

The effect of patient compliance on remission rates in pediatric noninfectious uveitis



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PURPOSE	To identify barriers to compliance in pediatric noninfectious uveitis, and to examine its association with achieving steroid-free remission.
METHODS	A retrospective analysis was performed on pediatric patients with noninfectious uveitis on immunomodulatory therapy treated at the University of Texas Southwestern Medical School and Children's Medical Center (Dallas, TX) between September 2015 and March 2017. Compliance barriers were identified and rates of achieving steroid-free remission were calculated.
RESULTS	A total of 57 patients with noninfectious uveitis requiring immunosuppressive therapy met inclusion criteria. Thirty-three (58%) of patients were compliant. Notable barriers to compliance included regimens requiring >3 medications, patient/parent negligence, transportation issues, family strife, and presence of an associated systemic autoimmune disease ($P < 0.050$). At a median follow-up of 24 months, a total of 28 (49%) achieved steroid-free remission. The presence of 3 or more compliance barriers was associated with decreased remission rates ($P < 0.050$). Poor compliance was associated with decreased rates of steroid-free remission (21% vs 79% [$P = 0.002$]).
CONCLUSIONS	Noncompliant patients with noninfectious pediatric uveitis requiring immunomodulatory therapy were found to have a lower rate of achieving steroid-free remission compared to patients who exhibited full compliance. (J AAPOS 2019;23:334.e1-6)

Uveitis is a diverse group of intraocular inflammatory conditions primarily involving the uvea and choroid and sometimes secondarily involving other ocular structures. The estimated prevalence of noninfectious pediatric uveitis increases with age and ranges from 0.003% to 0.03%.¹⁻⁴ Chronic uveitis in the pediatric population carries high visual morbidity. Up to half of the pediatric uveitis patients develop permanent visual sequelae, and up to one-quarter of them progress to legal blindness.^{1,5,6}

Pediatric uveitis patients are often burdened with a chronic clinical course requiring long-term immunomodulatory treatment.⁶ Patient compliance and adherence have long been recognized to be key elements in treatment success in a vast spectrum of chronic medical conditions.^{7,8}

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The World Health Organization categorizes compliance factors into socioeconomic, patient-related, disease-related, treatment-related, and healthcare system-related issues.⁹ The literature attempting to classify methods to improve uveitis treatment compliance or treatment outcomes is limited. The purpose of our study is to identify compliance barriers and investigate the association of patient compliance on the success rates of achieving the treatment end goal of steroid-free remission in noninfectious uveitis.¹⁰

Subjects and Methods

This study was approved by the Institutional Review Board at University of Texas Medical School and Children's Medical Center (Dallas, TX). Our research methods adhered to the tenets of the Declaration of Helsinki and were compliant with the US Health Insurance Portability and Accountability Act of 1996.

The medical records of pediatric patients with noninfectious uveitis treated at the University of Texas Medical School and Children's Medical Center (Dallas, TX) were reviewed retrospectively. The electronic medical records were searched for all patients treated by the uveitis fellowship-trained specialist (JHC). Patients with chronic, noninfectious uveitis requiring immunosuppressive therapy who were evaluated by a single fellowship-trained uveitis specialist (JHC) between September 2015 and March 2017 with a minimum follow-up of 12 months were identified. Only patients who had active inflammation at some point

during their treatment course were included. Patients with <3 visits over the study interval or who had ocular inflammation secondary to infectious and malignant etiologies were excluded. Patients without a diagnosis of uveitis or who were not managed by the uveitis specialist (eg, patients seen for a one-time second opinion) were excluded. Demographic data collected included age, race, sex, and laterality. Diagnosis, final logMAR visual acuity, method of medication administration (topical, oral, subcutaneous, intravenous, and otherwise), presence of an associated systemic disease, and disease remission status at the last clinic visit were recorded. Charts were reviewed to determine compliance over the most recent 12 months of treatment and then reviewed directly with the uveitis provider.

