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Milk allergy is a minor cause of milk avoidance due to perceived hypersensitivity among schoolchildren in Northern Sweden

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ABSTRACT

Aim: We investigated phenotypes of milk hypersensitivity among schoolchildren aged 11-12 in Northern Sweden. **Methods:** In a population-based cohort, 1,824 (98%) children aged 11-12 participated in a questionnaire survey, skin prick testing, interviews on food hypersensitivity and assessment of body mass index (BMI). Of the 265 children reporting milk hypersensitivity, milk avoidance and no celiac disease, 236 (89%) participated in a structured interview and blood samples for analyses of milk-specific Immunoglobulin E. The children were then categorised into milk hypersensitivity phenotypes according to preset criteria. **Results:** In all, 14.5% reported milk hypersensitivity. Of these, 3% were categorised as *current milk allergy*, 23% as *outgrown milk allergy*, 40% as *probable lactose intolerance* and 11% were *non-definable*. Furthermore, 23% had discontinued their elimination diet. *Milk allergy* was associated with other atopic disorders and lower BMI, with an odds Ratio of 0.82 and 95% confidence interval of 0.80-0.98. Only 2% had previously undergone an oral challenge. **Conclusion:** The most common symptom phenotypes among Swedish children aged 11-12 with self-reported milk hypersensitivity and milk avoidance, were *lactose intolerance* and *outgrown milk allergy* while *current milk allergy* was uncommon. Children with *milk allergy* had a lower BMI and most lacked a challenge proven diagnosis.

Key Words: body mass index, child, cow's milk, epidemiology, food allergy

Key Notes

- The phenotypes underlying reported food hypersensitivity are largely unexplored.
- Reported milk hypersensitivity was common in schoolchildren aged 11-12 in Northern Sweden, while the prevalence of current milk allergy was low. Milk allergy, current or outgrown, was associated with lower body mass index. Only 2% of children currently avoiding milk had previously undergone an oral challenge.

- Collectively, this emphasizes the need for proper, clinical evaluations of children with perceived milk hypersensitivity.

INTRODUCTION

Food hypersensitivity is a general term for adverse reactions to food. The term include allergies, which are reactions of immunological origin, and intolerances, which are caused by non-immunological mechanisms (1). Milk allergy is the most common food allergy in young children (2) but the majority of milk allergic children develop tolerance before school age (3). Despite this, the prevalence of reported milk hypersensitivity remains high in older children and adolescents in many studies, ranging from 0.1-13% (2,4-6). Since the onset of cow's milk allergy is uncommon after the first years of life (3) the majority of perceived symptoms following ingestion of dairy products in school-aged children are most likely to be explained by food hypersensitivity phenotypes other than milk allergy (6-9). However, this has not been thoroughly explored.

Lactose intolerance is thought to be uncommon in the Swedish population and the onset of symptoms usually occurs during adolescence (10). However, the prevalence of lactose intolerance has not been well studied (11). During the last few decades there has also been an increased awareness in the population regarding foods, cow's milk in particular, as possible triggers of various symptoms and diseases (9,12). Even when they are partially avoided, the elimination of dairy products may result in negative effects on nutritional status (11,13,14) and quality of life (15). Consequently, there is need for studies that clarify the food hypersensitivity phenotypes underlying perceived milk hypersensitivity and for appropriate selection of children in need of further evaluation and nutritional advice (7).

The aim of this study was to validate reported milk hypersensitivity and to describe the underlying phenotypes of reported milk hypersensitivity in Swedish 11 to 12-year-old children by the use of structured interviews and analyses of cow's milk-specific Immunoglobulin E (IgE) and a screening test for celiac disease. In addition, the association between the different milk hypersensitivity phenotypes and body mass index (BMI), living conditions, allergic sensitisation, allergic heredity and physician diagnosed asthma, rhinitis and eczema were analysed.

