

ORIGINAL PAPER/PRACA ORYGINALNA

Ocular complications of atopic dermatitis in children and adolescents

Powikłania oczne w przebiegu atopowego zapalenia skóry u dzieci i młodzieży

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ABSTRACT

Introduction: Atopic dermatitis (AD) is a prevalent inflammatory skin disease, often starts in childhood and tends to flare up periodically. Patients with AD may be at higher risk of several ocular complications.

Aim: To evaluate the relationship of frequency, type, and severity of ophthalmic complications in children and adolescents with AD.

Material and methods: This study included 64 patients between ages 0 and 18 who were diagnosed with AD between January 1, 2020 and June 30, 2020. Hanifin and Rajka criteria were used for diagnosis of AD, and the SCORAD score was used to assess severity. Data were statistically analyzed using IBM SPSS 22.

Results: A total of 64 patients diagnosed with AD with a mean age of 40.4 (4–198) months were included in the study. Periocular AD findings were detected in 12 (21%) cases and ocular findings in 15 (23%) cases. AD lesions were observed in the facial region of 35 patients. The mean age of the patients was 99.6 (52–192) months in the group with ocular findings and 22.2 (4–198) months in the group without ocular findings; there was a statistically significant difference between the two groups ($p < 0.001$). While ophthalmic involvement correlated with periocular involvement ($r = 0.585$, $p < 0.001$) and facial involvement ($r = 0.281$, $p = 0.024$), there was no correlation between SCORAD and ocular involvement ($r_{pb} = 0.129$, $p = 0.31$).

Conclusions: It was observed that the risk of eye involvement was increased in girls, older children, and in cases with facial and periorbital involvement. This study demonstrated that severe ophthalmic complications are rare in children with mild AD, but the risk of ocular involvement increases with age and in those with facial and periocular involvement.

KEY WORDS

atopic dermatitis, child, SCORAD, conjunctivitis, cataract.

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INTRODUCTION

Atopic dermatitis (AD), also known as eczema and atopic eczema, is a common, chronic, and progressive skin disease characterized by edema, vesicles, and weeping lesions in the acute phase, and erythema and thickening of the skin (lichenification) in the chronic phase [1]. AD is one of the most common inflammatory diseases, affecting 20% of children and 10% of adults in developed countries. Today, these rates are increasing, especially in developed countries. Lifetime incidence of AD has demonstrated an increasing trend worldwide [2]. The disease most often develops in childhood and is characterized by recurrent eczema and lesions causing intense discomfort [3].

AD is not an isolated disease affecting only the skin, but a disease accompanied by disorders of other organs. Common comorbidities in addition to skin findings include gastrointestinal diseases (eosinophilic gastroenteritis), kidney diseases (idiopathic nephritic disorder), autoimmune diseases (autoimmune thyroiditis in children), and psychological and psychiatric disorders (sleep disorder, abnormal interpersonal relationships) [4]. Besides these systems, AD patients are at lifetime risk of eye complications related to the clinical findings of the disease [5]. Although AD lesions around the eyes are frequently seen in adulthood, they can lead to vision loss. Ocular complications of AD include blepharitis, keratoconjunctivitis, keratoconus, uveitis, cataract, and retinal detachment, and their incidence varies between 25% and 50% [6].

Although many previous studies have investigated ophthalmologic findings in AD [7], further studies are needed to determine which clinical conditions correlate with ophthalmologic complications and to allow for the application of appropriate prophylaxis and treatment in patients with AD.

AIM

The aim of this study was to evaluate the relationship of the frequency, type, and severity of ophthalmologic complications in children and adolescents with AD.

MATERIAL AND METHODS

PATIENTS AND STUDY DESIGN

Patients who applied to the hospital between January 1, 2020 and June 30, 2020 and met the diagnostic criteria for AD were included in this retrospective study, conducted within the protocol of the Helsinki Declaration. Ethical approval was obtained from the Advisory Board of Scientific Research Projects of the Yüksek İhtisas University prior to the onset of the study. Patients with pediatric

