


# Prevalence, incidence and epidemiology of childhood uveitis

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## ABSTRACT.

**Purpose:** To analyse the prevalence, incidence and aetiology of paediatric uveitis.

**Methods:** A retrospective, population-based cohort study of Finnish children with uveitis in Northern Ostrobothnia Hospital District in 2008–2017. The data included parameters for age, gender, age at diagnosis, laterality, chronicity, anatomical distribution of the disease, aetiology and systemic association.

**Results:** One hundred fifty patients aged <16 years (mean age  $6.9 \pm 3.9$  years) with uveitis were included, out of whom 53% were girls. The first uveitis episode occurred at 1–6 years in 59%, and 62% of them were girls. In the age group of 7–15 years, boys were diagnosed with uveitis more frequently than girls (61% versus 39%, respectively). Seventy percent of the girls were diagnosed with their first uveitis episode at the age of 1–6 years, whereas only 48% of the boys were diagnosed at that age. The prevalence of uveitis increased from 64/100 000 children <16 years in 2008 (95% CI, 47.7–84.2) to 106/100 000 in 2017 (95% CI, 84.6–130.2). The incidence of childhood uveitis in 2008–2017 was 14/100 000 person-years in children <16 years (95% CI, 11.3–16.5). Eighty-seven percent of the cases were non-infectious, 9% were infectious, and 3% had masquerade syndromes. Sixty-one percent of patients had juvenile idiopathic arthritis (JIA).

**Conclusion:** The prevalence of paediatric uveitis has increased during the last decade in both genders. Uveitis is more frequent in girls, and they were diagnosed at a younger age than boys. Idiopathic cases and JIA accounted for a majority of aetiological features.

**Key words:** childhood – epidemiology – incidence – prevalence – uveitis

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The present study was supported by the grants from Eye Foundation, Eye and Tissue Bank Foundation, Mary and Georg C. Ehrnrooths Foundation and Finnish Ophthalmological Society.

Acta Ophthalmol. 2021; 99: e160–e163

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doi: 10.1111/aos.14535

## Introduction

Uveitis in children is relatively uncommon, accounting for 2–20 % of all uveitis cases worldwide (BenEzra et al. 2005; Nagpal et al. 2008; Chan et al. 2018; LaMattina & Koreishi 2018; Al-Haddad et al. 2019). The causes of uveitis in children may be non-infectious, infectious, caused by masquerade syndromes or related to systemic disorders but vary from those of adults (Smith et al. 2009; Ferrara et al. 2019). Juvenile idiopathic arthritis (JIA) is primarily associated with uveitis in children and is also a main cause for visual loss in paediatric patients (Mehta et al. 2013). The majority of paediatric uveitis is idiopathic, but the aetiological features vary greatly depending on the ethnic and geographic distribution, for example 97% of the childhood uveitis cases in the United States are non-infectious whereas infectious aetiologies in Colombia and JIA in Europe are the leading causes for paediatric uveitis (Chan et al. 2018; Lonngi et al. 2016; Ferrara et al. 2019).

Recent studies from Southern Finland and other Nordic countries have revealed a prevalence of 16–25% in childhood uveitis within JIA patients depending on study population (Kotaniemi et al. 1999; Kotaniemi et al. 2001; Kotaniemi et al. 2014; Nordal et al. 2017). Paediatric uveitis has been estimated to affect three in 100 000 children worldwide (Hamade et al. 2009;

Paroli et al. 2009; Rahimi et al. 2016; Curragh et al. 2017; Venkatesh & Takkar 2018).

Because of a great regional variability in the aetiology and the lack of up-to-date knowledge of local patterns of the disease, we evaluated the causes of childhood uveitis in Northern Finland. Previous studies of uveitis in the area are from the 1970s (Saari et al. 1975; Miettinen 1977). In addition, the prevalence and the incidence of uveitis in the current population-based paediatric cohort of age <16 years were assessed.

## Material

This work was carried out at Oulu University Hospital. The study followed the tenets of the Declaration of Helsinki, and it was conducted with the approval of the Oulu University Hospital Research Committee (89/2017).

The retrospective interventional case series was performed on all paediatric patients <16 years of age who presented at Oulu University Hospital with uveitis between 1 January 2008 and 31 December 2017. All cases of paediatric uveitis in the area are included in the study. The hospital's electronic patient database was used to search for the patients with uveitis by using the International Classification of Diseases-10 diagnose codes for anterior (H20.0 and H20.1), intermediate (H30.2) or posterior uveitis (H30.0-H30.9). Demographic data were collected and included parameters for age, gender, age during first episode, laterality, chronicity, anatomical distribution of the disease, aetiology and systemic association. Classification of the anatomical location and chronicity of uveitis was based on the Standardization of Uveitis Nomenclature classification (Jabs et al. 2005). We also classified patients according to their aetiology as non-infectious, infectious or masquerade. Juvenile idiopathic arthritis (JIA) was diagnosed in children according to the International League of Associations for Rheumatology Classification (Petty et al. 2004) and screening and the follow-up for JIA-uveitis was carried out according to the screening guidelines described earlier by Heiligenhaus et al. (2013). The prevalence of uveitis was determined in 2008 and in 2017, and the average incidence of childhood uveitis

was studied during the years 2008–2017. At the same time period, the average number of 1- to 15-year-old children was 81 528 in the area served by Oulu University Hospital. The population data were offered by Statistics Finland. The prevalence figures were calculated per 100 000 children and are presented with 95% confidence intervals (95% CI). The incidence of childhood uveitis was calculated per 100 000 person-years among children <16 years.