METHODS

Study population

As a part of the Obstructive Lung disease In Northern Sweden studies (OLIN), the second OLIN paediatric cohort was recruited in 2006 (16). The parents of all children in first and second grade, aged seven to eight years, in three municipalities were invited to a questionnaire study and 2,585 (97%) participated. The large majority of the cohort were Caucasians. The children in two of the municipalities, Kiruna and Luleå, were also invited to skin prick testing (SPT) with ten common airborne allergens and 1,700 (90%) participated. In 2010, the cohort was followed up when all children, now in the 5th and 6th grades, aged 11 to 12 years were invited (17). The same study methods were used at the follow up. Along with the skin prick testing, height and weight was measured and a short interview about food hypersensitivity was performed with the child, henceforth called the *child interview*. Of the 1,866 children in Kiruna and Luleå invited to the child interview 98% participated. These 1,824 children were included in this study. A study overview is presented in Figure 1. The study was approved by the Regional Ethical Review Board in Umeå, Sweden.

Questionnaire and child interview

The parental questionnaire included the International Study of Asthma and Allergies in Childhood core questions (18) with added questions about symptoms, physician diagnosis, medication and possible determinants of asthma, rhinitis and eczema. This questionnaire has been used in the OLIN cohort studies since 1996 (17, 19). The questionnaires were distributed by school personnel. For the current cohort, food hypersensitivity questions were added, including queries about reactions related to cow's milk (5-6). In the 2010 years survey, questions about food hypersensitivity were incorporated in both the parental questionnaire and the child interview.

In the current study, invitation to the structured interview was based on the following question from the child interview:

“To what extent do you avoid the following foods: cow’s milk, hen’s egg, fish, or wheat, due to allergy/ hypersensitivity?” The possible answers alternatives for each food were: *not at all, partially or completely.*

Children with physician-diagnosed celiac disease were not invited to the structured interview.

Data about celiac disease was collected from the parental questionnaire query:

“Has your child been diagnosed by a physician as having celiac disease?”

Further, the following definitions were used:

BMI: weight was measured to nearest 0.1 kg, height was measured to nearest 0.5 cm and BMI calculated as kg/m^2 .

Allergic heredity: questionnaire reported parental asthma, rhinitis and/or eczema.

FHS heredity: questionnaire reported parental food hypersensitivity

Skin prick test (SPT)

The SPT followed the European Academy of Allergology and Clinical Immunology recommendations. The Solu-prick panel included birch, timothy, mugwort, cat, dog, horse, two house dust mite extracts: *Dermatophagoides pteronyssius* and *farinae*, and two mold extracts: *Claudosporium* and *Alternaria* (ALK, Denmark). Histamine 10 mg/ml and glycerol were used as the positive and negative controls. A positive test was defined as at least one wheal ≥ 3 mm in diameter to any of the allergens tested, recorded after 15 minutes.

Structured interview

Children who reported milk hypersensitivity and milk avoidance were subsequently invited to a structured interview. Together with the children completely avoiding milk, their parents, usually the mother, were interviewed face to face (17), while the parents of children with partial milk avoidance were interviewed by telephone. The interview included food hypersensitivity related questions about age of onset, initial and current symptoms, symptom severity, time to symptom onset and symptom duration after intake of the culprit food, concomitant triggers, eliciting doses, dietary substitution products, allergic heredity, current eczema, rhinitis and, or, asthma, and current physician-diagnosed celiac disease. The interview was substantially shortened if the child had discontinued the elimination diet. Children who were still on an elimination diet were invited to donate blood for analysis of specific IgE to milk and tTGA. The structured interviews were performed between six to 12 months after the child interview.

Laboratory tests

The serum samples were analysed for specific IgE to cow's milk, the ImmunoCAP specific IgE food screen test fx5, (ThermoFisher Diagnostics, Uppsala, Sweden) that included cow's milk, hen's egg, cod, soy, wheat, and peanut and the ImmunoCAP inhalant allergen screen

test (ThermoFisher Diagnostics, Uppsala, Sweden) including birch, timothy, mugwort, cat, dog, horse, two dust mites - *Dermatophagoides pteronyssius* and *farinae* - and *Claudiosporium*. An IgE serum level > 0.35 kU/L was considered positive for all of the IgE tests. tTGA was measured in serum using the EliA Celikey IgA test (ThermoFisher Diagnostics, Uppsala, Sweden) and tTGA < 7 U/L was considered negative

Criteria for milk hypersensitivity phenotypes

Based on the structured interviews and the results of analyses of milk specific IgE and tTGA, the children were categorised according to milk hypersensitivity phenotype using preset criteria. The sorting criteria were based on current knowledge of common clinical presentations of food hypersensitivity phenotypes in childhood and adolescence (7,8) and have been used in a previous study of this cohort (17). The milk hypersensitivity phenotypes were defined as follows:

