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## Research Article

### ABO Blood Types in Atopic Dermatitis: A Danish Survey

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#### Abstract

**Introduction:** Atopic dermatitis (AD) is a multifactorial skin disease reducing quality of life in affected patients. This is partly due to lack of efficient treatment options that are currently limited to symptomatic management. The ABO blood type has been proposed as a predictive marker for a diverse range of pathogenesis, including dermatological conditions. The current study attempted to examine if any association exists between AD and the ABO blood type in Danish population.

**Methods:** A Danish questionnaire was developed and distributed online with the aid of the Atopic Eczema Association (Atopisk Eksem Forening). The questionnaire was open for two weeks. Statistical analysis was carried out on returned questionnaires from AD patients to identify whether certain blood types are more common among AD patients in Denmark.

**Results:** 60 AD patients with blood type A (28.3%), B (20.0%), AB (13.3%), and O (38.3%) were identified. Blood type B (OR=2.250, CI 95% 0.906-5.586) and AB (OR= 2.923, CI 95% 0.910-9.394) were found more frequent with AD, when comparison was done with ABO blood type distribution among Danes. No statistically significant difference was found between AD patients and the Danish population, in terms of having O or non-O blood types.

**Discussion:** Blood type B and AB showed a tendency of higher frequency among AD patients in the Danish population, which is in line with previous findings in other populations. These findings demonstrate the value of further investigation to identify a clear association between the ABO blood type and AD.

#### Introduction

Atopic dermatitis (AD) is a multifactorial, complex inflammatory skin disease characterized by severe itching, redness, and skin barrier disruption [1-3]. The occurrence of the disease varies worldwide, and the highest prevalence is found in industrialized countries, especially in Northern Europe with a life-time prevalence of 20-23% [3-5]. Recently, a mutation in the filaggrin (FLG) gene has been associated with AD [6]. Other studies suggest environmental factors such as climate, microbial exposure, and hygiene to be main drivers of the disease. Although the exact pathogenesis is not known, it is thought to be associated with hyperactivation of the immune system [7,8].

The clinical classification of AD patients varies depending on age and is additionally classified into either extrinsic or intrinsic, depending on the levels of IgE [7-9]. At present, no sufficient

treatment strategies are available, only the symptoms can be reduced [10]. The current treatment strategy does not take the classifications into consideration, leading to insufficient treatment of AD. Therefore, more individualized treatment is necessary, to facilitate a better management of the disease and possible increase in life quality [9].

In Denmark blood type A(44%) is more frequent than blood type O(41%), B(10%) and AB(5%) (<https://givblod.dk/fakta-om-blod/blodtyper/>). Some studies have demonstrated that non-O blood types might be associated with increased risk of developing several conditions such as cardiovascular diseases [11,12]. It has been suggested that an enzymatic dysregulation of glycosyltransferases might cause the association between various conditions and specific ABO blood types [12]. This may potentially influence immunological mechanisms, suggesting that the ABO blood type could affect development of skin diseases, in which

the immune system often plays an important role [13-15]. Balajee et al. suggested an increased risk of dermatophytosis with blood type A[16]. Some older studies [17,18] have identified incidence of ABO blood types in skin diseases. Only few studies have looked into an association between the ABO blood type and AD. In one study it was found that non-O blood types are more common in patients with atopic diseases [19]. A study of the Indian population demonstrated that non-O blood types were more frequent among AD patients [20]. However, no association between ABO blood type and AD has been examined in the Danish population. This study is an initial step for identifying if certain blood types are more prevalent among AD patients in Denmark.

## Methods

A Danish questionnaire was used to investigate the association between AD and the ABO blood types in Denmark. The questionnaire was distributed online, and quantitative and qualitative data were obtained and analyzed. According to the National Committee on Health Research Ethics guidelines, no ethical approval was needed.

### Questionnaire

In total, 12 questions were included in the questionnaire, which was prepared using SurveyXact (Version 12.6, Aarhus N, Denmark). Not all respondents received all 12 questions, as the process of reaching the next question depended on the given answers. Respondents were automatically excluded from the questionnaire, when stating they never suffered from AD.

The questionnaire consisted of two main parts. The first part focused on specific information about AD, treatment, and blood type. To ensure the reliability of answers regarding blood type, participants were asked how they knew it. Furthermore, the respondents were asked if they had other diseases than AD, to take confounding factors into consideration. The second part included demographic questions about age, gender, ethnicity, and country of residence. Questions were made as simple as possible, and additional background knowledge was provided where needed to avoid any misunderstandings. To obtain quantitative data, and to make sure answering the questionnaire would be straightforward, the questions were mainly designed as multiple choice. For answering some questions, it was possible to type a specific answer, if the provided choices did not apply. The average time to complete the questionnaire was approximately 4 minutes.