## Results

A total of 150 paediatric patients aged <16 years, who had been diagnosed with uveitis between the years 2008–2017, were included into the current retrospective, observational study. The mean age of the patients was  $6.9 \pm 3.9$  years (range 1–15), out of whom 53% ( $n = 79$ ) were girls. Over half (55%,  $n = 88$ ) of the patients had their first uveitis episode at the age of 1–6 years. Most of the patients (62%) diagnosed with uveitis at the age of 1–6 years were girls. In the age group of 7–15 years, boys were diagnosed with uveitis more frequently than girls (61% versus 39%, respectively). Seventy per cent of the girls were diagnosed with their first uveitis episode at the age of 1–6 years, whereas only 48% of the boys were diagnosed at that early age. HLA-B27-association was documented in 30 out of 131 patients (23%) evaluated for HLA-B27 status, and there was no statistical difference between the genders (25% in girls versus 21% in boys). Anti-nuclear antibody  $\geq 160$  was noted in 60 out of 133 patients (45%) evaluated, more commonly in girls (42 out of 74, 57%) compared with boys (18 out of 59, 31%). Serum auto-antibody ACE was evaluated from 40 of the patients but none of them had an ACE-level over the diagnostic value (112 U/l).

Uveitis was bilateral in 56% of the cases (62% in girls and 49% in boys). Anterior uveitis was present in 93%, intermediate in 5% and panuveitis in 2% of the patients (Table 1). None of the children had posterior uveitis. The course of the disease was acute in 22%, recurrent in 15% and chronic in 63%. Gender distributions of chronicity and the anatomical location of the disease are shown in Table 1.

The overall prevalence of uveitis was 64/100 000 children aged 1–15 years in 2008 ( $n = 51$ , 95% CI, 47.7–84.2) and 106/100 000 in 2017 ( $n = 87$ , 95% CI, 84.6–130.2). The uveitis prevalence in girls aged <16 years was 70/100 000 ( $n = 27$ , 95% CI, 46.0–101.5) in 2008 and 119/100 000 ( $n = 48$ , 95% CI, 88.0–158.3) in 2017. In 1- to 15-year-old boys the uveitis prevalence increased from 59/100 000 ( $n = 24$ , 95% CI, 37.5–87.2) in 2008 to 92/100 000 ( $n = 39$ , 95% CI, 65.7–126.3) in 2017.

The average incidence of paediatric uveitis during the years 2008–2017 was 14/100 000 children <16 years of age ( $n = 112$ , 95% CI, 11.3–16.5). There was no statistically significant difference between the genders in the incidence of uveitis [14/100 000 ( $n = 54$ , 95% CI, 10.2–17.7) in girls versus 14/100 000 ( $n = 58$ , 95% CI, 10.5–17.9) in boys].

Eighty-nine percent were found to be non-infectious in aetiology. Eighteen percent of the uveitis in children was idiopathic. Juvenile idiopathic arthritis (JIA) was the most frequent systemic association in the study cohort in 61% of all patients. In girls, JIA accounted for 76% of the systemic associations, whereas JIA was less common in boys (49%). Tubulointerstitial nephritis and associated uveitis syndrome were the second most common aetiological features diagnosed in one girl and five boys. Infectious cases accounted for 9%, and four of the patients (3%) had masquerade syndromes. All aetiological factors and gender distribution are presented in Table 2.

## Discussion

Uveitis in children differs from adult-onset disease and can often be challenging to diagnose in accordance to diagnostic and therapeutic aspects. Children with uveitis are mostly asymptomatic, or may not be able to verbalize possible complaints, which may lead to a delay in diagnosis (Pilly et al. 2013; Mehta et al. 2013). In addition, performing a comprehensive eye examination in a young child may be difficult. Childhood uveitis is commonly anterior, bilateral, chronic, recurrent and resistant to treatment, which all increase the risk of developing vision-threatening complications

**Table 1.** The course and anatomic classification of paediatric patients with uveitis.

Number (%)	Female	Male	All
<b>Course of uveitis</b>			
Acute	13 (16)	20 (28)	33 (22)
Recurrent	15 (19)	8 (11)	23 (15)
Chronic	51 (65)	43 (61)	94 (63)
All	79 (100)	71 (100)	150 (100)
<b>Type of uveitis</b>			
Anterior uveitis	75 (95)	65 (92)	140 (93)
Intermediate uveitis	4 (5)	3 (4)	7 (5)
Posterior uveitis	0 (0)	0 (0)	0 (0)
Panuveitis	0 (0)	3 (4)	3 (2)
All	79 (100)	71 (100)	150 (100)

Anatomic classification is based on the Standardization of Uveitis Nomenclature for reporting clinical data.