IgE-mediated milk allergy phenotype. Fulfilled mandatory criteria:

- A positive milk IgE-test – provided exposure to the milk within the last two years
- Symptoms are triggered by 100ml of milk or less

and at least two fulfilled secondary criteria:

- Onset before five years of age
- First symptom within 15 minutes of exposure
- Symptoms from more than one organ system
- Symptoms are triggered by trace amounts of milk
- Symptoms are triggered by skin exposure
- Symptoms are triggered by airborne exposure
- Anaphylaxis / exercise induced anaphylaxis

Non-IgE mediated milk allergy phenotype. Fulfilled mandatory criteria:

- A negative milk IgE-test
- Symptoms are triggered by less than 100ml of milk
- No celiac disease

and at least two fulfilled secondary criteria:

- Onset before five years of age
- First symptom more than 1 hour after exposure
- Symptom from more than one organ system
- Symptoms are triggered by treasure amounts of milk

Outgrown milk allergy phenotype. A convincing history of IgE-mediated or non-IgE mediated allergy, still avoids milk products but can now tolerate at least 100ml of milk without symptoms.

Probable lactose intolerance phenotype. Fulfilled mandatory criteria:

- Onset more than five years of age
- Symptoms limited to flatulence, stomach-ache and/or diarrhea
- Symptoms are triggered by 100 ml of milk or more
- Symptom-free on a lactose free/reduced diet
- No Celiac disease

Suspected lactose intolerance. All but one mandatory criteria fulfilled for the probable lactose intolerance phenotype.

Celiac disease phenotype: A doctor's diagnosis of Celiac disease and, or, a positive tTGA-test.

Non-definable phenotype: Avoids milk but does not fulfil the criteria for any of the listed phenotypes or declined donation of blood for analyses of milk specific IgE/tTGA.

Statistical analyses:

Data were analysed using the SPSS Software version 21 (IBM, New York, USA). The chi-square test was used for comparison of proportions and a p -value < 0.05 was considered statistically significant. Adjusted risk estimates, expressed as odds ratios (OR) with 95% confidence intervals (95% CI), for the FHS phenotype *milk allergy* were estimated by multiple logistic regression analysis. Factors that were significant or borderline significant in bivariate analyses were included in the model.

RESULTS

Prevalence of reported milk hypersensitivity

In the whole study sample of 1824 children, the prevalence of self-reported milk hypersensitivity was 14.5% ($n=265$). Of these, 193 children (73%) reported partial milk avoidance and 72 children (27%) reported complete milk avoidance. Of the 265 children with reported milk hypersensitivity, 236 (89%) participated in a structured interview (Figure 1).

Variables associated with reported milk avoidance were female sex ($p < 0.001$) physician diagnosed eczema ($p < 0.001$) allergic heredity ($p = 0.009$) and FHS heredity ($p < 0.001$). The associated variables were similar among children reporting partial or complete milk avoidance (Table 1). No significant differences were detected between children reporting milk avoidance (all, partial or complete) and children not avoiding milk for the variables: living area (Luleå/Kiruna), type of residence (house/apartment/both), socioeconomic status, parental smoking or siblings living at home (data not shown).

Milk hypersensitivity phenotypes

The results of the milk hypersensitivity phenotyping, based on the 236 children who participated in the structured interview, are presented in Table 2.

Milk allergy

Of 236 children with self-reported milk hypersensitivity, seven children (3%) were categorised as having *current milk allergy*, all of whom had reported complete milk avoidance. Further, 54 children (23%) were categorised as *outgrown milk allergy*. Children in this category had a convincing clinical history of a previous allergy to cow's milk, but could now tolerate at least 100 ml of milk without any symptoms. There was no significant difference in the prevalence of *outgrown milk allergy* between children reporting complete or partial milk avoidance.

Probable lactose intolerance

A total of 95 children (40%) were categorised as *probable lactose intolerance*. Of these, 35 children (15%) had a history of suspected lactose intolerance, that is they lacked one diagnostic criterion, which was most commonly symptom onset before five years of age. The prevalence of the *lactose intolerance* phenotype was more common among children reporting complete milk avoidance compared to children partially avoiding milk ($p=0.03$).

Celiac disease

Of the 236 children reporting milk avoidance, one child (0.4%) had a positive celiac screening test (tTGA).