A fellowship-trained uveitis subspecialist (JHC) examined and directly managed all treatment. Uveitis was classified according to the Standardization of Uveitis Nomenclature (SUN) criteria.¹¹ Disease remission was defined as <0.5+ anterior chamber cell, in the absence of haze or other clinical findings suggestive of disease activity on dilated fundus examination. Remission was confirmed by lack of activity on fluorescein angiography in cases of known or suspected posterior involvement. Steroid-free remission was defined as disease remission in the absence of corticosteroid therapy of any form (topical, periocular, oral, intravenous, or otherwise) for over 90 consecutive days. Patients who had perioperative steroid on board (eg, cataract surgery) were included in the category of steroid-free remission as long as they had had a minimum of 90 days of steroid-free remission prior to surgery and concluded steroid therapy within 90 days postoperatively.

As a practice pattern, the uveitis specialist was very meticulous in routinely inquiring and managing compliance barriers, particularly given that this clinic's population was comprised mostly of indigent patients with multiple and often complex financial and social needs. Compliance barriers were also assessed with every breakthrough flare, treatment failure, and during the decision-making process for each change in medication and/or dose. The uveitis specialist was also meticulous about documentation of compliance barriers in the chart and any follow-up with social work, foster care, the financial assistance office, and/or Child Protective Services (CPS), when applicable. Barriers to compliance were included in the analysis if they were noted at any visit within the 12-month study period. Noncompliance was defined as the presence of admitted and/or suspected deviance from the recommended treatment regimen or clinic visits, as noted in the record. For subanalysis, intermittent compliance was defined as patients who had periods of >3 months in which patient and family reported compliance, followed by periods of noncompliance.

Compliance barriers, subcategorized based on the WHO classifications for compliance factors, were identified as follows: socioeconomic (cost of treatment), patient-related (patient/parental neglect, transportation issues, poor health literacy, family strife, puberty, school absences, parental work issues, language barriers), disease-related (systemic disease, complex medical problems requiring multi-subspecialty care), treatment-related (side effects), and healthcare system related issues (access barriers due to insurance, undocumented immigrant status).⁹ Poor health literacy was defined as the inability to understand or verbally explain a basic 1-2 sentence definition of uveitis or purpose of

treatment, despite repeated one-on-one counseling with the uveitis specialist. This involved the use of a live and/or phone interpreter in the patient's primary language, when applicable. Family strife was defined as the presence of conflict or disagreement between parents regarding care and/or treatment decisions, non-amicable marital separation, the presence of a different relative or friend (who was most often unknowledgeable in the diagnosis or treatment of the patient) at every visit, or presence of any issues with guardianship, foster care, or CPS involvement. The presence of any barrier was defined as a compliance barrier when the patient, parent, or caregiver reported that the barrier hindered attending appointments and/or adhering to treatment regimen. Presence of compliance barriers was counted if it was present in any of the visit notes during the 12-month study period. In cases of variable and intermittent compliance, disease remission status during periods of compliance versus poor compliance were also compared. Rates of attendance to clinic and infusion appointments (total number of appointments attended by the patient divided by the overall number of scheduled appointments) were recorded. For those patients who achieved steroid-free remission, time to reach this treatment milestone was recorded.

Statistical analyses were performed using SPSS 25.0 (SPSS Inc, Chicago, IL) software package. When applicable, χ^2 analysis and/or the Fisher exact test were used to determine the relationships between our cohort characteristics and whether or not the following endpoints were achieved: steroid-free remission, compliance with treatment, and having the presence of ≥ 3 compliance barriers. Two-sided *P* values were recorded. Time to steroid-free remission was analyzed using Kaplan-Meier curves. Interquartile ranges were determined by log rank methods. Binary logistic regression analysis, using backward conditional entry of variables, was utilized to identify any statistical relationships between our 14 identified compliance barriers and the presence of steroid-free remission.

Results

Patient Characteristics

A total of 67 patients with noninfectious uveitis actively managed by the fellowship-trained uveitis subspecialist were identified. Fifty-seven patients had a minimum follow-up of 12 months and were included in this study. Baseline demographics are included in [Table 1](#).

