ORIGINAL REPORT

Referral Pathways for Children with Atopic Diseases in Denmark

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Atopic diseases such as atopic dermatitis, food allergy, allergic rhinoconjunctivitis, and/or asthma are common. In Denmark, however, there are multiple referral pathways for these diseases in the healthcare system and they are poorly understood. To describe how children with atopic diseases navigate their way through the Danish healthcare system, a questionnaire was distributed to children aged ≤17 years, who were being treated for atopic diseases between August 2020 and June 2021, either by a practising specialist or a hospital department, in the Capital Region of Denmark. A total of 279 children completed the questionnaire and most were referred to a specialist or to a hospital by their general practitioner. No "common track" to hospital existed for patients with ≥3 atopic diseases. These patients were more often referred to a hospital compared with children with 2 atopic diseases or fewer (odds ratio [OR] 3.79; 95% CI 2.07–7.24). The primary determinants for hospital treatment were food allergy (OR 4.69; 95% CI 2.07–10.61) and asthma (OR 2.58; 95% CI 1.18–5.63). In conclusion, children with multiple atopic diseases were more likely to be referred to hospital departments than to practising specialists, mainly due to food allergies.

Key words: allergic rhinitis; asthma; atopic dermatitis; disease management; food hypersensitivity; referral.

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SIGNIFICANCE

Atopic dermatitis, hay fever, food allergies, and asthma are common diseases, but little is known about how children with 1 or more of these diseases navigate through the healthcare system in Denmark. In this questionnaire study that included 279 children with atopic diseases, we mapped their pathway through the Danish healthcare system. Children with 3 or more atopic diseases were more likely to be referred to hospitals than to practising specialists. Food allergies and, to a lesser extent, asthma were the main reasons for referral.

Atopic diseases such as atopic dermatitis (AD), food allergy, asthma, and allergic rhinoconjunctivitis (ARC) are common diseases among children worldwide (1–3). Whereas AD and food allergy often develop during the first year of life (4), asthma and ARC usually occur later in childhood, with disease severities differing – from mild and transient, to severe and potentially fatal. The mechanisms underlying the development of 1 or several atopic diseases and the associated severity are poorly understood. Seven and 8 different disease trajectories for AD, asthma, and ARC have recently been described (5, 6). Early differentiation of patients with high vs low risk of persistent and severe atopic diseases is desirable to prevent disease progression and to offer the most appropriate level of care.

The Danish healthcare system is tax-supported and this ensures that all citizens have equal, cost-free access to healthcare services, including general practice, practising specialists, and hospital treatment (7). Some citizens may also have private health insurance cover and may be treated in private care, thus avoiding waiting lists. This option, however, may exclude some children, depending on their age and disease manifestations, as there is no private care for children with severe or complex atopic diseases.

In Denmark, children with atopic diseases are usually seen and treated initially in general practice, but may then be referred to practising specialists or hospital departments, e.g. paediatrics, dermatology, otorhinolaryngology, and allergology depending on the severity and complexity of their disease (8). According to paediatric specialty standards, children with complex or severe atopic diseases should be referred to a hospital department with a high level of specialization. To date, however, no disease management programme exists for patients with multiple atopic diseases, and the referral pathways in the Danish healthcare system are poorly understood (8). The management of these patients requires different levels of knowledge and support, depending on the number and severity of atopic diseases, family resources, and needs (9).

From 2006 to 2015, the number of patients with atopic diseases treated in a hospital setting in Denmark increased by 177% (8). A UK national survey reported that the number of paediatric allergy appointments for

newly referred patients has increased sevenfold from 2006 to handle rising demand (10). A South Korean study also found increased prevalence of ARC and asthma in hospital settings, but not AD (11). To ensure optimal quality of care and effective use of healthcare services for individuals with atopic diseases, an efficient referral pathway to the appropriate level of care is warranted.

The aim of the present study was to describe the current referral pathways in the Danish healthcare system for children with AD, food allergy, ARC, and/or asthma.

MATERIALS AND METHODS

The study included children and adolescents (0–17 years) who had consulted a hospital department (paediatric, dermatology, or allergy) or a practising specialist (2 paediatricians, 1 dermatologist, and 1 otorhinolaryngologist) in the Capital Region of Denmark between August 2020 and June 2021. Patients diagnosed with AD, food allergy, ARC, and/or asthma by a physician from 1 of the hospital departments or practising specialists were invited to answer a questionnaire.