diseases that could cause ocular complications or ocular findings and patients with isolated ocular pathologies were excluded from the study. Hanifin and Rajka criteria were investigated for the diagnosis of AD; patients who met 3 major and 3 minor criteria were diagnosed with AD [8]. A total of 64 children aged 0–18 years who met the study criteria were included in the study. Detailed anamnesis was taken from all patients, and physical examinations were performed. The age, gender, onset of clinical findings of AD, history of treatment, comorbidities, and family history of disease of the patients were questioned. The severity of the disease was determined using the Severity Scoring of Atopic Dermatitis Index (SCORAD). A score of < 25 was considered mild, between ≥ 25 and ≤ 50 moderate, and > 50 as severe AD [9]. The patients were investigated for signs of periocular atopic dermatitis, atopic keratoconjunctivitis, keratoconus, tear dysfunction, cataracts, retinal detachment, glaucoma, bacterial blepharoconjunctivitis, herpetic eye disease, uveitis, and other AD-related eye complications, and examination findings were noted.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS software version 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for demographic variables (such as age, gender), and were expressed as number, percentage (%), ratio, median, interquartile range, mean, and standard deviation. The Shapiro-Wilk test was used to evaluate the suitability of the parameters for normality distribution. The χ^2 test and one-way ANOVA were used to assess the significance of difference between groups. The Kruskal-Wallis test was used for comparisons between parameters without normal distribution, and the Mann-Whitney *U* test was used to determine which group was the cause of the difference. Student's *t*-test was used for comparisons between two groups of normally distributed parameters, and the Mann-Whitney *U* test for parameters without normal distribution. The χ^2 test was used to compare qualitative data. A *p*-value less than 0.05 was considered statistically significant.

RESULTS

In this study, ophthalmologic examinations were performed on 64 patients (42 boys, 22 girls) diagnosed with AD, with a mean age of 40.4 (4–198) months. While 18 (28.1%) of the patients had a family history of AD, none of the patients had a family history of ophthalmologic disease. Mean age of onset of AD was 24.8 (4–72) months. AD lesions were observed in the facial region of 35 (54.6%) patients. In terms of treatment history,

53 (82.8%) patients previously used moisturizers and 27 (42.1%) used mild and moderately potent steroids. None of the patients had a history of using topical calcineurin inhibitors and steroid use around the eye region. Demographic and clinical characteristics of the patients are displayed in Table 1.

Ocular findings of AD were present in 15 (23%) patients, atopic keratoconjunctivitis (AKC) in 10, bacterial conjunctivitis in 2, blepharitis in 2, and amblyopia in 1 patient. None of the cases were observed to have severe ophthalmologic complications such as keratoconus or cataracts. The mean age of the patients in the group with ocular findings was 99.6 (52–192) months and 22.2 (4–198) months in the group without ocular findings; this difference was statistically significant ($p < 0.001$). Mean age of onset of AD was 62.8 (36–72) months in the group with ocular findings, and 13.2 (4–36) months in the group without ocular findings. There was a statistically significant difference between the two groups in terms of age of onset ($p < 0.001$). In addition, there was a statistically significant difference between the genders in terms of eye involvement ($p = 0.005$). It was observed that eye complications were more common among girls. The mean SCORAD score was 24.8 in the group with ocular findings and 22.7 in the group without ocular findings; there was no statistically significant difference between the two groups in terms of SCORAD scores ($p = 0.24$). Clinical characteristics of patients with and without ocular complications are presented in Table 2.

Three different periocular findings were observed in 12 (18%) cases; 8 had only Dennie-Morgan infraorbital folds (DMIF), 1 only orbital darkening, and both DMIF and orbital darkening were observed in 3 patients. Aside from these three findings, no other periocular findings were encountered. Prevalence of periorbital involvement was 80% among the patient group with eye involvement and 40% among the patient group without eye involvement; this difference was statistically significant ($p < 0.001$).

According to point-biserial correlation analysis, no correlation was found between AD severity according to SCORAD with ocular involvement ($r_{pb} = 0.129$, $p = 0.31$), facial involvement ($r_{pb} = -0.01$, $p = 0.991$), and periorbital involvement ($r_{pb} = -0.057$, $p = 0.656$).

A correlation was found between eye involvement and periocular involvement ($r = 0.585$, $p < 0.001$), demon-

TABLE 1. Demographic and clinical characteristics of the patients

Parameter	Results
Age [months]	40.4 (4–198)
SCORAD score	23.2 ± 7.0
Mean age of onset of disease [months]	24.86 (4–72)
Treatment history:	
Moisturizing	53 (82.8%)
Steroid	27 (42.1%)

strating a positive, moderate, statistically significant linear relationship between eye involvement and periocular involvement.