There was a better logMAR visual acuity in the worse-seeing eye of the steroid-free remission cohort compared with the non-remission cohort (0.22 ± 0.25 vs 0.4 ± 0.31 [$P = 0.038$]). There was no difference in the logMAR visual acuity of the worse-seeing eye in the compliant group compared with the noncompliant group (0.25 ± 0.25 vs 0.39 ± 0.33 [$P = 0.130$]).

Time to Steroid-Free Remission

The median clinic follow-up time from presentation to the uveitis clinic was 24 months (IQR, 22-31), with 28 patients (49%) achieving steroid-free remission. The median time to steroid-free remission was 4 months (IQR, 2-9). There was a trend toward faster time to steroid-free remission

Table 1. Patient demographics and baseline characteristics^a

Patient characteristic	Total ^b	Compliant ^b	Noncompliant ^b	P value ^c
Sex				0.999
Male	32 (56)	14 (43)	11 (34)	—
Female	25 (44)	19 (76)	13 (52)	—
Age, years				0.788
Median	12 [9-16]	12 [9-16]	12 [10-15]	—
<12	26 (46)	16 (62)	10 (38)	—
≥12	31 (54)	17 (55)	14 (45)	—
Race				0.601
White	14 (25)	7 (50)	7 (50)	—
Black	14 (25)	7 (50)	7 (50)	—
Hispanic	25 (43)	17 (68)	8 (32)	—
Other	4 (7)	2 (50)	2 (50)	—
Eyes				0.631
Bilateral	53 (93)	30 (57)	23 (43)	—
Unilateral	4 (7)	3 (75)	1 (25)	—
Systemic diagnosis				—
JIA only	11 (65)	6 (55)	5 (45)	—
HLA B27+	1 (6)	1 (100)	0 (0)	—
JIA and HLA-B27+	2 (12)	0 (0)	2 (100)	—
Neurosarcoidosis	2 (12)	1 (50)	1 (50)	—
VKH	1 (6)	0 (0)	1 (100)	—
Diagnosis				0.999
Anterior uveitis	15 (26)	10 (67)	5 (33)	—
Intermediate uveitis	18 (32)	10 (56)	8 (44)	—
Posterior uveitis	0 (0)	0 (0)	0 (0)	—
Panuveitis	23 (40)	12 (52)	11 (48)	—
Scleritis	1 (2)	1 (100)	0 (0)	—
BCVA, logMAR				—
BSE median	0.050 [0-0.200]	0 [0-0.150]	0.100 [0-0.200]	—
WSE median	0.300 [0-0.425]	0.200 [0-0.400]	0.300 [0.150-0.600]	—

BCVA, best-corrected visual acuity; HLA-B27+, human leukocyte antigen B27; IQR, interquartile range; JIA, juvenile idiopathic arthritis; VKH, Vogt-Koyanagi-Harada disease.

^aAll of the 57 patients included had a diagnosis of chronic autoimmune uveitis requiring immunosuppressive therapy.

^bUnless otherwise indicated, results are numbers of patients. Percentages are given in parentheses; IQRs, in square brackets.

^cP values determined by the Fisher exact test.

(≤6 months) in patients with anterior uveitis compared with those with posterior involvement (90% vs 54% [$P = 0.060$]). Patients with pars planitis often took longer than 6 months to achieve steroid-free remission compared with patients with other ocular diagnoses (75% vs 21% [$P = 0.067$]). However, there was no difference in rates of compliance between patients with pars planitis versus non-pars planitis cohorts (59% vs 56% [$P = 0.811$]). Figure 1 includes a Kaplan-Meier curve of the time to steroid-free remission in the compliant versus noncompliant groups and in patients with ≥3 versus <3 cumulative barriers.