For patients aged < 15 years, one parent/caregiver answered the questionnaire; while patients aged 15 to 17 years were encouraged to answer the questionnaire together with their parent/caregiver.

The Ethics Committee of the Capital Region of Denmark (H-19041695) and the Data Protection Agency (P-2020-659) approved the study.

The questionnaire covered baseline characteristics, referral pathways, and details of the 4 atopic diseases including symptoms and severity. In the analysis, parent/patient-reported diseases confirmed by a physician were used. Answers were multiple choice and/or blank space for comments.

All data were manually entered into REDCap (Research Electronic Data Capture; https://www.project-redcap.org/) by two investigators (GF and VL) (12, 13).

Statistical analysis

A χ^2 test was used to compare groups, but when expected values were below 5, Fisher's exact test was used instead. Normal distribution was assessed for the data. For non-parametric values (e.g. Visual Analog Scale [VAS] scores for severity), a Mann–Whitney *U* test was applied. We used logistic regression to calculate the odds ratio (OR) of being referred to a hospital, with AD, food allergy, asthma, and ARC as the independent variables.

P-values were considered as statistically significant if they were below 0.05. A 95% confidence interval was used for ORs.

Data management and statistical analyses were performed using R version 4.2.0 (R Core Team, 2022; R Foundation for Statistical Computing, Vienna, Austria), and SAS® Enterprise Guide®, version 7.15 (SAS Institute, Cary, NC, USA).

RESULTS

In total, 301 children and adolescents were included in the study and the completed questionnaire was returned by 279 (completion rate: 92.7%). In the subsequent analysis, only patients who completed the questionnaires were included. Of the 279 patients, 166 came from hospital departments and 113 from practising specialists. Patient characteristics are listed in **Table I**. Overall, median age was 10 years (CI 9–10). Approximately 80% of all patients had a family history of atopic diseases, mainly ARC (more than 60%). The socioeconomic differences (parent education, household income, parents living together) between patients from different inclusion sites were minor (Table SI).

Patients from the Department of Dermatology and the practising dermatologist differed slightly from the rest. They were younger compared with patients from other specialties (median 4 years [Department of Dermatology] and 0 years [practising dermatologist] vs ≥ 10 years [other specialties]). Dermatologic patients more commonly had a first-degree relative with AD compared with patients from other specialties (57% vs ≤32%) (see Table SI). Among patients with AD, there was no significant difference in the self-reported severity of AD within the last 6 months between those treated by practising specialists and those treated at hospital departments ($p = 0.12$). However, a significantly higher proportion of patients from hospital departments had required urgent visits to a physician within the previous 12 months due to AD (**Table II**).

Hospital vs practising specialists

The children were divided into 2 groups depending on their site of inclusion: hospital department or a practising specialist. Hospital patients more often had AD ($p = 9$ x

Table I. Characteristics of children 0–17 years with atopic dermatitis, food allergy, allergic rhinoconjunctivitis, and/or asthma

	All participants	Practising specialist % (*n*/*N* of total)	Hospital % (*n*/*N* of total)		
Factor	Total	Total	Total	Paediatric department	Dermatology department
Gender, boys	63% (175/277)	61% (68/112)	65% (107/165)	65% (79/122)	65% (28/43)
Age, years, median (95% CI)	10 (9–10)	10 (9–12)	9 (8–10)	10 (9–11)	4 (3–9)
Parents living together, yes	82% (227/277)	83% (93/112)	81% (134/165)	79% (96/121)	86% (38/44)
Family history of atopic diseases					
All	80% (220/274)	81% (89/110)	80% (131/164)	77% (94/122)	88% (37/42)
AD	36% (98/274)	32% (36/110)	38% (62/164)	31% (38/122)	57% (24/42)
Food allergy	29% (79/274)	28% (31/110)	29% (48/164)	26% (32/122)	38% (16/42)
ARC	62% (169/274)	60% (66/110)	63% (103/164)	62% (76/122)	64% (27/42)
Asthma	34% (94/274)	34% (38/110)	34% (56/164)	34% (42/122)	33% (14/42)
None	18% (49/274)	17% (19/110)	18% (30/164)	21% (26/122)	9% (4/42)

Data are summarized as percentage (number of total) or median (95% confidence interval).
AD: atopic dermatitis; ARC: allergic rhinoconjunctivitis; CI: confidence interval; *n*: number.