Non-definable cases

In 25 children (11%), the symptoms and findings from the structured interviews and blood tests did not fulfil the criteria for any of the pre-set phenotypes. These children were thus categorised as *non-definable*. The *non-definable* group included eight children (3%) reporting symptoms that were non-specific and 17 children (7%) that declined blood sampling.

Discontinued milk avoidance

At the time of the structured interviews, 54 children (23%) who reported milk hypersensitivity were no longer avoiding dairy products. All of these had reported partial milk avoidance. These children were not further evaluated. Reported reasons for reintroduction milk were lack of positive effects of the milk elimination or that the child was now symptom-free independently of diet (data not shown).

Factors associated with milk hypersensitivity phenotypes

Variables associated with *milk allergy*, current or outgrown, were: female sex ($p=0.02$) FHS heredity (<0.001) physician diagnosed asthma (0.006) rhinitis (0.003) and eczema (<0.001). Children with *milk allergy* had a lower BMI, although the p -value did not reach statistical significance ($p=0.058$) in the bivariate analysis (Table 3). In a multivariate analysis the association to the variables female sex (OR 1.90, CI (1.02-3.55) FHS heredity (OR 4.45, CI 2.42-8.29) and physician-diagnosed eczema (OR 3.53, CI 1.79-6.98) remained statistically significant and decreased BMI reached statistical significance (OR 0.82, CI 0.80-0.98) (Table 4).

In children categorised as having *probable lactose intolerance* the variables female sex ($p<0.001$) and FHS heredity (<0.001) were more common compared to children with no milk avoidance. In addition, the variables any positive SPT ($p=0.034$) a positive inhalant screen ($p=0.031$) and a positive food screen ($p=0.023$) were negatively associated with the *lactose intolerance* phenotype. No significant associations were seen for any of the milk hypersensitivity phenotypes for the variables living area (Luleå/Kiruna), type of residence (house/apartment/both), socioeconomic status, parental smoking or siblings living at home.

Health care contacts due to milk hypersensitivity

Among the 181 children with reported milk hypersensitivity and current milk avoidance, 77 children (43%) reported that their milk hypersensitivity diagnosis had been established by a physician. The proportion with a physician diagnosed milk hypersensitivity was highest (62%) among children with *milk allergy*, current or outgrown. Only 17 children (9%) reported that they had ever been referred to a dietician for nutritional advice and only four children (2%) reported that they had been diagnosed by an oral challenge.

DISCUSSION

Even though the prevalence of reported milk hypersensitivity among Swedish 11 to 12-year-olds was as high as 14.5%, only 3% of them were categorised as *current milk allergy*. The most common milk hypersensitivity phenotypes were *probable lactose intolerance* and *outgrown milk allergy*. Children with *outgrown milk allergy* could at the time during the assessment tolerate a portion size of dairy products without symptoms but had remained on a milk elimination diet. Current and outgrown *milk allergy* was associated with other atopic disorders and lower BMI. Only 9% of the children currently avoiding milk reported that they had ever been referred to a dietician for nutritional advice and only 2% had a milk hypersensitivity diagnosis established by an oral challenge.

Cow's milk is currently a hot topic and the debate includes potential positive and negative effects of dairy products (12-14). Concerns have been expressed regarding elimination of cow's milk from the diet of a growing child (13,14). In this study, the prevalence of reported milk hypersensitivity was 14.5%, with a quarter reporting complete milk elimination and three-quarters reporting partial elimination of milk. This prevalence was high compared to most previous studies (2,4). During recent years, studies have suggested that milk elimination could lead to negative effects on growth (14) and on the intake of important nutrients such as vitamin D (20,21). In our study, children categorised as current or outgrown *milk allergy* had

a lower BMI compared to children with no milk avoidance and to the other milk hypersensitivity phenotypes. A possible explanation is that children with *milk allergy* had been avoiding dairy products since early life and were still avoiding them, even though the children with *outgrown milk allergy* probably did not have to (14,17).