Compliance

The overall compliance rate in our cohort was 58% (33/57). In the compliant group, a higher percentage of patients achieved steroid-free remission than in the noncompliant group (22/28 [79%] vs 6/28 [21%]; $P = 0.002$). See Table 2. A subanalysis was performed on patients who had intermittent and poor compliance. Forty-four patients (77%) were quiet when compliant but had active inflammation when noncompliant, with 28 (64%) achieving steroid-free remission at some point in their treatment course. Ten

subjects (18%) never exhibited enough compliance to determine whether their regimen would allow them to achieve disease quiescence for a period of time >90 days. Median show rate to infusion appointment was 81% in the steroid-free remission group (range, 73%-90%) and 74% (range, 60%-85%) in the non-remission group. Median show rate to clinic appointment was 85% (77%-90%) in the steroid-free remission group and 71% (66-84%) in the non-remission group.

Compliance Barriers

The overall prevalence of compliance barriers is provided in Table 3. Barriers to compliance that had an associated adverse effect on achieving steroid-free remission were patient/parent negligence, transportation issues, family strife, and the presence of a systemic autoimmune disease associated with uveitis ($P < 0.050$). The presence of 3 or more compliance barriers was associated with decreased rates of steroid-free remission ($P = 0.011$). See Figure 2. Patients with fewer than 3 medications had a higher rate of steroid-free remission (56% vs 11% [$P = 0.025$]). There was no association between the route of medication

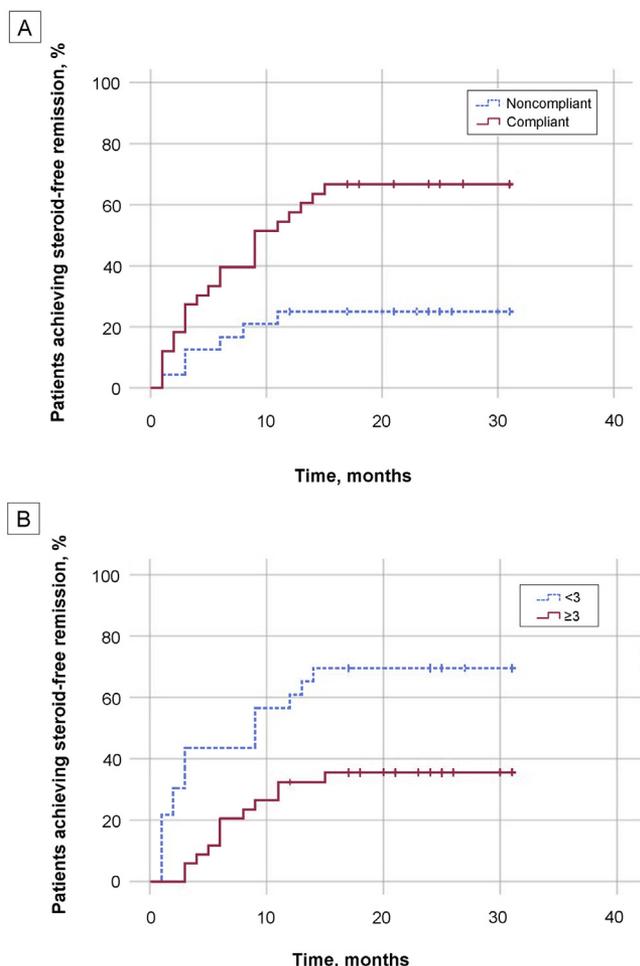


FIG 1. Time to steroid-free remission. This Kaplan-Meier curve illustrates the time required for pediatric noninfectious uveitis patients to achieve steroid-free remission based on the presence or absence of compliance (A) and total number of compliance barriers (B).

administration (oral, subcutaneous, intravenous) and rates of achieving steroid-free remission.

Fourteen (25%) patients reported at least 1 side effect to medications: anxiety and/or pain related to injections (11 [19%]), nausea (3 [5%]), and systemic reaction related to immunomodulatory therapy (4 [7%]). Systemic reactions included the following: anaphylaxis related to infliximab (1 [2%]), neutropenia related to infliximab (1 [2%]), elevated liver enzymes in the context of methotrexate and fatty liver disease (1 [2%]), and a possible localized allergic rash related to subcutaneous adalimumab injections (1 [2%]). A medication change was enacted in 9 (16%), but was not associated with the presence or absence of patient compliance.