Table II. Distribution, severity, and impact of the children's atopic diseases stratified by inclusion site

Factor	Practising specialist % (*n*/*N* of total)	Hospital % (*n*/*N* of total)	*p*-values[b]
Distribution of diseases[a]			
AD	32% (36/111)	56% (92/163)	**9 x 10^{-5}**
Food allergy	21% (23/111)	52% (85/164)	**2 x 10^{-7}**
ARC	69% (77/111)	62% (99/159)	0.23
Asthma	37% (40/109)	51% (84/165)	**0.02**
Number of diseases			
1 disease	42% (45/107)	24% (38/157)	**0.002**
2 diseases	35% (37/107)	29% (46/157)	0.36
3 diseases	13% (14/107)	27% (42/157)	**0.008**
4 diseases	2% (2/107)	15% (24/157)	**0.0003**
Severity last 6 months, VAS 0–100 (0 is no symptoms and 100 is severe symptoms), mean (SD)			
AD	36 (31)	44 (28)	0.12
Food allergy	44 (30)	41 (33)	0.65
ARC	41 (26)	43 (25)	0.64
Asthma	29 (22)	27 (24)	0.38
Any days missed from day care and school in the previous 12 months due to the diseases, yes	26% (29/112)	39% (65/165)	**0.02**
1 to 2 days	9% (10/112)	12% (20/165)	0.40
< 1 week	10% (11/112)	17% (28/165)	0.09
1 week–1 month	4% (5/112)	6% (10/165)	0.76
> 1 month	1% (1/112)	3% (5/165)	0.41
Unknown	2% (2/112)	1% (2/165)	1
Urgent visits to a physician in the previous 12 months due to the diseases, yes	13% (15/113)	29% (48/166)	**0.002**
AD	3% (3/113)	10% (17/166)	**0.02**
Food allergy	2% (2/113)	8% (13/166)	**0.03**
ARC	3% (3/113)	2% (4/166)	1
Asthma	4% (5/113)	9% (15/166)	0.14
Other allergic symptoms	2% (2/113)	2% (4/166)	1
Affecting the family in general, scale 0–100 (0 is not affected and 100 is very affected), mean (SD)	27 (25)	34 (32)	0.33

[a]Parent/patient-reported physician-based diseases. [b]*P*-values were obtained using the χ^2 test, Fisher's exact test, Welch, and Student's *t*-test.
Data are summarized as percentage (number of total) or mean (SD).
AD: atopic dermatitis; ARC: allergic rhinoconjunctivitis; *n*: number; SD: standard deviation; VAS: visual analogue scale. Significant *p*-values ($p \leq 0.05$) are shown in bold.

10^{-5}), food allergy ($p = 2 \times 10^{-7}$) and/or asthma ($p = 0.02$) than patients from practising specialists; no differences were found in the number of patients with ARC (see Table II). Hospital patients were more likely to have 3 (27% vs 13%, $p = 0.008$) or all 4 of the atopic diseases (15% vs 2%, $p = 0.0003$) compared with patients from practising specialists, who often had only 1 of the diseases (42% vs 24%, $p = 0.002$).

There was no difference in the self-reported severity of the atopic diseases, how they affected the families' daily lives, and their quality of life (see Table II). However, 39% of patients from hospital departments had missed days from day care compared with 26% from practising specialists ($p = 0.02$), although no differences were found in the number of days missed. Besides planned visits to their physician, patients from hospital departments were more likely to require urgent visits (29% vs 13%, $p = 0.002$), because their AD flared up (10% vs 3%, $p = 0.02$) or their food allergy worsened (8% vs 2%, $p = 0.03$).

Referral pathways

Generally, about 80% of patients had previously consulted their GP regarding atopic disease and around 75% had either seen a practising specialist in the past or were seeing one at the time of study inclusion. Patients were divided into 2 groups depending on their number of atopic diseases: 164 had 1 or 2 diseases, and 81 had 3 or 4 diseases. In the group with ≥3 diseases, 80% received treatment at a hospital department, compared with 51% in the group with ≤2 diseases (OR 3.87, CI 2.07–7.24) (**Table III**). Patients from both groups followed the general referral pattern from their GP to a practising specialist or to a hospital department. No "common track" directly from general practitioner to hospital existed for patients with ≥3 atopic diseases (Table III) (**Fig. 1**). More than half of all patients had visited their GP only once or twice before their referral to a practising specialist or hospital department, and this typically occurred within 6 months of their first visit. Five percent of patients with 1 or 2 diseases, and 12% of patients with 3 or 4 diseases had consulted a private hospital or a private specialist, covered by either family resources or a private health insurance company.

