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Original article

Pattern and determinants of ocular complications in leprosy patients in eastern Nepal

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Abstract

Background: Ocular complications of leprosy can lead to blindness.

Objective: To report the pattern and determinants of ocular complications in patients with leprosy from eastern Nepal.

Methods: A cross-sectional study was carried out analyzing one hundred and eighty six patients of leprosy presenting between Jan 2002-Nov 2004. All the patients were categorized using WHO and Ridley and Jopling classification. After determining bacillary indices in all of them, a detailed ocular examination was carried out. Independent risk factors were determined for ocular involvement.

Results: Ocular complications were found in 30.65 % of the leprosy patients; lagophthalmos (17.74%) was the most frequent followed by uveitis (8.60%). Most of the patients having visual loss had it due to corneal complications and none of the patients with uveitis had vision <6/18. The patients released from treatment (83.33%) and those currently on treatment (31.63%) had higher occurrence of complications. Risk factors for ocular involvement were higher bacillary index, longer disease duration (p=0.031, RR=1.109, 95% CI=1.009-01.218) and decreased corneal sensation (p=0.001, RR=3.564; 95% CI =2.014-6.306). Higher Schirmer values (p=0.012, RR=0.935, 95% CI=0.888-0.985) were found to be protective for ocular complications.

Stastics: SPSS ver 10.0 was used for data analysis. The P value of <0.05 was considered as significant.

Conclusions: The prevalence of complications is high in patients released from treatment for leprosy. Cornea-related complications are the most important cause of visual disability and blindness. Risk factors for ocular complications are higher bacillary index, longer disease duration and decreased corneal sensation.

Key words: leprosy, Nepal, ocular complications and risk factors

Introduction

Leprosy is a chronic disease, which may result in cosmetic stigma, various malformations and disability in humans. Ocular involvement in leprosy is frequent (10-50%) and is responsible for 5% of blindness worldwide (Kagame, 1983; Hobbs, 1971).

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Of various reported ocular complications due to leprosy, the potentially sight-threatening ones are iridocyclitis and its sequelae, corneal anesthesia, lagophthalmos and exposure keratitis, leprous keratitis, scleritis, scleral perforation and secondary glaucoma (Lubbers et al 1994, Rathinam et al 2008).

The pattern of ocular complications may differ from one part of the world to the other. The factors determining the complications include type of leprosy (paucibacillary and multi-bacillary), age of the patients, multidrug therapy (MDT) coverage, socioeconomic

status and availability of eye care services (Courtright & Lewallen, 1998; Gupta et al 2007).

The prevalence of leprosy in Nepal is reported to be 4.4/10,000 population, making it an important public health problems (HMG Nepal report, 2002). Considerable difference in the prevalence of ocular complications in patients with leprosy between the pre- and post-MDT era has been reported (Malla et al1981; Brandt et al1981; Knuuttila, 1998; Nepal, 2004). Moreover, the pattern of ocular complications is not known.

This study was carried out to report the prevalence and pattern of ocular complications of leprosy in patients from the eastern region of Nepal.

Materials and methods

The patients with leprosy (either on treatment or released from treatment) presenting between Jan 2002 and Nov 2004 to the B P Koirala Institute of Health Sciences were included in this study. The majority of leprosy patients from the eastern part of Nepal attend this institute as it is the only tertiary care hospital in this region with modern dermatological and eye care facilities. All the patients were subjected to detailed dermatological evaluation, which included history pertaining to duration of symptoms, duration of treatment and lepra reactions. Bacillary indices (BI) were determined by skin-slit smear examinations (from 6 predetermined sites, namely one from each ear lobe and medial part of eyebrow and from the skin lesions).

Ophthalmic history included determination of presence or absence of diminution of vision in the past or ocular redness with or without pain. Best-corrected visual acuity measurement and detailed slit-lamp bio-microscopy were performed for every patient.

Uveitis was classified as active or inactive. Active uveitis was defined as eyes having > 5 cells in the anterior chamber with or without presence of flare or keratic precipitates (KPs), whereas inactive uveitis was defined as eyes having either iris pearls, patchy iris atrophy, fine multiple peripheral anterior synechiae (PAS) on gonioscopy, ectropion uveae, diffuse loss of iris pattern, heavily pigmented trabecular meshwork (>180 degrees or presence of pigmentation in the superior trabecular meshwork without any history of trauma or surgery) and KPs or posterior synechiae in the absence of cells.

