

Ocular Manifestations among Jordanians with Inflammatory Bowel Disease. Hospital-Based Study in Asymptomatic Patients

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ABSTRACT

Objectives: To study the ocular manifestations of inflammatory bowel disease and to investigate whether they are related to disease activity, site of occurrence, and presence of arthritis.

Methods: A randomized controlled prospective study that was conducted at King Hussein Medical Center during the period between June 2008 and December 2008. One hundred and thirty patients attending inflammatory bowel disease clinic were enrolled in the study. First five patients attending the clinic were selected each week to ensure randomization. Data collected included type of disease, duration, treatment, presence of active disease, site of involvement and presence of arthritis. The randomly selected patients were referred to ophthalmology clinic where they had anterior and posterior segment examination by the same senior ophthalmologist. We investigated the relationship between ocular involvement and type of disease, site of involvement, presence of disease activity and presence of arthritis. Data was collected and compared with a control group of 130 normal subjects. Relatives of patients attending ophthalmology clinic for various reasons were randomly selected as a control group. P-value was calculated to see statistical significance.

Results: A total of 130 patients were studied. Mean age of patients was 46.8 years (range 16.2 to 82.2 years) with a male to female ratio of 1.1:1. Seventy patients had ulcerative colitis and 60 patients had crohn's disease. Episcleritis was seen in 12 patients, dry eyes in 9 patients and iritis in 8 patients. One patient was found to have uveitic glaucoma. None of the patients had corneal involvement, scleritis, or retinal vascular involvement. Fifty patients had active disease and 80 were in remission. All patients with episcleritis and iritis had active bowel disease. Tortuous episcleral vessels were seen in 16 patients; the majority of them had inactive disease. Patients with history of arthritis or colonic involvement had more risk of ocular involment.

Conclusion: The results of our study showed that ocular manifestations of inflammatory bowel disease are related to disease activity, site of involvement and presence of arthritis.

Key words: Dry eyes, Episcleritis, Inflammatory bowel disease, Iritis and arthritis.

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Introduction

Inflammatory bowel disease is an idiopathic disease, probably involving an immune reaction of

the body to its own intestinal tract.⁽¹⁻²⁾ Two major types of this disease are described: ulcerative colitis and Crohn's disease. Both types usually run

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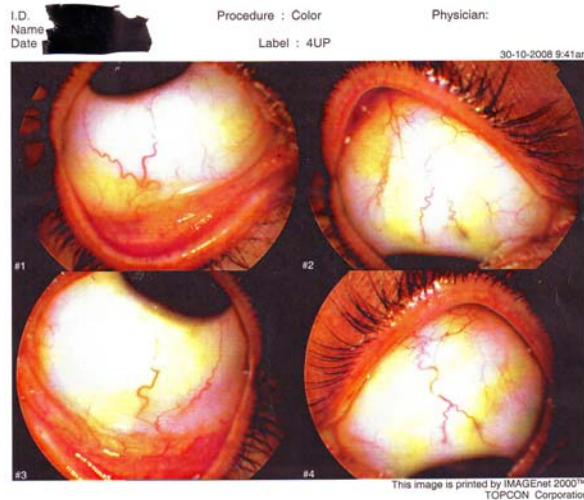


Fig. 1. Tortuous episcleral blood vessels

a waxing and waning course in the intensity and severity of illness.⁽³⁾

As its name implies, inflammatory bowel disease primarily affects the intestines. It also affects other systems. Examples of extra intestinal manifestations are arthritis, skin, urinary tract, haematological, cardiac and eye involvement.⁽⁴⁻⁶⁾

A number of ocular abnormalities have been described, most commonly anterior uveitis and episcleritis. Other ocular complications are described more incidentally such as corneal involvement, intermediate uveitis, retinal vasculitis, and multifocal choroiditis.⁽⁷⁾

We aimed from this study to investigate the ocular manifestations of inflammatory bowel disease and to see whether they are related to disease activity, site of occurrence, and presence of arthritis.