Notably, there were 13 cases (23%) in which compliance was hindered by lack of insurance approval of medications: methotrexate (2), mycophenolate (1), adalimumab (3), infliximab (6), and cyclosporine (1). Eventually, insurance approved the desired medication in 11 cases (85%). Of

Table 2. Compliance was associated with increased rates of remission in pediatric noninfectious uveitis requiring immunosuppressive therapy

Remission status	Total, no. (%)	Compliant, no. (%)	Noncompliant, no. (%)	<i>P</i> value ^a
Steroid-free remission	28 (49)	22 (79)	6 (21)	0.002
No steroid-free remission	29 (51)	11 (38)	18 (62)	

^a*P* value was determined by the Fisher exact test.

those, 7 patients (64%) achieved steroid-free remission. The 2 patients who were challenged by continued barriers to insurance approval of recommended medications (adalimumab in one, cyclosporine and infliximab in another) have been unable to achieve steroid-free remission. Children under 12 years of age had fewer access barriers related to insurance compared with those aged 12 and over (3 [5.3%] vs 10 [18%]; *P* = 0.063); the majority (83%) carried a diagnosis of JIA.

Discussion

We herein demonstrate that compliance has a beneficial effect on outcomes in pediatric uveitis patients with increased success in achieving steroid-free remission. Furthermore, even in patients who were unable to achieve long-term remission, 77% were determined to be quiet when compliant but had active inflammation when non-compliant.

Previous studies have demonstrated the importance of treatment compliance in achieving treatment outcomes and goals. A study by Feldman and colleagues⁷ demonstrated that adherence to medications and exercise regimens was associated with favorable outcomes in the control of active joint count, pain related to illness, degree of overall pain, functional scores, and quality of life scores in pediatric juvenile idiopathic arthritis. Mohanty and colleagues⁸ identified that 69% of patients in their cohort of 84 all-cause uveitis subjects at an international tertiary care facility had poor adherence to treatment due to financial limitations, where 40% of poor adherence were the results of inadequate counseling, and 69% were due to prolonged duration of treatment. Our study attempts to relate compliance barriers to uveitis remission rates more comprehensively.

Barriers to compliance that had a negative impact in achieving steroid-free remission were patient/parent negligence, transportation issues, family strife, and having the presence of systemic autoimmune disease associated with uveitis. We additionally found that having 3 or more compliance barriers was associated with a decreased prevalence of steroid-free remission. This suggests screening patients for the above compliance barriers can help identify patient subpopulations that may be at higher risk for failing to achieve treatment goals.

Table 3. Incidence of compliance barriers on uveitis remission rates

Compliance barrier	Total number patients (N = 57), no. (%)	Steroid-free remission (n = 28), no. (%)	No steroid-free remission (n = 29), no. (%)	P value ^a
Patient related				
Patient/parental neglect	21 (37)	4 (14)	17 (59)	0.001
Family strife	10 (18)	6 (21)	4 (14)	0.034
Parental work conflicts	17 (30)	6 (21)	11 (38)	—
Language barriers	12 (21)	5 (18)	7 (24)	—
Poor health literacy	19 (33)	5 (18)	14 (48)	—
Puberty	6 (11)	2 (7)	4 (14)	—
Socioeconomic				
Transportation	13 (23)	3 (11)	10 (34)	0.027
Cost of treatment	4 (7)	1 (4)	3 (10)	—
Healthcare System related				
Non-private insurance	40 (70)	17 (61)	23 (79)	—
Insurance approval of medications	13 (23)	6 (21)	7 (24)	—
Disease related				
Presence of associated systemic disease	17 (30)	11 (39)	6 (21)	0.042
Presence of unrelated systemic disease	8 (14)	3 (11)	5 (17)	—
Treatment related				
Any side effects	14 (25)	8 (29)	6 (21)	—
Side effects resulting in treatment change	9 (16)	4 (14)	5 (17)	—

^aP values determined using a binary logistic regression model, using backward conditional entry of all variables included in the table.