In all except 10 eyes (5 eyes with phthisis bulbi, 3 with perforated ulcers and one each with interstitial keratitis and corneal opacity), intraocular pressure (IOP), Schirmer test, tear break-up time and corneal sensations were determined.

Intraocular pressure (IOP) was determined using the Goldmann applanation tonometer and an average of three readings for each eye was recorded. Schirmer test and tear break-up time (TBUT) were determined using standard means. IOP, Schirmer and TBUT values in both the eyes were averaged for analysis; in cases where measurement in one eye was not possible, the available eye was considered for evaluation.

All patients were tested for any facial weakness. The corneal sensation was determined using a cotton wisp. Decrease in corneal sensation in any of the four corneal quadrants was classified as abnormal. Syringing was performed in all to evaluate the lacrimal apparatus.

Leprosy was classified using both WHO (1988) and Ridley and Jopling (1966) immunological classifications. The patients were divided into multibacillary (BI>0) and paucibacillary types (BI=0) (WHO, 1988). The patients grouped according to Ridley and Jopling classification were further categorized into tuberculoid type (TT), Intermediate type (BB, BT & BL) and (LL) Lepromatous type (Dharmendra, 1985).

Statistics

SPSS ver 10.0 was used for data analysis. The Student's 't' test was used for continuous variables, Mann-Whitney Rank sum test and Chi square test for categorical variables. Multivariate analysis and logistic regression were used to determine the independent risk factors. The p value of < 0.05 was taken as significant.

Results

Demography

One hundred and eighty six patients with leprosy were evaluated [136 (73.02%) males and 50 (26.88%) females]. The mean age was found to be 37.0753 ± 15.179 years (range 6-72 years).

The mean duration between onset of the disease symptoms and diagnosis of the disease was found to be 2.76 ± 4.87 years (range=1 month to 40 years). At the time of evaluation, 52.69% of the patients were

receiving MDT, 9.68% had been released from treatment (RFT) and 37.63% were not on any treatment.

Leprosy type

The dermatological diagnoses at the time of presentation were: TT (10.75%), BT (49.46%), BB (2.15%), BL (13.98%) and LL (23.66%). The mean BI was 1.36±2.04 (95% CI=1.06-1.66). Paucibacillary disease was found in 58.06% of the patients.

Type 1 lepra reaction was encountered in 5 patients and type 2 in 2 patients, but none of the patients had any evidence of eye involvement at the time of presentation.

Ocular involvement (Table 1)

Ocular involvement due to leprosy was found in 57 (30.65%) patients (94 eyes; 20 unilateral and 37 bilateral). Lagophthalmos (17.74%) was the most common complication encountered followed by uveitis (8.60%).

Loss of iris pattern (7 eyes), ectropion uveae (6 eyes), peripheral anterior synechiae (5 eyes), and pigmented trabecular meshwork (2 eyes) were found in isolation and were categorized as inactive uveitis.

Corneal complications were identified in 64 eyes, which included prominent corneal nerves (32.81%), superficial punctuate keratitis (21.86%), interstitial keratitis (18.75%), corneal opacity (18.75%) and perforated corneal ulcers (4.69%). Details of the other complications are given in Table 1.

Ocular complications were not related to age, gender, paucibacillary or multi bacillary involvement and treatment status. However, they were found to be independently associated with patients having BI > 5 and longer disease duration (Table 3).

Though the treatment status was not related to ocular complications, 11 (5.9%) of the newly-diagnosed patients and 15 (83.33%) of the 18 patients released from treatment were found to have complications.

Patients with the disease in the lepromatous (p=0.006, RR=0.244 95% CI=0.089-0.669) end of the spectrum had complications less frequently than those on the tuberculoid.

Table 1
Ocular complications of leprosy

SN	Complications	Number of complications
1	Uveitis	
	Inactive uveitis	20
	1. Iris pearl	4
	2. Loss of iris pattern (7)	15(7†)
	3. Ectropion uveae (6)	8(6†)
	4. PAS (5)	6(5†)
	5. Pigmented TM (2)	4(2†)
	6. Posterior synachieae	2
	Active uvietis	6
2	Corneal	
	Lagophthalmos	34
	Corneal opacity	12
	Prominent corneal nerves	21
	Interstitial keratitis	12
	Superficial punctuate keratitis	14
	Perforated ulcer	3
	Trichiasis	2
3	Sclearal	
	Nodular scleritis	2
4	Extraocular	
	Madarosis	8
	Dacryoadenitis	6
	Phithisis Bulbi	5
	Total (no of complications)	145
	Investigations	
1	Intraocular pressure (eyes)	
	6 - 10 mm Hg	11(6‡)
2	Corneal sensations (eyes)	
	Decreased (abnormal)	54 (25‡)
3	Schirmer values (eyes)	
	< 5 mm	10 (0‡)
	5-10 mm	21 (8‡)
4	TBUT (eyes)	
	< 5 s	8 (2‡)