**Table 2.** Aetiology of uveitides. Some patients had several aetiological features.

Aetiology Number (%)	Female	Male	All
Non-infectious (all)	73 (92)	60 (85)	133 (89)
Idiopathic	10 (13)	17 (24)	27 (18)
Systemic disease (all)	61 (77)	38 (54)	99 (66)
JIA	60 (76)	35 (49)	95 (61)
TINU	1 (1)	4 (6)	5 (3)
Kawasaki disease	0 (0)	1 (1)	1 (<1)
Scleroderma	0 (0)	1 (1)	1 (<1)
Postoperative	2 (3)	1 (1)	3 (2)
Post-traumatic	0 (0)	4 (6)	4 (3)
Infectious (all)	6 (8)	7 (10)	13 (9)
Chickenpox	4 (5)	5 (7)	9 (6)
Other	2 (3)	2 (3)	4 (3)
Masquerade (all)	0 (0)	4 (6)	4 (3)
HOGA	0 (0)	1 (1)	1 (<1)
Coats	0 (0)	2 (3)	2 (1)
PHPV	0 (0)	1 (1)	1 (<1)
All	79 (100)	71 (100)	150 (100)

HOGA = hyperornithinaemia gyrate atrophy, JIA = juvenile idiopathic arthritis, PHPV = persistent hyperplastic primary vitreous, TINU = tubulointerstitial nephritis and uveitis.

(Chan et al. 2014). Complications of uveitis, such as cataract, glaucoma, amblyopia and band keratopathy, may be present already during an early phase of the disease and may have lifelong sequelae on the visual function of young patients (Pilly et al. 2013, Chan et al. 2014, Al-Haddad et al. 2019).

In the previous Finnish study published in 2000, the overall incidence and prevalence of childhood uveitis were 4.3/100 000 and 27.9/100 000 in Turku area in Southern Finland, respectively (Päivönsalo-Hietanen et al. 2000). Our results show the increased incidence of paediatric uveitis in up to 14/100 000 children ≤16 years during the years 2008–2017. In addition, the prevalence of uveitis in children has increased by 50% from 2008

to 2017 in both genders and doubled during the past two decades (Päivönsalo-Hietanen et al. 2000). This might be explained by the rising prevalence of JIA in children (Marzetti et al. 2017), and possibly by more accurate monitoring of uveitis and developed diagnostic methods in paediatric patients with JIA during the last decade (Heiligenhaus et al. 2013). Children also tend to be diagnosed with uveitis at younger age, which may affect the overall prevalence. Girls were more commonly affected than boys in our cohort, which is in agreement with the previous studies (Paroli et al. 2009; Rahimi et al. 2016; Lonngi et al. 2016; Curragh et al. 2017). In contrast, male predominance has also been shown, for example, in India (Hamade et al. 2009; Venkatesh & Takkar 2018).

The mean age of uveitis onset in our patients was 6.9 years (median 5 years), which is less than 7.7–12.5 years reported in several studies previously (Smith et al. 2009; Paroli et al., 2009; Couto et al. 2016; Lonngi et al. 2016; Rahimi et al. 2016; Al-Haddad et al. 2019; Ferrara et al. 2019). Girls were diagnosed with uveitis even earlier, at the average age of 6.2 years, whereas boys were diagnosed at 7.6 years on average. In part, this difference might be explained by regional variability in healthcare organizations and management of uveitis screening in children. The asymptomatic nature of childhood uveitis and difficulties of comprehensive eye evaluation in children can also lead to the delay in diagnosis of uveitis. The associated aetiological features may affect the time-course of the uveitis onset as well, for example in most patients with JIA-uveitis develops during the first 4 years of the disease (Kotaniemi et al. 2014).

The aetiology of paediatric uveitis varies worldwide. In developed countries, non-infectious autoimmune aetiology predominates, whereas infectious aetiology is more common in developing countries (La Mattina & Koreishi 2018). In agreement with this, 89% of the uveitis cases in children were non-infectious and only a minority of the cases in the present study were of infectious background. Several studies have shown that JIA accounts for 9–48% of the systemic association of paediatric non-infectious uveitis (Hamade et al. 2009; Rahimi et al. 2016; Curragh et al. 2017). In our cohort, the amount of children with uveitis associated with JIA was even higher, 61%, and only one fifth was idiopathic.

In conclusion, the incidence and prevalence of childhood uveitis have markedly increased during the last decade. Most of the cases were non-infectious. In addition, young age, female gender and JIA seem to be predictive factors for paediatric uveitis. Regular screening of uveitis and reliably performed eye examination in paediatric JIA patients is of great importance for preventing the development of ocular complications and visual loss due to delayed diagnosis and treatment of uveitis. The specific challenges of children’s eye examination and the beneficial investments for

the long-term, continual patient relationships should be kept in mind.

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Received on February 21st, 2020.

Accepted on June 3rd, 2020.

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The present study was supported by the grants from Eye Foundation, Eye and Tissue Bank Foundation, Mary and Georg C. Ehrnrooths Foundation and Finnish Ophthalmological Society.