DISCUSSION

Atopic dermatitis is a chronic, inflammatory skin disease that may emerge with ocular comorbidities. Ocular complications are more common among individuals with AD compared to the general population and may cause morbidity [10]. Ophthalmologic examination is not routinely performed in AD cases, despite complications that may lead to vision loss [11]. In our study, ocular findings of 64 AD patients aged 0–18 years were evaluated. While the most common ocular finding among our cases was atopic keratoconjunctivitis, severe ocular complications of AD were not observed in any of our cases. According to studies performed in adult AD patients [12, 13], ocular findings of AD were rarer in children compared to adults. Ocular involvement was found to be more prevalent among cases with late onset, facial and periocular involvement, and older children and adolescents with AD.

In this study, the mean age of patients with ocular findings was 99.6 months, and was 22.2 months among those without ocular findings. There was a statistically significant difference between the two groups, demonstrating that ocular complications of AD occurred among older children and adolescents. Mean age of onset of AD was 62.8 months in patients with ocular findings, and 13.2 months in patients without ocular findings; there was a significant difference between the two groups. Accordingly, it was observed that eye complications of AD were more common in patients with late-onset disease. The patient group with ocular signs of AD consisted of

TABLE 2. Clinical characteristics of patients with and without ocular complications

Variable	With ocular complications (n = 15)	Without ocular complications (n = 49)	P-value
Face involvement (%)	80	48	0.024
SCORAD score	24.8	22.7	0.24
Periorbital involvement (%)	60	40	< 0.001

older patients with late-onset disease. This may be related to the fact that the ocular findings of AD are more common in adolescence [3]. Some studies have proposed that repetitive trauma secondary to eye rubbing and itching during the clinical course of the disease may also be the cause of ocular complications in AD [14, 15]. A significant proportion of very early-onset (3 months to 2 years) AD cases enter complete remission before the age of two; on the other hand, it is known that early-onset AD cases (2–6 years) are at high risk for chronic disease [16]. Longer and more severe exposure to traumas such as rubbing and itching of the eye during the chronic disease period may also be the reason why these complications are seen in older children and adolescents. It is known that the eye region is affected more frequently in adult women with AD [11]. In our study, it was observed that ocular findings were more common in the female group.

In our study, the rate of AD ocular findings (23.4%) among patients aged 0–18 was found to be lower than similar studies in the literature [6, 17]. In a study by Garrity and Liesegang, this rate was reported as 42.5% [12]. We believe that the lower rate in our study may be due to the younger patient population compared to other studies.

In general, eyelid and periocular skin involvement with spongiotic changes and lichenification occurs in 20–42% of cases. The most common periocular findings in AD are DMIF and orbital darkening [5]. First described in 1948, DMIF is characterized by wrinkles that form on the skin under the lower eyelids [18]. DMIF is a minor diagnostic criterion [8] for AD and is present in 84% of patients, with 78% sensitivity and 76% specificity. Orbital darkening is another minor criterion of AD defined by Hanifin-Rajka and has a lower sensitivity than DMIF. These two minor findings are not specific for AD and are known to occur in patients with allergic rhinitis and asthma [19]. Besides these, rarer periocular findings associated with AD include Hertoghe's sign (loss of the outer third of the eyebrow due to chronic itching), madarosis, ptosis, trichiasis, and lagophthalmos. In addition, malposition of the eyelid may develop as a result of scar formation [5].

In our study, periocular findings were detected in 12 (21%) cases, in whom 8 patients had only DMIF, 1 patient had only orbital darkening, and 3 patients had both DMIF and orbital darkening. Prevalence of periorbital involvement was 60% in the group with ocular findings and 40% in the group without ocular findings; the difference was statistically significant. In addition, a correlation between ocular findings and periocular involvement was observed; accordingly, there was a moderate statistically significant positive linear relationship between eye involvement and periocular involvement. DMIF is an indicator of atopy, and it was associated with atopy in AKC, which is the

most common ocular finding in our cases. The relationship between periocular ocular findings of AD and ocular findings detected in our study may be due to the fact that both clinical conditions are associated with atopy. Furthermore, Uehera [20] observed that DMIF was more prevalent among patients who had eczematous lesions of the lower eyelids compared to patients who did not. Although none of our cases had active eczematous lesions in their lower eyelids, they may have experienced such complaints in the past.