† - Isolated findings in eyes categorized as uveitis
‡ - Findings in eyes without any ocular complications

Variables considered for the regression analysis were: sex, BI, paucibacillary/multibacillary status, diagnosis, disease duration, treatment status, average Schirmer values, TBUT and corneal sensation.

Table 2
Variables with and without ocular complications

Variables	Patients with ocular complications	Patients with no complications	p value
Patients (total = 186)	57	129	
Age			
Mean (95% CI)	39.597(35.145 - 42.048)	35.105 (30.958 -39.2526)	P = 0.365
SD	13.008	15.630	
Median	36	34	
Sex			
Males	50	86	P = 0.005
Females	7	43	
Disease duration			
Mean (95% CI)	4.287(2.233-6.341)	2.126(1.456-2.795)	P = 0.004
SD	7.740	2.523	
Median	1.5	1	
Treatment			
On treatment	31	67	P=0.001
Released from treatment	15	3	
Not on treatment(new patients)	11	59	
BI			
Mean (95%CI)	1.719 (1.171-2.268)	1.158(0.600-1.716)	P = 0.074
SD	2.068	2.103	
Median	1	0.00	
Paucibacillary	27	81	P= 0.048
Multibacillary	30	48	
Schirmer			
Mean (CI)	14.456(12.430-16.479)	17.0(15.129-18.871)	P = 0.036
SD	7.489	6.920	
Median	13	15	
TBUT			
Mean	13.283(11.911-14.655)	16.302(14.915-17.689)	P = 0.003
SD	4.978	5.033	
Median	14	16	
IOP			
Mean (CI)	12.943(12.107-13.779)	13.00(12.283-13.717)	P = 0.612
SD	3.035	2.602	
Median	12	13	
Sensations (eyes, 176)			
Abnormal	25	29	P = <0.001
Normal	59	249	

Intraocular pressure (IOP)

Mean IOP in the right and left eye was 13.044 ± 2.848 mm of Hg (6-26 mm Hg) and 13.167 ± 2.793 mm of Hg (8-20 mm of Hg) respectively. Eleven (3.04%) eyes had IOP < 10 mm of Hg, of which 6 had no complications related to leprosy. There was no statistically significant difference in IOP in eyes with ocular complications or patients with multibacillary or paucibacillary involvement.

Table 3
Variables for regression analysis

	Variables	RR	95% CI		P value
			Lower	Higher	
1	BI (bacillary index)				0.091
	1	0.486	0.117	2.028	0.323
	2	0.409	0.091	1.830	0.242
	3	0.208	0.046	0.944	0.042
	4	0.514	0104	2.530	0.413
	5	5.952	1.047	33.828	0.044
	6	0.292	0.046	1.849	0.191
2	Diagnosis				0.010
	Non-lepromatous	0.729	0.078	6.787	0.782
	Intermediate	0.618	0.126	3.024	0.553
	Lepromatous	0.244	0.089	0.669	0.006
3	Disease duration (increasing)	1.109	1.009	1.218	0.031
4	Schirmer values (increasing)	0.935	0.888	0.985	0.012
5	Decreased corneal sensation	3.564	2.014	6.306	0.000

Tear Film
Mean Schirmer values were found to be higher in eyes with no ocular complications (p=0.012, RR=0.935, 95% CI=0.888 - 0.985). Values of 5-10 mm were detected in 21 eyes (8 of them had no ocular complication). Abnormal TBUT (<5s) was encountered in 2 eyes which did not have any complications due to leprosy.

Corneal sensation
Decreased corneal sensation was observed in 54 eyes (14.51). It was more commonly found in eyes with ocular complications (p=0.001, RR=3.564; 95% CI=2.014-6.306).

