and face validity by socio-economic group^{11,12}. The food frequency part of the questionnaire was designed to cover the whole of the Irish diet and included 149 food items, arranged by food group. Each food item was assigned a standard portion size. Mothers were asked to indicate their average use of each food item during pregnancy.

We estimated the average number of servings per day of fruit and vegetables for each mother based on number of servings consumed per day over a notionally recorded week. Data were categorized into quartiles of fruit and vegetable consumption for this analysis. We also estimated the average number of servings per week of oily fish, and the average number of servings per day of added or spreadable fats. Added or spreadable fats considered included butter, margarine and other spreads, salad dressings and mayonnaise. We focused for this analysis only on pure fat products, rather than considering total fat intake based on foods that have partial or hidden fats. Constituent foods included in each group are shown in Table 1.

Statistical Methods

Mantel-Haenszel tests were used to assess the univariate associations between quartiles of added fat and of fruit and vegetable intake and categorical covariates, and linear regression

Table 1 Constituents of food groups considered	
Group	Individual Foods
Fruit	Apples, Pears, Oranges satsumas & mandarins, Grapefruit, Bananas, Grapes, Melon, Peaches plums & apricots, Strawberries raspberries & kiwi fruit.
Vegetables	Carrots, Spinach, Broccoli spring greens & kale, Brussels sprouts, Cabbage, Peas, Green beans & runner beans, Marrow & courgettes, Cauliflower, Parsnips & turnips, Leeks, Onions, Garlic, Mushrooms, Sweet peppers, Bean sprouts, Green salad & lettuce, Cucumber & celery, Watercress, Tomatoes, Sweetcorn, Beetroot, Coleslaw, Avocado.
Oily fish	Oily fish, fresh or canned, eg mackerel, kippers, tuna, salmon, sardines, herring.

using median values for each quartile was used to assess the associations with continuous covariates.

To examine the relationships between maternal dietary factors and asthma in children at age three we used multivariate logistic models. These were stratified by hospital of birth. To assess the effect of potentially confounding covariates we examined the association of dietary factors with asthma before and after including the covariates in the model. These were maternal age, maternal BMI, maternal