Only 3% of the 11 to 12-year-old children with self-reported milk hypersensitivity were categorised as *current milk allergy*, all of whom had reported complete milk avoidance. Assuming a similar distribution of this phenotype among the non-participants would have given a prevalence of *current milk allergy* in the entire cohort of 0.4%. As opposed to the high reported prevalence of milk hypersensitivity, the prevalence of *current milk allergy* in this study was relatively low compared to the findings of others (2,3). The prevalence of challenge proven milk allergy was likely to be even lower. In a previous study of this cohort, about half of the children categorised as having a *current allergy* to milk, egg, cod or wheat had a positive double-blind food challenge (17).

In addition, 23% of the children were categorised as having an *outgrown milk allergy*. This finding was consistent with the natural history of allergy to cow's milk (3,22). As for reported milk hypersensitivity, the variables female sex, physician diagnosed eczema and heredity for food hypersensitivity were more common in children with *current* or *outgrown milk allergy* compared to children not avoiding milk. Previous studies have showed that childhood eczema is a risk factor for the development as well as the persistence of food allergies (23,24). It has also been shown that even though food allergies and sensitisation to food allergens are more common among boys than girls, there seems to be a shift during adolescence that renders a higher prevalence of food allergies in women (25). Children categorised as having an *outgrown milk allergy*, could now tolerate at least 100ml of milk without symptoms. Despite this, they were still on a milk elimination diet due to uncertainty about whether they had fully outgrown their allergy or because they disliked the taste or texture of dairy products. These findings emphasise the importance of recurrent evaluations

of tolerance development and dietary restrictions in children with cow's milk allergy (7).

The most commonly occurring phenotype was a *probable lactose intolerance*. Children in this phenotype were less sensitised to aeroallergens and food allergens compared to children with no reported milk hypersensitivity. A prevalence of the *lactose intolerance* phenotype of 40% among children with reported milk hypersensitivity would suggest a prevalence of *probable lactose intolerance* in the entire cohort of about 6%. In our study, the *probable lactose intolerance* phenotype was based on symptoms and the absence of milk allergy and celiac disease and these children were not further evaluated. Even though a former study showed a higher-than-expected prevalence of lactase down-regulation (14%) among Swedish schoolchildren (26), others have shown that over-reporting of lactose intolerance is frequent even in populations in which lactase down-regulation is common (27). These findings suggest that symptoms of lactose intolerance might be caused by underlying mechanisms other than lactase down-regulation (9). Further evaluation of these children including genotype testing and oral challenges would be necessary to differentiate symptoms caused by lactase down-regulation from lactose intolerance like symptoms due to other gastrointestinal conditions like irritable bowel disease (7,9,11).

Previous studies have shown a high prevalence of celiac disease among people with symptoms of lactose intolerance (28). In our study only one child with reported milk hypersensitivity (0.4%) had a positive celiac screening test. A previous study from this cohort showed a prevalence of reported physician diagnosed celiac disease of 0.3% and a prevalence of a positive celiac screening test of 1% (17). Taken together, this gives a likely prevalence of diagnosed and undiagnosed celiac disease which is somewhat lower than other recent studies in this region (29) and the prevalence of celiac disease was equally low among children with reported milk hypersensitivity.

By the time of the structured interviews, 30% of the children reporting milk hypersensitivity were no longer avoiding milk. This high prevalence of discontinued elimination diet complies with the high remission of reported milk hypersensitivity between eight and 12 years of age seen in a previous study from this cohort (6). All children who no longer avoided milk had reported partial milk avoidance. The majority of these children had tried a milk reduced diet during a period, seeking alleviation of various symptoms, but had returned to a non-avoidance diet due to lack of positive effects or because they were now symptom-free independent of the type of diet.

A major strength of our study was its population based design, the well-defined study participants and the high participation rates. The participants who underwent the structured interviews were representative of the children in the study cohort. The invitation to the structured interview was based on the children's reports of milk hypersensitivity. However, based on another cohort of children of the same ages, we found a very high agreement between parental and children reports of allergic diseases (30). A possible study limitation was the lack of further evaluation of the milk hypersensitivity phenotypes with oral challenges and genotype testing for lactase non-persistence (7). This could have resulted in an over-diagnosis, especially of the *probable lactose intolerance* phenotype (9,11) while the tolerance cut-of-level of 100 ml of cow's milk, might have resulted in an under-diagnosis of *current milk allergy* (7,8). Also, since the interviews included questions about events from further back in time the answers could be affected by recall bias.