A large epidemiological study revealed a significantly higher prevalence of ophthalmic manifestations in the AD population compared to the general population, depending on disease severity [10]. These complications include blepharitis, keratoconjunctivitis, keratoconus, uveitis, subcapsular cataract, retinal detachment and ocular herpes simplex [5, 6], with prevalence in the range 25–50% [6]. The etiology of ophthalmic complications caused by AD is rather complicated and multifactorial. Immune system dysregulation, physical trauma caused by rubbing the eyes, genetic factors, and side effects of certain drugs used in treatment are thought to be affecting factors. While some of these complications occur during the chronic disease period, some of them occur suddenly, and it is important to note that both cases may result in vision loss [10].

Atopic keratoconjunctivitis is among the most common ophthalmic complications of AD [5]. AKC was first identified by Hogan in 1953 in an atopic patient group [21]. Conjunctivitis and keratitis risk is increased in adults with AD. Especially caused by multifactorial causes, AKC is an important health problem for AD patients. AD is present in 95% of AKC cases, and AKC is present in approximately 20–68% of AD patients. AKC is more common in adults than children and usually occurs in the second and fifth decades [5].

In our study, ophthalmic manifestations of AD were observed in 15 cases. In our study, the presence of allergy, skin prick tests, or specific IGEs were not examined, but when compared to the general population, it is known that aeroallergen sensitivity is higher in AD patients than in the general population [22]. Hence, the most common ophthalmic manifestation among our patients was AKC, as expected.

Disruption of skin barriers facilitates bacterial colonization, especially *S. aureus*, in patients with AD. Typically, bacterial blepharoconjunctivitis occurs when patients touch their eyes after scratching eczematous lesions [17]. In our study, it was found that ophthalmic involvement of AD was more common in patients with facial AD lesions. It was thought that this may be related to the fact that they infect the eyes by scratching the lesions on their face. This contamination process was thought to be further fa-

cilitated, considering that the study population comprised children and adolescents.

In a study by Thyssen *et al.*, adults with AD were found to have a significantly higher risk of developing conjunctivitis, keratitis, and keratoconus compared to the general population, depending on the severity of the disease [23]. In a study by Carmi *et al.* that included pediatric AD patients, no correlation was found between the severity of the disease and eye involvement. In our study, no relationship was found between disease severity and eye complications. The reason for this may be that although the study by Thyssen *et al.* covered the adult population, our study included the pediatric population, as in the study by Carmi *et al.* [6]. In addition, AD lesions are frequently observed on the cheeks in infants and on the face in children, unlike adults [16]. In our study, a statistically significant difference was found in terms of the presence of AD lesions on the face between the groups with and without ophthalmic manifestations. Furthermore, a correlation was demonstrated between facial involvement and eye involvement; there was a statistically significant weak positive linear correlation between facial involvement and eye involvement. The fact that the SCORAD scores of patients with and without ophthalmic manifestations were not statistically significantly different suggests that ocular involvement is more related to the localization of lesions than to the severity of the disease.

AD patients are ten times more likely to develop keratoconus than the general population. Although keratoconus may occur at a younger age and may progress more rapidly in AD [23], this complication was not observed in any of our cases. The risk of developing cataracts due to AD is quite low in childhood, but is an expected complication in advanced ages [24]. The exact pathogenic mechanisms of cataract development in AD are unclear. Although many studies have suggested that the development of cataract in patients with AD is directly related to facial involvement that causes repeated trauma secondary to rubbing and itching the eyes [14, 15], there are also studies that do not support this theory [25]. In our study, cataracts were not detected in any of the cases. The absence of these two major eye complications was attributed to the 0–18 age range of the study population.

There were certain limitations of our study, the most important of which is the inability to examine patients for the presence of allergy with the skin prick test or specific IgE. Another limitation was that the majority of our patients were young children and infants with mild AD. Additionally, the data of our study cannot be fully compared with similar studies in the literature, as those studies include adults. A strong point of our study is that it is one of the few studies to evaluate ophthalmic manifestations of AD in rare pediatric and adolescent cases.

In this study, it was determined that severe ophthalmic complications are rare in young children with mild AD, and eye complications are more common in those with facial and periocular involvement, regardless of the severity of the disease.

Although severe ophthalmic manifestations found in adults are not encountered in children with AD, ocular involvement, regardless of the severity of the disease, may indicate the presence of eye involvement in mild cases, which may delay the diagnosis of complications as late as the progression of vision loss. Cases with facial and periocular involvement should be carefully followed up in terms of ocular findings to prevent delayed diagnosis and treatment. Eye examinations should also be performed routinely in patients diagnosed with AD, a disease which has potential complications that can lead to vision loss.

In memory of Mert Şimşek.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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