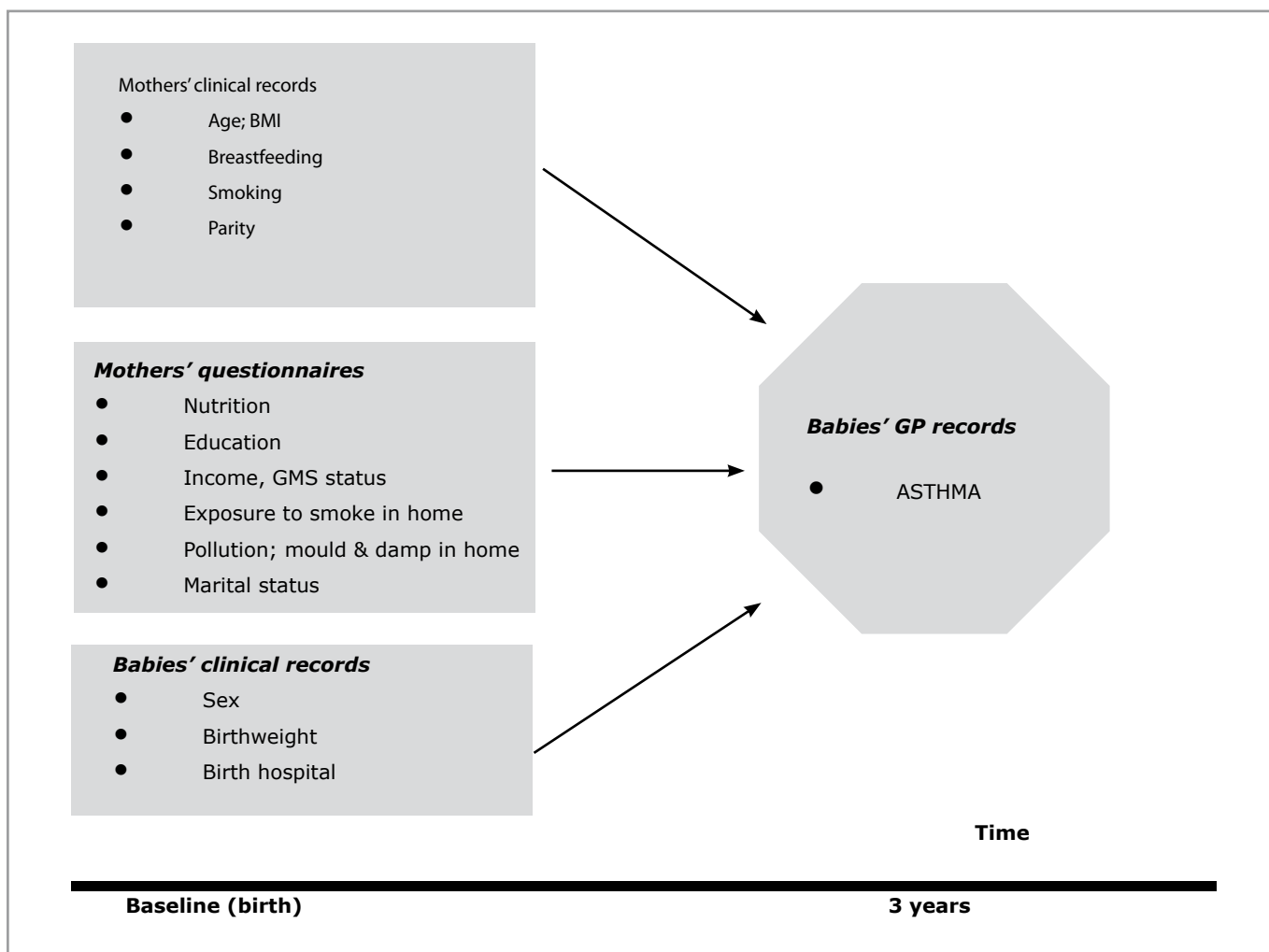


Figure 1

Table 2 Baseline characteristics of 1001 mother-singleton baby pairs with GP follow-up at 3 years

Baseline characteristic	N	No follow-up	Follow-up	P *
Number	1001	370	631	
Mother's age yrs mean(sd)	996	29.2(5.9)	30.3(5.9)	0.006
Mother's BMI kg/m ² mean(sd)	833	23.8(4.2)	24.0(4.2)	0.60
Galway	1001	96(26%)	219(35%)	0.004
GMS	993	71(19%)	105(17%)	0.31
Low income	910	64(19%)	107(19%)	0.83
3 rd level education	977	177(49%)	304(49%)	0.87
Single	993	86(23%)	109(18%)	0.03
First baby	984	169(47%)	268(43%)	0.27
Mould/damp in home	996	57(15%)	76(12%)	0.14
Pollution a problem	983	123(34%)	212(34%)	0.88
Smoking at delivery	957	96(28%)	115(19%)	0.002
Exposure to smoke in home	999	116(31%)	157(25%)	0.03
Fruit & veg servings mean(sd)	1001	5.6(3.8)	5.6(3.2)	0.80
Added fat servings mean(sd)	1001	2.6(2.4)	2.5(2.3)	0.46
Oily fish weekly	983	77(21%)	145(23%)	0.39
Birthweight grams mean(sd)	980	3528(564)	3523(563)	0.88
Breastfeeding	888	139(42%)	238(43%)	0.92

* Follow-up at 3 years versus no follow-up group

smoking during pregnancy, exposure to smoke in the home, mould or damp in home, problems with pollution in the local area, maternal university education, GMS status, income, maternal parity, child's birthweight, child's gender, and breast feeding (see Figure 1). Potential confounders were retained in the model based on change to the log-likelihood of the model. From the parameter estimates we calculated the odds ratio and 95% confidence intervals of a record of asthma by age three in relation to the selected dietary factors. For mothers' fruit and vegetable consumption, divided into quartiles, we calculated the p-value for the contrast between the highest quartile and the three lower quartiles. Models were fitted using SAS version 9 (SAS Institute, Cary, NC).