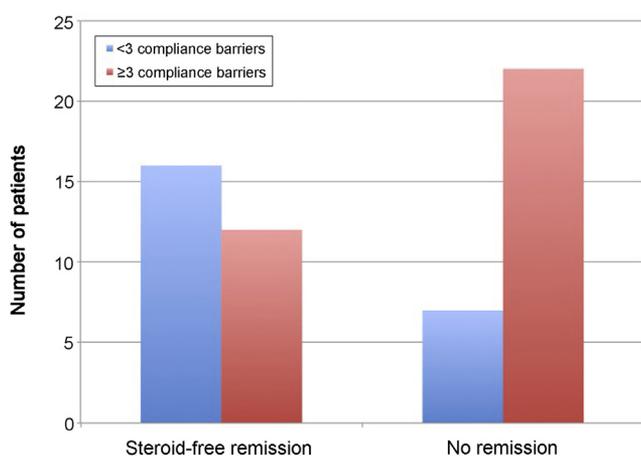


FIG 2. The association of compliance barrier burden and pediatric uveitis remission rates. The presence of at least 3 cumulative compliance barriers is associated with decreased rates steroid-free remission ($P = 0.011$).

Because almost all treatments for uveitis are off-label use, insurance approval for medications often requires lengthy multitier prior authorization, and sometimes, despite insurance approval, prohibitively high out-of-pocket costs.¹² Nearly a quarter of our cohort had barriers to insurance approval that delayed their therapy by more than 2 months. If approved, 77% achieved steroid-free remission, thereby underscoring a significant health policy issue. Although legislative provisions have improved access to vision screening and healthcare coverage for children, even insured patients continue to struggle with healthcare access barriers.^{13,14} Ballenger and colleagues¹⁵ demonstrated that system issues and access to care were key factors in poor adherence to uveitis screening of patients

with JIA. In our cohort, patients under 12 years of age had fewer access barriers; a higher percentage of these patients carried a diagnosis of JIA and, therefore, had better access to dedicated screening programs and Food and Drug Administration approval of medications.

There were several limitations to our study, which included a sample size of 57 patients. We attempted to optimize our analysis by choosing this specific clinical population because of the widely mixed socioeconomic diaspora (30% with private insurance and 70% dependent on federal, state, and locally funded healthcare). This was a retrospective analysis that relied on the medical records to identify the presence of compliance barriers. However, as a practice pattern, the uveitis specialist was meticulous in routinely inquiring about, documenting, and addressing compliance barriers, with marked involvement from support staff, including social work, foster care, and CPS. We maximized the number of captured barriers by reviewing all visit notes within the 12-month period. A benefit of the uveitis specialist's practice pattern is that during multiple one-on-one counseling sessions face-to-face between families, the uveitis specialist may actually capture more compliance barriers than an impersonal paper survey, even if prospective.

Despite these practice patterns and generally good rapport, as perceived by the uveitis specialist—prospective studies may shed further light on patient-perceived patient/physician relationships with patient families—we recognize that compliance barriers are difficult to identify and record, and any study on compliance barriers will be intrinsically underreported.

Because the same endpoint was assessed multiple times within subgroups, it is possible that some barriers may not have been truly significant; however, there is no consensus regarding whether statistical adjustment is

necessary in such cases of multiple testing.^{16,17} To reduce confounding bias and further support our findings would require studies using a multivariate analysis of a larger cohort. Further investigations will be needed to determine whether findings in our cohort are translatable to the adult uveitis population. We also recognize that the association between presence of compliance barriers and steroid-free remission may not be causative. It is possible that among patients who are compliant there are generally more cases than in the noncompliant population of milder disease that is “easier” to control; however, the severity of disease and ease of control is difficult to quantify. In our cohort, the pars planitis group took longer to achieve steroid-free remission and thus could be perceived as being more difficult to control. Nonetheless, there was no difference in the prevalence of compliance in the cohort with pars planitis compared with the remaining patients in our cohort.