Methods

One hundred and thirty patients were enrolled in this randomized controlled prospective study that was conducted at King Hussein Medical Center during the period between June 2008 and December 2008. All patients were diagnosed to have inflammatory bowel disease based on biopsy examination with duration of illness ranging from 9 months to 37 years. Patients were treated by either

steroids, aminosalicylates, immune modifiers, anti-tumor necrosis factor or combination. As our patients are randomly distributed in each clinic list, we selected first five patients attending inflammatory bowel disease clinic each week as a method of randomization. Data collected included type of disease, duration, treatment, presence of active disease, site of involvement and presence of arthritis. The randomly selected patients were referred to ophthalmology clinic. Best corrected visual acuity was recorded for each patient. Ocular examination which was done by the same senior ophthalmologist included anterior segment examination via slit lamp, Schirmer test, Goldmann applanation tonometry and posterior segment examination after mydriasis by +78 lens. Dry eye was diagnosed if Schirmer test result was less than 6 mm in 5 minutes. We investigated the relationship between ocular involvement and type of disease, site of involvement, presence of disease activity and presence of arthritis. Data was collected and compared with a control group of 130 normal subjects. Relatives of patients attending ophthalmology clinic for various reasons were randomly selected as a control group. We chose a group of relatives rather than from other patients attending ophthalmology clinic for other

reasons to ensure that our control data represents a randomly selected sample of population not known to have any ocular abnormality. P-value was calculated and was considered statistically significance if it was less than 0.05.

Results

A total of 130 patients were studied. Mean age of patients was 46.8 years (range 16.2 to 82.2 years) with a male to female ratio of 1.1:1. Patients were matched with control data according to sex and age (Table I). Seventy patients had ulcerative colitis and 60 patients had crohn's disease. Episcleritis was seen in 12 patients, dry eyes in 9 patients and iritis in 8 patients. In control group, only one patient was found to have episcleritis and one patient had idiopathic uveitis. Glaucoma, cataract and posterior segment abnormalities occurrence did not show statistical difference in both groups. None of the patients had corneal involvement, scleritis, or retinal vascular involvement (Table II).

Table III shows the distribution of patients according to site of involvement. The vast majority of patients had colonic involvement. Fifty patients had active disease and 80 were in remission. All patients with episcleritis and iritis had active bowel disease. Tortuous episcleral vessels were seen in 16 patients; the majority of them had inactive disease. Patients with active disease, history of arthritis or colonic involvement had more risk of ocular involment (Table IV).

Discussion

Inflammatory bowel disease is recognized as an important cause of intestinal and extraintestinal disease in children and adults. Extraintestinal manifestations are thought to be immune mediated and related to intestinal disease activity and may precede or develop concurrently with intestinal symptoms.⁽¹⁾ Many systems be involved such as joints, skin, urinary tract, haematological, cardiac and eye.

Ocular involvement had been previously studied in patients with inflammatory bowel disease with reported incidence from 6% to 60%.⁽⁷⁻¹¹⁾ In our study, episcleritis, dry eyes and iritis were the most common ocular abnormalities seen in inflammatory bowel disease patients with incidence of 9.2%, 6.9% and 6.2% respectively. The association between these three abnormalities and inflammatory bowel disease was statistically significant (Table II). An

important point we would like to mention is the occurrence of subclinical iritis; one of our patient representing 12.5% of uveitic patients was discovered to have asymptomatic iritis. Early detection of such patients and early intervention may avoid further visual complications.

The most common ocular finding we found was tortuous episcleral vessels (Fig. 1) with an incidence of 12.3% compared to 2.3% in control group ($p < 0.01$). As far as we know this finding was not previously described and we think it needs further studies to show the importance of this sign in patients with inflammatory bowel disease. It may be a sign of a previous attack of episcleritis. Other ocular abnormalities in our patients did not show statistically significant association with inflammatory bowel disease included cataract (8 patients), age related macular degeneration (2 patients) and glaucoma (1 patient).

The prevalence of dry eye in IBD is currently unknown and the specificity of this finding to IBD can be questioned.⁽⁹⁾ Taxiarchis Fleckis studied 60 patients with inflammatory bowel disease and found a prevalence of dry eyes of 22% compared to 11% in control group.⁽⁹⁾ In our series, the prevalence of dry eyes was 6.9% in study group and 1.5% in control group ($0.02 < p < 0.05$).