Results

Table 2 shows maternal characteristics during pregnancy that may be associated with asthma in children for those with and without GP follow-up at 3 years. There were 1001 singleton babies born, whose mothers had completed the FFQ during pregnancy, of which 631 had GP follow-up. Twins were excluded. Mainly due to a higher follow-up rate for the Galway mothers, who were on average older than the Dublin mothers, more likely to be married and less likely to smoke, these factors were significantly different for the follow-up and non follow-up groups. Mothers' dietary habits and other characteristics were not significantly different for the groups with and without follow-up.

Tables 3 and 4 show the associations between maternal added fat and fruit and vegetable consumption during pregnancy and potentially confounding factors. Mothers in the lowest quartile of fat consumption were more likely to be single, first time mothers, to have GMS cards and to smoke during pregnancy. They also tended to consume a smaller quantity of fruit and vegetables. Mothers who

consumed more fat during pregnancy were more likely to breast feed, more likely to eat oily fish and more likely to be from Galway. Mothers who consumed a small quantity of fruit and vegetables were more likely to be of lower socio-economic level: having no university education, low income, GMS card and single. Mothers who ate a large quantity of fruit and vegetables were more likely to breast feed and to eat oily fish, and to be from Galway rather than Dublin.

65 (10.4%) of children had a diagnosis of asthma by age 3. In the multivariate logistic model, the factors included in the model for asthma in children at 3 years were birth-weight (babies with low and high birth-weights were at higher risk of asthma than those in the middle of the range), gender (boys at higher risk of asthma than girls), smoke exposure in the home, and means-tested General Medical Services eligibility. Socio-demographic and lifestyle variables that were not significant and had no effect on parameter estimates were mother's age, mother's BMI, education levels of mother, marital status, parity, breastfeeding, self-reported pollution in the environment and mould and damp in home. Notably maternal smoking during pregnancy was not significant.

Table 5 gives the odds ratios and 95% confidence intervals for asthma in children aged 3 by maternal fruit and vegetable consumption during pregnancy, and tests the odds of asthma in the highest quartile of fat consumption against the three lower quartiles. Adjusting for fat consumption increased the risk of asthma to children whose mothers were in the highest quartile of fruit and vegetable consumption, and controlling for other covariates further increased the significance of this. However, adjusting for the consumption of oily fish decreased the risk of asthma in this group. There was no evidence of significant interactions between

Table 3 Associations between fruit and vegetable consumption and potentially confounding covariates

	Quartile of mother's fruit & vegetable consumption during pregnancy (servings per day)				P trend*
	Q1	Q2	Q3	Q4	
Median	2.3	4.1	6.0	8.9	
Range	0-3.4	3.4-5.0	5.0-7.1	>7.1	
N	146	166	146	173	
Mother's age mean (sd)	27.9(5.9)	30.4(5.7)	31.5(5.5)	31.2(5.9)	0.19
Mother's BMI mean (sd)	24.3(4.3)	24.2(4.4)	23.5(3.8)	23.9(4.3)	0.39
Galway	42(29%)	53(32%)	52(36%)	72(42%)	0.01
GMS	44(30%)	26(16%)	17(12%)	18(10%)	<0.0001
Low income	35(27%)	26(17%)	22(16%)	24(15%)	0.01
3 rd level education	52(37%)	76(48%)	77(53%)	99(59%)	0.0001
Single	40(29%)	28(17%)	17(12%)	24(14%)	0.0006
First baby	71(49%)	69(42%)	56(37%)	72(42%)	0.22
Mould/damp in home	22(15%)	18(11%)	17(12%)	19(11%)	0.35
Pollution a problem	44(31%)	52(32%)	56(39%)	60(35%)	0.32
Smoking at delivery	47(34%)	35(22%)	17(12%)	16(10%)	<0.0001
Exposure to smoke in home	49(34%)	39(23%)	30(21%)	39(23%)	0.03
Fat servings mean(sd)	1.7(1.9)	2.3(2.0)	2.6(2.3)	3.1(2.8)	0.02
Oily fish weekly	16(12%)	28(17%)	36(25%)	65(38%)	<0.0001
Birthweight grams mean(sd)	3412(564)	3552(596)	3560(535)	3557(548)	0.27
Breastfeeding	40(29%)	58(40%)	62(48%)	78(53%)	<0.0001
Male baby	70(48%)	78(47%)	61(42%)	82(49%)	0.85

*P trend based on Mantel-Haenszel tests for categorical variables and linear regression against median fruit and vegetables consumption for continuous variables.

the dietary factors.

