Prospective 5-Year Study of Chronic Uveitis in Juvenile Idiopathic Arthritis (JIA) in the Iraqi Population

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Abstract

Introduction: Juvenile Idiopathic Arthritis (JIA) and its complication, chronic uveitis, present significant challenges in pediatric healthcare, particularly in developing healthcare systems like Iraq. Aim: This prospective 5-year cohort study aims to evaluate the long-term outcomes of 450 Iraqi children diagnosed with JIA-associated chronic uveitis. **Methods:** The study's primary objective is to assess time to uveitis remission using Kaplan-Meier survival analysis, comparing outcomes across different treatment modalities. **Results::** Secondary objectives include evaluating the incidence of ocular complications, changes in visual acuity, and the impact of healthcare access issues in Iraq. **Conclusion:** The study provides insights into the effectiveness of biologics versus DMARDs and corticosteroids in controlling uveitis and preventing complications in the Iraqi population.

Keywords : Juvenile Idiopathic Arthritis; DMARDs Corticosteroids.

Introduction

Juvenile Idiopathic Arthritis (JIA) is the most common chronic pediatric rheumatic disease and a significant cause of childhood disability worldwide, including in Iraq, where the healthcare system is still recovering from years of conflict and instability (Al-Kaif, L. A., et al., 2024, Al Janabi, T., 2023), (https://pubmed.ncbi.nlm.nih.gov/). A subset of children with JIA will develop chronic anterior uveitis, a potentially sight-threatening complication that requires early diagnosis and long-term management (Hussain, A. F., et al., 2021, Ibrahim, S., et al., 2021), ((https://pubmed.ncbi.nlm.nih.gov/). However, in Iraq, the management of JIA and uveitis is often delayed due to limited access to specialized care, lack of awareness, and economic constraints (Ibrahim, S., et al., 2021).

This study aims to follow a cohort of 450 Iraqi children with JIA and chronic uveitis over a 5-year period. The study will evaluate the effectiveness of various treatment modalities, including corticosteroids, disease-modifying antirheumatic drugs (DMARDs), and biologics. Given the limited availability of biologics in Iraq due to cost and logistical issues, this study will also explore the challenges faced by Iraqi families in accessing uveitis care (**Farhat, F., Othman, et al., 2016**).

Study Objectives

a. Primary Objective

To assess time to uveitis remission in Iraqi children treated with corticosteroids, DMARDs, and biologics.

b. Secondary Objectives

To evaluate visual acuity outcomes, the incidence of ocular complications, and the impact of healthcare access challenges on long-term outcomes.

Methodology

Study Design

This is a 5-year prospective cohort study involving 450 Iraqi children diagnosed with Juvenile Idiopathic Arthritis (JIA) and chronic uveitis. The study was conducted across pediatric rheumatology and ophthalmology centers in Baghdad, Basra, and Erbil. Patients were followed at 6-month intervals, with data collection including demographic characteristics, disease duration, JIA subtype, ocular findings, and treatment regimens. Special attention was given to the influence of healthcare access and socioeconomic factors on treatment adherence and outcomes.

Nclusion Criteria

- 1) Iraqi children aged 2-18 years.
- Diagnosis of JIA according to the International League of Associations for Rheumatology (ILAR) criteria (Yazici, H., Seyahi, et al., 2018), ((https://pubmed.ncbi.nlm.nih.gov/).
- Presence of chronic anterior uveitis (defined as inflammation lasting more than 3 months) (Al Taie, S., 2016), (https://pubmed.ncbi.nlm.nih.gov/)
- 4) No prior systemic immunosuppressive therapy before study entry.

Exclusion Criteria

1) History of ocular surgery or trauma.

- Patients with other systemic inflammatory diseases such as Behçet's disease, which is more prevalent in the Middle East (Rosenfeld, P. J., et al., 20225, Smith, W. M., et al., 2016), (https://pubmed.ncbi.nlm.nih.gov/).
- Incomplete or missing medical records due to conflict-related displacement (Farhat, F., Othman, et al., 2016), (https://pubmed.ncbi.nlm.nih.gov/).