Other ocular abnormalities reported in inflammatory bowel disease patients include granulomatous conjunctivitis,⁽¹²⁾ peripheral corneal ulcers, keratitis, scleritis,⁽¹³⁾ Salzmann nodules,⁽¹⁴⁾ myositis,⁽¹⁵⁾ ocular myasthenia gravis⁽¹⁶⁾ and posterior segment abnormalities such as serous retinal detachment, choroidal infiltrates, retrobulbar neuritis, papillitis, retinal pigment epithelium disturbance, and choroidal folds.⁽¹⁷⁾ Although no posterior segment abnormality was found in our series, fundus examination is vital in inflammatory bowel disease patients as it may prevent devastating complications.

Colonic involvement was the commonest site of involvement in our patients (94.5%). Entire colon involvement was seen in almost half of the patients. Other sites affected included rectum, gastroduodenum and ileum (1.5% each). All patients with iritis, dry eyes and tortuous episcleral vessels and 92.6% of episcleritis patients had colonic involvement (either pan or partial). This supports what was previously mentioned by Salmon JF, *et al*⁽⁸⁾ that patients with colitis or ileocolitis were more likely to suffer from ocular inflammation.

Other risk factors for ocular involvement were the

Table I. Demographic data

		Study group	Control group
Age	mean	46.8 years	45.1 years
	range	range 16.2 to 82.2 years	16.4 to 79.8 years
Gender (male to female)		67 to 63	68 to 62

Table II. Ocular involvement in inflammatory bowel disease and control groups

Ocular abnormality	IBD* group				Control group	P-value	
	UC**	CD [^]	total	incidence			
Episcleritis	7	5	12	9.2%	1	<0.01	
Dry eyes	5	4	9	6.9%	2	<0.05	
Iritis	symptomatic	5	2	7	5.4%	1	<0.01
	asymptomatic	1	-	1	0.8%	-	<0.5
	total	6	2	8	6.2%	1	<0.01
Tortous episcleral vessels	12	4	16	12.3%	3	<0.01	
Cataract +	5	3	8	6.2%	7	>0.1	
Glaucoma	-	1	1	0.8%	1	>0.1	
ARMD ^{^^}	2	-	2	1.5%	2	>0.1	

* Inflammatory bowel disease ** Ulcerative colitis + defined by presence of any type of lens opacity

[^] Crohn's disease ^{^^} Age related macular degeneration of either wet or dry type

Table III. Patient distribution according to site of involvement

Site of involvement	Number of patients	%
Pan colon	52	49
Left colon	51	39.2
Ilio-colonic junction	21	16.2
Rectum	2	1.5
Gastroduodenum	2	1.5
Ileum	2	1.5
Total	130	100
Arthritis	8	6.2

Table IV. Distribution of statistically significant ocular abnormalities according to disease activity, site of involvement and presence of arthritis

Factor		Episcleritis	Dry eyes	Iritis	Tortous episcleral vessels
Disease activity	Active n=50	12	8	8	4
	Inactive n=80	-	1	-	12
	P-value	<0.01	<0.01	<0.01	<0.3
	pan colon	6	5	2	7
Site of involvement	left colon	5	4	4	8
	gastroduodenum	1	-	-	-
	ilio-colonic junction	-	-	2	1
	P-value (colonic to others)	<0.01	<0.01	<0.01	<0.01
Presence of arthritis	Present n=8	4	3	2	1
	Absent n=122	8	6	6	15
	P-value	<0.01	<0.01	<0.01	<0.5

Table V. Distribution of statistically significant ocular abnormalities according to disease category

Eye involvement	Ulcerative colitis	Crohn's disease	P-value
	(Number and percentage of patients)	(Number and percentage of patients)	
Episcleritis	7 (10)	5 (8.5)	>0.5
Dry eyes	5 (7.1)	4 (6.7)	>0.5
Iritis	6 (8.6)	2 (3.3)	<0.3
Tortous episcleral vessels	12 (17.1)	4 (6.7)	<0.3

presence of active intestinal disease and arthritis. All patients with episcleritis and iritis and 88.9% of patients with dry eyes had active disease. The association between active disease or arthritis with either episcleritis, dry eyes or iritis was statistically significant (Table V). On the other hand, the presence of tortuous episcleral vessels did not show such significant association with disease activity or arthritis.