CONCLUSION

In summary, in this large cohort of Swedish 11 to 12-year-old schoolchildren, there was a high prevalence of self-reported milk hypersensitivity of 14.5%. Of these, only 3% were categorised as *current milk allergy* while 23% were categorised as *outgrown milk allergy*. The most common milk hypersensitivity phenotype was *probable lactose intolerance* (40%). Children with *milk allergy*, either current or outgrown, had a lower BMI than children with no

milk avoidance. Only 9% of the children currently avoiding milk had ever been referred to a dietician for nutritional advice and only 2% reported that their milk hypersensitivity diagnosis had been established by an oral challenge. These findings highlight the importance of recurrent and thorough clinical evaluations of children with perceived milk hypersensitivity in order to prevent unnecessary food avoidance and consequent side effects on nutrition and growth.

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Conflict of interest and funding

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Abbreviations:

BMI: Body Mass Index

IgE: Immunoglobulin E

OLIN: The Obstructive Lung disease In Northern Sweden Studies

SPT: Skin Prick Test

tTGA: Tissue transglutaminase IgA

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self-completed questionnaires about allergic diseases and environmental factors in teenagers. *J Clin Epidemiol* 2010;63:783-9. **Table 1. Prevalence (%), and comparison of the listed variable between children reporting milk avoidance, complete milk avoidance, partial milk avoidance and no milk avoidance, respectively.**

	Milk avoidance (all) n=265	Complete milk avoidance n=72	Partial milk avoidance n=193	No milk avoidance n=1559	p-value 1*	p-value 2**	p-value 3***	p-value 4****
Female sex	61.9%	63.9%	61.1%	47.1%	<0.001	0.682	0.005	<0.001
Physician diagnosis;								
Asthma	13.4%	12.5%	13.8%	10.6%	0.184	0.790	0.615	0.194
Rhinitis	14.2%	18.1%	12.7%	10.9%	0.118	0.267	0.058	0.447
Eczema	24.9%	25.7%	24.6%	14.0%	<0.001	0.855	0.006	<0.001
Allergic heredity	63.4%	72.2%	60.1%	54.8%	0.009	0.068	0.004	0.165
FHS heredity#	44.9 %	52.8 %	42.0 %	19.9 %	<0.001	0.116	<0.001	<0.001
Allergic sensitization	36.6%	38.2%	36.0%	40.5%	0.246	0.740	0.708	0.242

* p-value 1 = comparison avoids milk – no milk avoidance

** p-value 2 = comparison complete milk avoidance – partial milk avoidance

*** p-value 3 = comparison complete milk avoidance – no milk avoidance

**** p-value 4 = comparison partial milk avoidance – no milk avoidance

FHS heredity = parentally reported food hypersensitivity

Table 2. Distribution, n (%), of different food hypersensitivity phenotypes among children reporting any milk avoidance, complete milk avoidance and partial milk avoidance.

FOOD HYPERSENSITIVITY PHENOTYPE	Milk avoidance (All) (n=236)	Complete milk avoidance (n=56)	Partial milk avoidance (n=180)	p-value*
CURRENT MILK ALLERGY	7 (3%)	7 (12 %)	0 (0%)	<0.001
IgE-mediated Allergy	2 (1 %)	2 (4 %)	0 (0%)	
Non-IgE-mediated Allergy	5 (2 %)	5 (9 %)	0 (0%)	
OUTGROWN MILK ALLERGY	54 (23 %)	16 (28.1%)	38 (21.1%)	0.281
PROBABLE LACTOSE INTOLERANCE	95 (40 %)	30 (53 %)	65 (36 %)	0.030
Lactose intolerance	60 (25 %)	22 (39 %)	38 (21 %)	
Suspected Lactose intolerance	35 (15 %)	8 (14 %)	27 (15 %)	
CELIAC DISEASE	1 (0.4 %)	0 (0 %)	1 (0.5%)	1.000
NON-DEFINABLE	25 (11 %)	3 (5 %)	22 (12 %)	0.214
Symptoms not definable	8 (3 %)	1 (2 %)	7 (4 %)	
No blood analyses (specific IgE/tgA)	17 (7 %)	2 (4 %)	15 (8 %)	
DISCONTINUED MILK AVOIDANCE	54 (23 %)	0 (0 %)	54 (30.6%)	< 0.001

* complete milk avoidance versus partial milk avoidance

Table 3. Prevalence, n (%), and comparison of the listed variables between the different food hypersensitivity (FHS) phenotypes and children with no milk avoidance.