To our knowledge, this is the first study to analyze in detail compliance barriers and their association with rates of achieving treatment end goals in noninfectious uveitis requiring immunomodulatory therapy.¹⁰ Despite our study’s retrospective nature and limited sample size, we were able to demonstrate a positive association between compliance and achieving the end treatment goals of steroid-free remission. We hope that this study will pave the way for the design and completion of larger, prospective studies to further elucidate the role of compliance barriers in the treatment of uveitis.

Literature Search

PubMed was searched on July 15, 2016, without language or date restriction, using the following terms: *uveitis* AND *compliance*.

References

1. Nagpal A, Leigh JF, Acharya NR. Epidemiology of uveitis in children. *Int Ophthalmol Clin* 2008;48:1-7.
2. Thorne J, Suhler E, Skup M, et al. Prevalence of noninfectious uveitis in the United States: a claims-based analysis. *JAMA Ophthalmol* 2016;134:1237-45.
3. Rajaraman R, Kimura Y, Li S, Haines K, Chu DS. Retrospective case review of pediatric patients with uveitis treated with infliximab. *Ophthalmology* 2006;113:308-14.
4. Siddique S, Shah R, Suelves AM, Foster CS. Road to remission: a comprehensive review of therapy in uveitis. *Expert Opin Investig Drugs* 2011;20:1497-515.
5. Angeles-Han S, Rabinovich CE. Uveitis in children. *Curr Opin Rheumatol* 2016;28:544-9.
6. Mehta P, Alexander JL, Sen HN. Pediatric uveitis: new and future treatments. *Curr Opin Ophthalmol* 2013;24:453-62.
7. Feldman DE, De Civita M, Dobkin PL, Malleson PN, Meshhefedijan G, Duffy CM. Effects of adherence to treatment on short-term outcomes in children with juvenile idiopathic arthritis. *Arthritis Rheum* 2007;57:905-12.
8. Mohanty G, Dash S. Adherence to treatment regimen in uveitis patients in a tertiary hospital in Orissa. *Sch J App Med Sci* 2017;7:2710-15.
9. Dolz-Marco R, Gallego-Pinazo R, Diaz-Llopis M, Cunningham ET Jr, Arevalo JF. Noninfectious uveitis: strategies to optimize treatment compliance and adherence. *Clin Ophthalmol* 2015;9:1477-81.
10. Foster CS, Kothari S, Anesi SD, et al. The Ocular Immunology and Uveitis Foundation preferred practice patterns of uveitis management. *Surv Ophthalmol* 2016;61:1-17.
11. Jabs D, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol* 2005;140:509-16.
12. Remicade. Medication cost support. Janssen Biotech Inc; Nov 2017. Available at <https://www.remicade.com/ankylosing-spondylitis/remicade-support/medication-cost-support/commercial-insurance>.
13. Wallace DK, Morse CL, Melia M, et al. American Academy of Ophthalmology Preferred Practice Pattern Pediatric Ophthalmology/Strabismus Panel. Pediatric Eye Evaluations Preferred Practice Pattern®: I. Vision Screening in the Primary Care and Community Setting; II. Comprehensive Ophthalmic Examination. *Ophthalmology* 2018;125:184-227.
14. Simacek K, Ko JJ, Moreton D, Varga S, Johnson K, Katic BJ. The impact of disease-modifying therapy access barriers on people with multiple sclerosis: mixed-methods study. *J Med Internet Res* 2018;20:e11168.
15. Ballenger L, Ardoin SP, Driest KD. Assessing barriers to uveitis screening in patients with juvenile idiopathic arthritis through semi-structured interviews. *Pediatr Qual Saf* 2018;3:e084.
16. Perneger T. What’s wrong with Bonferroni adjustments. *BMJ* 1998;316:1236.
17. Nakagawa S. A farewell to Bonferroni; the problems of low statistical power and publication bias. *Behav Ecol* 2004;15:1044-5.