Table 6 gives the odds ratios and 95% confidence intervals for asthma in children aged 3 by maternal added fat consumption during pregnancy, and tests the odds of asthma in the highest quartile of fat consumption against the three lower quartiles. Adjusting for other dietary factors (fruit and vegetables and oily fish) increased the risk of asthma to children whose mothers were in the highest quartile of fat consumption, and controlling for other covariates further increased the significance of this.

Discussion

This analysis demonstrates a significant relationship between maternal diet, social circumstances and diagnosis of asthma by the age of three. Broadly speaking women who reported meeting a recommended healthy diet, that is high fruit and vegetable and fish oil intake and relatively sparing fat intake¹² were less likely to have children who developed asthma. The follow up rate, at 63% was reasonable and a function of GP's rather than respondents' cooperation, so systematic bias is unlikely. The prevalence of asthma at 10.4% is consistent with that of the United Kingdom's Millennium Birth Cohort findings for children recruited in the same

period, which reports that by age 3, 12.3% of children had ever had asthma and 20.3% had wheezed in the past 12 months¹³, suggesting a reasonably accurate prevalence estimate in the current study. However the problem of ascertainment bias, particularly for younger mothers with less social support, who might be more likely to present to a general practitioner, remains an issue¹⁴. The impact of socio-economic circumstances on asthma as an outcome is as might be expected and is the obvious confounding possibility for an apparent influence of diet, as less affluent families are more likely to have both a more limited diet and concurrent exposures to other risk factors. Nonetheless maternal nutrition factors during pregnancy were significant predictors of asthma in children at 3 years after controlling for socio-demographic, lifestyle and clinical variables. It is possible that asthma in this cohort is related to the relative balance of omega-3 and omega-6 content of the maternal diet, or to other antio-oxidant or micronutrients, but the data are preliminary and a more detailed dietary assessment would be necessary to assess this.

We are not yet able to control for children's diet in itself as such information has not yet been collected, though it is proposed to do

Table 4 Associations between fat consumption and potentially confounding covariates.

	Quartile of mother's added fat consumption during pregnancy (servings per day)				P trend*
	Q1	Q2	Q3	Q4	
Median	0.57	1.3	2.6	5.1	
Range	0-1.0	1.0-1.9	1.9-3.2	>3.2	
N	200	135	136	160	
Mother's age mean (sd)	28.8(6.2)	30.2(5.5)	30.9(5.8)	31.8(5.6)	0.06
Mother's BMI mean (sd)	24.3(4.5)	23.8(3.8)	24.1(4.7)	23.6(3.7)	0.26
Galway	54(27%)	52(39%)	47(35%)	66(41%)	0.01
GMS	51(26%)	12(9%)	18(13%)	24(15%)	0.01
Low income	39(22%)	23(19%)	18(14%)	27(18%)	0.24
3 rd level education	87(46%)	76(58%)	66(49%)	75(47%)	0.95
Single	54(26%)	24(18%)	14(10%)	17(11%)	<0.0001
First baby	103(53%)	57(44%)	58(43%)	50(31%)	<0.0001
Mould/damp in home	31(16%)	10(7%)	17(13%)	18(11%)	0.38
Pollution a problem	71(37%)	35(26%)	45(33%)	61(38%)	0.67
Smoking at delivery	49(26%)	23(18%)	20(15%)	23(15%)	0.007
Exposure to smoke in home	57(29%)	30(22%)	34(25%)	36(23%)	0.25
Fruit & veg servings mean(sd)	4.6(2.9)	6.1(3.5)	5.8(3.1)	6.4(2.8)	0.26
Oily fish weekly	34(18%)	30(23%)	35(26%)	46(29%)	0.01
Birthweight grams mean(sd)	3546(559)	3494(503)	3480(631)	3555(560)	0.70
Breastfeeding	61(35%)	53(43%)	56(48%)	68(48%)	0.01
Male baby	90(45%)	68(51%)	63(46%)	70(44%)	0.68