### Procedure

Before posting the questionnaire, pilot testing was carried out to ensure that the questions were clear. the Atopic Eczema Association (Atopisk Eksem Forening) assisted to distribute the link with the questionnaire for AD patients. The link was shared in two Facebook groups (Atopisk Eksem - Atopic Syndrome and Atopisk Dermatitis - Denmark) for people diagnosed and registered with AD, along with additional information about the study and how to complete the questionnaire. The participants were informed that the survey was anonymous and can be answered in less than 5 minutes. The questionnaire was available online for 2 weeks in November 2017, and reminders were posted in both Facebook groups.

### Statistical Analysis

Data analysis was carried out using SurveyXact and Excel 2013 (Microsoft Office Professional Plus 2013, version 15.0.4981.1001, Redmond, Washington, USA). Data were presented as numeric, percentages, and arithmetic means  $\pm$  standard deviation (SD). Statistics were performed using the Statistical Package for Social Sciences software (IBM SPSS, version 24, Armonk, New York, USA).

Odds ratios (OR) and 95% confidence intervals (CI) were calculated, to examine the association between the occurrence of each blood type in the AD patients and the Danish population. A Chi-squared Goodness-of-fit test was carried out to compare the blood type distribution in AD patients with the Danish blood type distribution. An assumption of this test is that 80% of the cells in the cross-tab have a value above 5. To meet this assumption, data from non-O blood groups were pooled together and compared to the O blood group.  $p \leq 0.05$  was considered statistically significant. Power of the Chi-squared Goodness-of-fit test was calculated using G\*Power (version 3.1.9.2, Franz Faul, Kiel University, Germany). Graphics were designed using GraphPad Prism 7 (La Jolla, California, USA).

### Results

In total, 125 returned questionnaires were included for analysis. Out of 125, 57 did not know their blood type, and 8 did not answer the question regarding blood type, leaving 60 respondents that were included for the final analysis. Out of the 60 respondents, 4 (6.7%) were males and 56 (93.3%) were females. The mean age of the respondents was  $37 \pm 12.08$  years within a range of 16-68 years (Table 1). The ethnic origin among the respondents included countries from Northern Europe (Denmark, Faroe Islands, Norway, Sweden, Germany, and Holland).

|                     |                           | A     | B     | AB     | O      | Total  |
|---------------------|---------------------------|-------|-------|--------|--------|--------|
| Respondents with AD |                           | 17    | 12    | 8      | 23     | 60     |
| Gender              | Men                       | 1     | 2     | 1      | -      | 4      |
|                     | Women                     | 16    | 10    | 7      | 23     | 56     |
| Age (years)         | Mean                      | 37.59 | 38.42 | 42.13  | 34.04  | 37     |
|                     | Standard deviation        | ±3.35 | ±9.92 | ±15.75 | ±10.21 | ±12.08 |
| Condition           | Diabetes                  | -     | -     | -      | -      | -      |
|                     | Allergy                   | 10    | 5     | 5      | 16     | 36     |
|                     | Cardiovascular diseases   | -     | -     | -      | -      | -      |
|                     | Other skin diseases       | -     | 2     | 1      | 1      | 4      |
|                     | Other diseases            | 2     | 2     | 3      | 1      | 8      |
|                     | No other disease          | 2     | 3     | 3      | 1      | 9      |
| Treatment           | Fat creme                 | 15    | 10    | 7      | 21     | 53     |
|                     | Corticosteroid creme      | 11    | 10    | 7      | 20     | 48     |
|                     | Corticosteroid tablets    | 2     | 5     | 3      | 3      | 13     |
|                     | Corticosteroid injections | -     | -     | -      | 2      | 2      |
|                     | Phototherapy              | 2     | 2     | 2      | 2      | 8      |
|                     | Other treatments          | 7     | 4     | 2      | 8      | 21     |
|                     | No treatment              | -     | 1     | -      | -      | 1      |

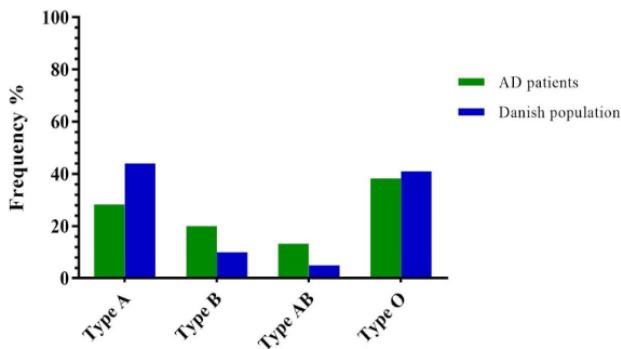
**Table 1:** Distribution of blood types among the 60 atopic dermatitis (AD) patients along with age, gender, indicated treatments, and other known conditions than AD. Data are presented as number of respondents. ±: standard deviation (SD).