Yilmaz and his colleague⁽¹⁰⁾ reported higher incidence of ophthalmologic manifestations in patients with crohn's disease than in those with ulcerative colitis. In our series, ophthalmologic abnormalities occurred in crohn's disease and ulcerative colitis patients with no statistically significant difference.

We would like to stress on some points:

1. Early referral of inflammatory bowel disease patients to ophthalmology clinic as some patient may have asymptomatic eye involvement.
2. Patients with colonic involvement, active intestinal disease and arthritis have more risk of ocular involvement.
3. The presence of tortuous episcleral vessels requires further studies and evaluation. We found it to be statistically significant in patients with inflammatory bowel disease but not related to disease activity or arthritis.

Conclusion

The results of our study showed that ocular manifestations of inflammatory bowel disease are related to disease activity, site of involvement and presence of arthritis.

References

1. **Veloso FT, Carvalho J, Magro F.** Immune-Related Systemic Manifestations of Inflammatory Bowel Disease: A Prospective Study of 792 Patients. *J Clin Gastroenterol* 1996; 23: 29-34.
2. **Chang JH, McCluskey PJ, Wakefield D.** Toll-like receptors in ocular immunity and the immunopathogenesis of inflammatory eye disease. *Br J Ophthalmol* 2006; 90: 103-108.
3. **Jenkins HR.** Inflammatory bowel disease. *Arch Dis Child* 2001; 85: 435-437.

4. **Jose FA, Heyman MB.** Extraintestinal Manifestations of Inflammatory Bowel Disease. *JPGN* 2008; 46: 124-133.
5. **Veloso FT.** Review article: skin complications associated with inflammatory bowel disease. *Aliment Pharmacol Ther* 2004; 20: 50-53.
6. **Amy SO, Edward VL, Jae K, Gordon KD, Thomas FM.** Constrictive pericarditis in chronic ulcerative colitis. *J Clin Gastroenterol* 2002; 34: 247-251.
7. **Verbraak FD, Schreinemachers M, Tiller A, van Deventer, SJH.** Prevalence of subclinical anterior uveitis in adult patients with inflammatory bowel disease. *Br J Ophthalmol* 2001; 85: 219-221.
8. **Salmon JF, Wright JP, Murray ADN.** Ocular inflammation in Crohn's disease. *Ophthalmology* 1991; 98: 480-484.
9. **Felekis T, Katsanos K, Kitsanou M, et al.** Spectrum and Frequency of Ophthalmologic Manifestations in Patients with Inflammatory Bowel Disease: A Prospective Single-Center Study. *Inflamm Bowel Dis* 2009; 15: 29-34.
10. **Yilmaz S, Aydemir E, Maden A, Unsal B.** The prevalence of ocular involvement in patients with inflammatory bowel disease. *Int J Colorectal Dis* 2007; 22: 1027-1030.
11. **Mintz R, Feller ER, Bahr RL, Shah SA.** Ocular manifestations of inflammatory bowel disease. *Inflamm Bowel Dis* 2004; 10:135-139.
12. **Blasé WP, Knox DL, Green WR.** Granulomatous conjunctivitis in a patient with Crohn's disease. *Br J Ophthalmol* 1984; 68: 901-903
13. **Petrelli EA, McKinley M, Troncale FJ.** Ocular manifestations of inflammatory bowel disease. *Ann Ophthalmol* 1982; 14: 356-360.
14. **Lang AP, Bahar I, Sansanayudh W, et al.** Salzmann nodules-a possible new ocular manifestation of crohn's disease: a case report. *Cornea* 2009; 28: 85-86.
15. **Ramalho J, Castillo M.** Imaging of orbital myositis in Crohn's disease. *Clin Imaging* 2008; 32: 227-279.
16. **Foroozan R, Sambursky R.** Ocular myasthenia gravis and inflammatory bowel disease: a case report and literature review. *Br J Ophthalmol* 2003; 87: 1186-1187.
17. **Ernst BB, Lowder CY, Meisler DM, Gutman FA.** Posterior segment manifestations of inflammatory bowel disease. *Ophthalmology* 1991; 98:1272-1280.