*P trend based on Mantel-Haenszel tests for categorical variables and linear regression against median fat

Table 5 Odds ratios (95% CIs) for asthma in children aged 3 by mother's consumption of fruit and vegetables during pregnancy

	Quartile of mother's fruit and vegetable consumption during pregnancy (servings per day)				p-contrast Q4 vs Q1+Q2+Q3
	Q1	Q2	Q3	Q4	
Median	2.3	4.1	6.0	8.9	
Range	0-3.4	3.4-5.0	5.0-7.1	>7.1	
N	146	166	146	173	
Asthma n cases(%)	N	OR	OR (95%CI)	OR (95%CI)	
Univariate n=66(10.4%)	631	1.00	0.99 (0.51,1.9)	0.80 (0.39,1.6)	0.07
Multivariate n=66(10.4%) +fat	631	1.00	0.99 (0.50,2.0)	0.71 (0.33,1.5)	0.04
Multivariate n=64(10.4%) +oily fish fat	618	1.00	1.1 (0.55,2.3)	0.81 (0.37,1.7)	0.09
Multivariate n=63(10.3%) +birthweight, sex, Smoke exposure, fat, Oily fish,	610	1.00	1.1 (0.53,2.3)	0.93 (0.42,2.0)	0.06
Multivariate n=62(10.2%) +birthweight, sex, Smoke exposure, fat, Oily fish, GMS	605	1.00	1.1 (0.53,2.3)	0.89 (0.39,2.0)	0.07
Multivariate n=64(10.4%) +birthweight, sex, Smoke exposure, fat, GMS	618	1.00	1.0 (0.49,2.1)	0.76 (0.34,1.7)	0.04

Table 6 Odds ratios (95% CIs) for asthma in children aged 3 by mother's consumption of added fats during pregnancy
Mothers' dietary patterns during pregnancy and risk of asthma symptoms in children at 3 years

		Quartile of mother's added fat consumption during pregnancy (servings per day)				P contrast Q4 vs Q1+Q2+Q3
		Q1	Q2	Q3	Q4	
Median		0.57	1.3	2.6	5.1	
Range		0-1.0	1.0-1.9	1.9-3.2	>3.2	
N		200	135	136	160	
Asthma n cases(%)	N	OR	OR (95%CI)	OR (95%CI)	OR (95%CI)	
Univariate n=66(10.4%)	631	1.00	0.66 (0.30,1.5)	0.57 (0.26,1.3)	1.5 (0.81,2.8)	0.01
Multivariate n=64(10.4%) +fruit&veg, Oily fish	618	1.00	0.65 (0.28,1.5)	0.54 (0.23,1.4)	1.8 (0.93,3.5)	0.002
Multivariate n=63(10.3%) +birthweight, sex, Smoke exposure.	610	1.00	0.68 (0.29,1.6)	0.62 (0.28,1.6)	1.9 (0.95,3.7)	0.003
Multivariate n=62(10.2%) + GMS	605	1.00	0.78 (0.33,1.9)	0.70 (0.30,1.6)	2.1 (1.0,4.2)	0.003

so as part of the 5 year follow-up with families in 2007. It may be that maternal diet during pregnancy is a proxy for children's own diets or for mothers' ongoing diets, rather than the causal factor in itself and as such reflects more prolonged household exposure to a particular type of diet. Given that the data were collected at a single time point as part of a food frequency questionnaire during pregnancy, it is in fact remarkable that any impact was demonstrated. There is a mounting literature suggesting the biological coherence of a link between maternal diet and asthma with which this analysis is consistent²⁻¹⁰. In a similar cohort study in Aberdeen with follow-up of 700 children by the age of 5 years, maternal vitamin E and zinc intakes during pregnancy were found to be negatively associated with wheeze and asthma in the last year, supporting the hypothesis that maternal diet can have long term consequences. That study adjusted also for children's own intakes⁵.

In conclusion these findings merit a more detailed dietary assessment and analysis of this issue in the Lifeways cohort, which will be elucidated further in the next sweep of data collection.

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