Even though patients with more than 3 atopic diseases were referred to hospital, further analysis showed that

Table III. Referral pathways for children with atopic dermatitis, food allergy, allergic rhinoconjunctivitis, and/or asthma

Factor	Number of atopic diseases		OR (95% CI)
	1–2 diseases (*n* = 164)	≥ 3 diseases (*n* = 81)	
Referred to a hospital (total)	84	65	3.87 (2.07, 7.24)
From GP and practising specialist	31	38	3.73 (2.08, 6.71)
Instantly from GP	33	14	0.83 (0.42, 1.66)
Instantly from home	18	8	0.89 (0.37, 2.14)
Referred to practising specialist (total)	80	16	0.26 (0.14, 0.48)
From GP	72	15	0.29 (0.15, 0.55)
Instantly from home	8	1	0.24 (0.33, 1.98)

CI: confidence interval; GP: general practitioner; *n*: number; OR: odds ratio.

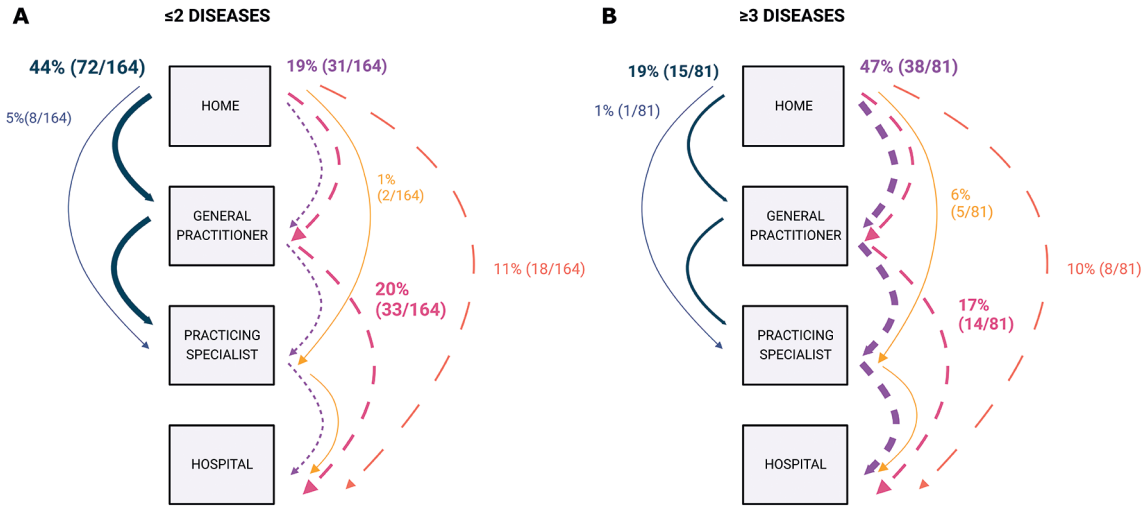

Fig. 1. Referral pathways for children 0 to 17 years with atopic dermatitis, food allergy, allergic rhinoconjunctivitis, and/or asthma stratified by number of diseases. (A) Children with ≤2 atopic diseases and (B) children with ≥3 atopic diseases. Each arrow shows the referral pathway for a group of patients. The width of the arrow illustrates the proportion of patients in each group, also shown as percentage and numbers in parentheses. On the left side in each figure are referral pathways ending at a practising specialist and on the right side referral pathways ending at a hospital. The figure was created with BioRender.com.

food allergy (OR 4.69, 2.07–10.61) was the primary determinant for the referral. Asthma (OR 2.58, 1.18–5.63) also played a role, but AD (OR 2.31, 0.97–5.52), ARC (OR 0.54, 0.25–1.17), or the fact of having ≥3 atopic diseases (OR 1.17, 0.34–4.04) had no influence.

DISCUSSION

This study provides new insight into the referral pathways in Denmark for children with atopic diseases. Children with 1 or 2 atopic disease(s) were often treated by practising specialists, while those with 3 or more atopic diseases were almost 4 times more likely to be referred to a hospital department. Subsequent analysis showed that food allergy and, to a lesser extent, asthma were the primary determinants for referral to a hospital department, rather than the number of diseases. We found no common track to hospital for patients with ≥3 diseases, and the general referral pattern was from the GP to a practising specialist and to a hospital department.