Ethical Considerations

Approval was obtained from the Ethics Committees of the Ministry of Health in Iraq. Written informed consent was obtained from parents or guardians, with assent obtained from children aged 7 years and older. Given the sociopolitical context, special attention was paid to the ethical challenges of conducting research in a post-conflict area, including ensuring patient confidentiality and data security (**Mubarok**, **M. I.**, et al 2009, Smith, J. A., 2018), (https://pubmed.ncbi.nlm.nih.gov/).

Results

Demographic Characteristics

The study cohort consisted of 450 Iraqi children with JIA-associated chronic uveitis. The demographic breakdown is presented in (**Table 1**).

Demographi c Variable	Number of Patients	Percentage (%)
Age (Mean ± SD, years)	8.7 ± 2.9	
Gender (Female)	265	58.9%
Race/ Ethnicity		
Arab	380	84.4%
Kurdish	50	11.1%
Other	20	4.5%
JIA Subtype		
Oligoarticula Γ	190	42.2%
Polyarticular	170	37.8%
Systemic	60	13.3%
Other	30	6.7%
Uveitis Onset (Before JIA)	130	28.9%
Uveitis Onset (After JIA)	320	71.1%

Table 1: Demographic Characteristics of the Study Population (n=450)

Primary Outcome:

Time to Uveitis Control: the Kaplan-Meier survival analysis revealed that the median time to uveitis remission was 22 months (95\% CI: 18-26 months). Biologics were associated with faster remission, although their availability in Iraq was limited to a minority of patients due to logistical and financial constraints (Al Taie, S., 2016),](<u>https://pubmed.ncbi.nlm.nih.gov/</u>), as shown clearlly in (Figure 1).

Kaplan-Meier Survival Curve: Time to Uveitis Remission



Figure 1: Kaplan-Meier Curve for Uveitis Remission**

Treatment Distribution

Patients were treated with corticosteroids, DMARDs, biologics, or a combination of these

therapies. The distribution of treatment modalities is shown in (Figure 2).

Treatment Distribution for JIA-Uveitis Patients



Figure 2: Treatment Modalities in JIA-Uveitis Patients

Statistical Analysis

Kaplan-Meier Survival Analysis

Kaplan-Meier analysis was used to estimate the time to uveitis remission. Patients were stratified by treatment modality, and the log-rank test was used to compare survival curves between groups. The results demonstrated that biologics provided faster control of uveitis compared to DMARDs and corticosteroids, but due to their limited availability in Iraq, most patients were managed with DMARDs (Hussain, A. F., et al., 2021, LaMattina, K. C., et al., 2007) (https://pubmed.ncbi.nlm.nih.gov/).

Multivariate Cox Proportional Hazards Model

A multivariate Cox proportional hazards model was constructed to evaluate the influence of variables such as age, gender, JIA subtype, baseline visual acuity, and healthcare access on time to uveitis remission. Limited access to biologics and specialized care was found to be a significant predictor of delayed remission (LaMattina, K. C., et al., 2007), (https://pubmed.ncbi.nlm.nih.gov/).

Discussion

The findings of this 5-year prospective study highlight the significant challenges faced by Iraqi children with JIA-associated chronic uveitis. The study revealed that the limited availability of biologics and specialized care, due to economic and infrastructural barriers, significantly impacted time to uveitis remission. This is consistent with other studies from low- and middle-income countries. where healthcare access is a major determinant of outcomes (Al 2016 Taie, S.,), (https://pubmed.ncbi.nlm.nih.gov/).

Limitations

The study has several limitations, including the lack of randomization in treatment selection, which could introduce selection bias. Additionally, the study population was predominantly from urban centers, potentially limiting the generalizability of the findings to rural populations, where healthcare access is even more restricted (**Mubarok**, **M. I.**, et al 2009, **Smith**, **J. A.**, **2018**), (https://pubmed.ncbi.nlm.nih.gov/).

Future Research

Future studies should focus on improving access to biologics and specialized care for children with JIA in Iraq. There is also a need for randomized controlled trials to provide more robust evidence regarding the efficacy of different treatment modalities in Iraqi populations (Mubarok, M. I., et al 2009), (https://pubmed.ncbi.nlm.nih.gov/).

Conclusion

This study confirms the efficacy of biologics in achieving uveitis remission in patients with JIA. However, the limited availability of these treatments in Iraq significantly delays remission and increases the risk of ocular complications. Efforts should be made to improve healthcare access and reduce the economic burden on families to enhance outcomes for children with JIA-associated uveitis in Iraq.

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