One respondent stated, that no treatment was used against the eczema, while the remaining used one or several types of treatments. The most common treatments among all patients were fat creme (88.3%) and corticosteroid creme (80.0%). Corticosteroid injections (3.3%), corticosteroid tablets (21.7%), phototherapy (13.3%), and other treatments (35.0%), including other medications and alternative therapies were also stated (Table 1). No structured pattern was found between each blood type and used treatments.

The respondents were also asked about comorbidities, and 60% stated that they also suffered from allergy. Beyond that, no pattern was identified in other diseases present among the respondents.

Of the 60 AD patients included in the study, 23 (38.3%) had blood type O, 17 (28.3%) type A, 12 (20.0%) type B, and 8 (13.3%) type AB (Table 1). 81.7% of the patients knew their blood type from a blood type test, 3.3% were told from their parents, and 15.0% did not remember from where they knew their blood type or did not answer the question.

The ORs between the blood types in AD patients and the Danish population, showed that AD patients less often had blood type A and O (OR=0.503, CI 95% 0.250-1.000 and OR=0.895, CI 95% 0.4641.723, respectively) and more often had blood type B and AB (OR=2.250, CI 95% 0.906-5.586 and OR=2.923, CI 95% 0.9109.394, respectively) than the Danish population (Figure 1).



**Figure 1:** Frequencies of the blood types among atopic dermatitis (AD) patients (type A=28.3%, type B=20.0%, type AB=13.3%, and type O=38.3%) and the Danish population (type A=44.0%, type B=10.0%, type AB=5.0%, and type O=41.0%).

The Chi-squared Goodness-of-fit test, in which the distribution of the non-O and O blood type in AD patients was compared to the distribution in the Danish population, yielded no significant difference between the frequency of non-O and O blood types in the two groups ( $p=0.675$ ). The power of the test was 28.6%.

## Discussion

In the current study, the distribution of blood types among the included AD patients was compared to the general distribution of blood types in Denmark. A Chi squared Goodness-of-fit test revealed no significant difference when comparing the distribution of non-O and O blood types. The ORs indicated no significant difference between the distributions of each of the blood types in the AD patients, compared to the general Danish population. These results are contrary to previous findings from Gangopadhyay et al., who found significantly lower occurrence of blood type O in AD patients than in controls [20]. The correlation between multiple atopic diseases, including AD, and the ABO blood types was also investigated by Brachtel et al., wherein a higher incidence of blood type A and B was found among patients with atopic diseases, though it was not statistically significant [19]. Similarly, in this present study no significant difference was identified in the distribution of blood types among the AD patients and the general Danish population. Although, the ORs pointed towards a tendency that blood type B and AB were more prevalent among AD patients. Altogether, the above-mentioned studies and the current results indicate that blood type O might be less associated with AD.

In people with non-O blood types, either A, B or both antigens are expressed on the surface of not only erythrocytes, but also cells in the skin [21]. This implies that the presence of the B antigen might influence the development of AD, as it has been cited in the literature. Based on the tendencies observed in the current study, blood type B and AB might be associated with AD.

The association between the different blood types and AD has shown to differ slightly between various studies [19]. This might be explained by variations in the included AD patients from different parts of the world. The frequency of the blood types varies worldwide, and since research has shown that environmental factors affect the development of AD [4], both genetic distribution of ABO blood types and environmental factors may contribute to the diversity in the results. The AD patients in the current study are Danish, where the exposure to UV, outdoor temperatures, and microbial- and allergen exposures deviate from countries outside Scandinavia. Several of these mechanisms are proposed to affect the development of AD [6], and these factors may vary between the AD patients included in the different studies, emphasizing the challenge of comparing studies from different parts of the world.

The majority of patients included in the current study used treatment for their eczema, and in most cases several types of treatments were applied. That indicates how AD is a burden for the affected patients, being dependent on daily treatments or recurrent visits for phototherapy. This is also associated with increased costs from a societal point of view [3]. 60% of the patients included in this study were also affected by allergy, consistent with previous findings that AD often occurs along with other atopic diseases [3]. It has previously been proposed that prevention of AD might also inhibit or delay progression of the atopic march [22].

## Conclusion

The present study investigated the association between the ABO blood type and AD in Denmark. No statistically significant difference was found between AD patients with different blood types, even though blood type B and AB were more prevalent among AD patients. Based on previous studies and the recent findings, it is proposed that blood type O might be less associated with AD compared to other blood types. However, larger cohorts are required before any sharp conclusion can be made.

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