Previous referral pathway studies have been register-based in the main and often dealing with a single atopic disease (7, 14, 15). According to a study that included 2 atopic diseases, children with both AD and asthma visited hospital emergency departments and outpatient clinics more frequently than those with asthma alone (16). This is in line with our findings: that children with multiple atopic diseases were more frequently referred to a hospital department and a higher percentage needed urgent care. However, a corresponding study showed that adults with both AD and asthma, compared with adults with only 1 of these diseases, more frequently consulted their GP or a practising specialist rather than hospital departments (outpatient clinics) (17), indicating that the referral pathways for atopic diseases change from childhood to adulthood. Interestingly, when ARC was included in the study, adults with both AD and asthma more often had ARC consultations in a hospital than adults with only 1 of the diseases (17). This result supports our finding concerning multiple atopic diseases and hospital referrals.

We found that food allergy was a main determinant for referral to a hospital department and it might suggest that children with food allergy are primarily receiving medical investigation at hospital departments. This is consistent with Danish national guidelines that hospital-based allergy centres perform the diagnostic tests such as oral food challenges, and provide care for patients with food allergy and anaphylactic reactions (8). Both international and national recommendations from other countries are consistent with these guidelines (18, 19).

Another, albeit less significant, determinant that affected hospital referral was asthma. Previous research has emphasized the importance of receiving specialized care for severe asthma (20, 21), partly due to access to a greater variety of asthma treatments including biological treatment (21, 22).

We did not find a common track to hospital for children with multiple atopic diseases and many had seen both their GP and a practising specialist before a hospital referral. This may be due to the time-varying onset of the diseases (5, 6), as only 1 or 2 diseases had evolved at the time point for referral from their GP. However, there is ongoing work to categorize atopic diseases into various subtypes based on genetic factors and clinical characteristics (23, 24). One study showed that persistent AD might be predicted by a child's prior usage of especially potent AD medication (25). If these findings could be used to accurately predict how the diseases will

develop, they could help to determine where patients should be referred to get the best care at the right time.

Disease management programmes include stratification of patients, adopting a patient-centred approach and ensuring coherence in healthcare services (26). Clinical practice guidelines are part of these disease management programmes, yet a study revealed that within the scope of applied clinical practice standards in General Practice, fragmented healthcare was a concern for patients with multiple diseases (27). Further, it was difficult to integrate these patients' individual needs and preferences into the stratification, which, in any case, is not always accurate as the most vulnerable patients with fewer resources are often dismissed rapidly in the secondary and tertiary healthcare sectors because of, e.g., missed appointments or low adherence to treatment (27). The limited options to personalize guidelines are the main reasons for non-adherence, according to the Allergic Rhinitis and Its Impact on Asthma (ARIA) collaboration (28); but a personalized, integrated patient care approach has been suggested as a solution (28, 29).

Strengths and limitations

We included patients from practising specialists as well as from hospitals. To reduce selection and non-response bias, all eligible patients at, e.g., a hospital department on a given day were invited to participate, and they were encouraged to fill out the questionnaire while they were at the department. The completion rate in our study was 92.7%.

A potential limitation is recall bias, for example in the questions concerning previous experiences of referral pathways in the healthcare system. The patients in this study were children and adolescents, which meant that the onset of their disease(s) and referral pathways were within recent years, thus reducing the risk of recall bias. The primary and secondary healthcare sectors in Denmark use different electronic medical record systems that do not automatically share information. This made it difficult to confirm patients' responses concerning their referral pathways and we therefore had to rely on parent/patient-reported data.

Family history of atopic diseases was reported in the questionnaire, but we did not have data on family members' encounters with the healthcare system. Prior experience may influence expectations regarding referral to and navigation of the healthcare system.

Severity of the diseases was not clinically assessed, since we did not have validated patient/parent-reported measurements for all 4 diseases. We therefore chose to use VAS to assess severity, both for the specific day that patients completed the questionnaire, and for the previous 6 months, to ensure comparability and consistency across all 4 diseases. Furthermore, ARIA guidelines for ARC recommend the use of VAS to assess severity (28).

Conclusion

This study shows that children with multiple atopic diseases were more likely to be referred to hospital departments than to practising specialists, specifically for food allergies. Further research in the form of qualitative, in-depth interviews with the parents of children with atopic diseases could obtain more insight into their needs, experiences, and preferences.

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