	Milk allergy (current and outgrown) n=61	p-value *	Probable Lactose intolerance n=95	p-value **	Non-definable n=25	Discontinued milk avoidance n=55	No milk avoidance n=1559
Female sex	38 (62 %)	0.020	64 (67 %)	<0.001	16 (64 %)	31 (56 %)	735 (47%)
Asthma	13 (22 %)	0.006	10 (10 %)	0.976	3 (12 %)	5 (9 %)	163 (10 %)
Rhinitis	14 (23 %)	0.003	8 (8 %)	0.475	6 (24 %)	2 (4 %)	168 (11 %)
Eczema	25 (42 %)	<0.001	16 (17 %)	0.435	6 (24 %)	11 (20 %)	214 (14 %)
Allergic heredity	37 (61 %)	0.371	58 (61%)	0.237	15 (60 %)	36 (66%)	855 (55 %)
FHS heredity #	32 (52 %)	<0.001	45 (47 %)	<0.001	10 (40 %)	18 (33 %)	310 (20 %)
Any positive SPT	30 (53 %)	0.068	27 (29 %)	0.034	8 (42 %)	16 (31 %)	564 (40 %)
Food screening	16 (26 %)	0.104	8 (8 %)	0.023	-	-	103 (18%) ##
Inhalant screening	29 (48 %)	0.335	28 (30 %)	0.031	-	-	239 (41 %) ##
	mean		mean		mean	mean	mean
BMI	18.66	0.058	19.50	0.884	18.59	19.90	19.55

* Milk allergy versus no milk avoidance

** Lactose intolerance versus no milk avoidance

FHS heredity = parentally reported food hypersensitivity

Children donating blood samples n=581

Table 4. Prevalence (%) of milk allergy in relation to risk factors and adjusted risk analysed by multiple logistic regression analysis expressed as odds ratios (OR) with 95% confidence intervals (CI).

		MILK ALLERGY (current or outgrown)			
		%	p-value	Crude OR (95%CI)	Adjusted OR* (95% CI)
Sex	Boys	2.5	0.041	1.0	1.0
	Girls	4.2		1.73 (1.02-2.93)	1.90 (1.02-3.55)
Physician diagnosed asthma	No	2.9	0.008	1.0	1.0
	Yes	6.6		2.37 (1.26-4.47)	1.24 (0.55-2.76)
Physician diagnosed rhinitis	No	2.9	0.005	1.0	1.0
	Yes	6.8		2.43 (1.31-4.49)	1.25 (0.54-2.88)
Physician diagnosed eczema	No	2.3	<0.001	1.0	1.0
	Yes	9.0		4.16 (2.45-7.07)	3.53 (1.79-6.98)
FHS heredity#	No	2.1	<0.001	1.0	1.0
	Yes	7.5		3.80 (2.27-6.35)	4.45 (2.42-8.19)
Any positive SPT	No	2.7	0.049	1.0	1.0
	Yes	4.6		1.70 (1.00-2.89)	1.05 (0.53-2.06)
BMI			0.059	0.92 (0.84-1.00)	0.82 (0.80-0.98)

* Significant variables in the bivariate analyses (table 3) were included in the multivariate analysis

FHS heredity = parentally reported food hypersensitivity

Table 5. Reported methods for establishing the milk hypersensitivity diagnosis and reported referrals to a dietitian for nutritional advice between children in the different food hypersensitivity (FHS) categories.

	Milk hypersensitivity (All) n=181	Milk allergy (current and outgrown) n=61	Probable Lactose intolerance n=95	Non-definable n=25
Physician diagnosis FHS	77 (43%)	38 (62 %)	30 (32 %)	9 (36 %)
Lactose challenge	4 (2%)	3 (5 %)	0	1 (4 %)
Gene test	15 (8%)	5 (9 %)	9 (9 %)	1 (4 %)
IgE testing milk	22 (12%)	17 (29 %)	1 (1 %)	4 (16 %)
Oral challenge	4 (2%)	2 (3 %)	1 (1 %)	1 (4 %)
Dietician	17 (9%)	12 (20 %)	1 (1 %)	4 (16 %)

FIGURE LEGENDS

Figure 1. STUDY OVERVIEW

Figure 1.