Visual acuity
According to the WHO criteria for the visually impaired, we found 6 (3.23%) patients having visual impairment (6/60-6/24) and 2 (1.08%) each with severe blindness (<3/60) and moderate blindness (3/60-5/60). Forty seven (12.63%) eyes were found to have vision of less than 6/18 (6/60-6/18=23 eyes, 5/60-3/60=11 eyes and <3/60 in 13 eyes). Of these, the majority were due to superficial punctate keratitis associated with lagophthalmos (19 eyes), interstitial keratitis and corneal opacity (10 eyes each); and the remainder were due to phthisis bulbi (5) and perforated corneal ulcer (3). None of the patients with uveitis had vision <6/18.

Discussion
The majority of the visual disability and blindness in leprosy patients is produced by corneal and uveal diseases. A higher cure rate is possible in patients with leprosy after the induction of MDT (Lewallen et al 2000), though a substantial number of them continue to suffer from leprosy-related disability due to the earlier-sustained nerve or tissue damage following treatment. There is evidence that chronic uveitis may be progressive in patients thought to be bacteriologically cured (Lewallen et al 2000).

Ocular complications are more frequently reported in developing countries. The majority of patients come from rural areas, are poor and have less access to health care facilities.

In this series of 186 patients evaluated over a period of around 3 years, we found the prevalence of ocular complications to be 30.65%. Earlier studies from this region showed a prevalence rate of 37.3% (Lubbers et al 1994), which is similar to ours. However, studies done by Nepal et al in 2004 showed a somewhat higher prevalence (57%), which may be attributed to geographical factors. Earlier studies from Nepal reporting the higher prevalence probably replicate the pre-MDT era with poorer control of the disease (Malla et al 1981; Brandt, 1981; Hogeweg, 2005). Studies done later from the same region and other parts of the world showed a prevalence similar to ours (Knuuttila, 1998; Orefice et al 1998; Fytche 1981), suggesting better ocular disease control with MDT.

Though it is reported that multi-bacillary disease is more prevalent in East and South-East Asian countries, data from the health survey in Nepal showed otherwise (Courtright and Lewallen, 1998), which may be due to the fact that the majority of our patients had paucibacillary disease. It is also known that there is a higher incidence of paucibacillary disease in the endemic zones (Indian subcontinent and Africa), probably due to better cell-mediated immunity (Courtright and Lewallen, 1998).

In the present study, ocular complications were

encountered more frequently in patients who had been released from treatment (83.33%, Table 2) and those on treatment (31.63%), though the treatment status was not found to be an independent risk factor. Gupta et al 2007 have reported similar observations in a study from mid-Nepal. None of our patients presenting with lepra reactions had ocular complications at the time of presentation.

The large number of patients with complications among those who had been released from treatment may be due to the higher incidence of neural (VIIth and Vth cranial nerves) complications. In general, regular monitoring of patients released from treatment may help reduce the incidence of blindness due to ocular complications.

Lubbers et al (1984) in a study from Nepal reported 5% prevalence of leprosy-related sight-threatening complications in newly diagnosed patients of leprosy as compared to 15.71% in our study. We cannot find a plausible explanation for the difference. The most common ocular complications reported in leprosy patients are corneal followed by uveitis (Courtright and Lewallen, 1998).

Our series also had a higher prevalence of lagophthalmos and corneal complications than reported in other studies of this region.

A high prevalence of lagophthalmos (32.5%) is commonly reported among leprosy patients with multibacillary disease (Courtright et al 1995). Unlike our data, patients with leprosy from India and Nepal having paucibacillary disease were found to have a lower prevalence of lagophthalmos, though a study in similar leprosy patients from Pakistan reported a higher prevalence of lagophthalmos (25.17%) and ectropion (9.01%), (Khan et al 2002).

Higher prevalence of lagophthalmos among paucibacillary patients is generally reported early in the course of the disease. Patients with facial patches and reversal reaction also have a higher prevalence of lagophthalmos (Courtright and Lewallen, 1998), though this was not found to be the case in our series.

Decreased corneal sensation was more prevalent in our patients with ocular complications, which may have a cause - effect relationship. Uveitis is common among leprosy patients, particularly in those with a longer duration of the disease, inadequate treatment and with the multi-bacillary type (Courtright and Lewallen, 1998). Most of the studies generally underestimate the prevalence of uveitis either due to improper methods of examination, miotic pupils or co-existing corneal lesions. Histopathological studies of the iris of leprosy patients with no ocular findings have revealed inflammatory changes (Brandt et al 1990). Lower prevalence (1-4.3%) of chronic uveits is reported in leprosy patients from various regions of Nepal and China (Courtright and Lewallen, 1994; Lubbers, 1995).

A recently-conducted study from western Nepal reported prevalence of uveitis to be 7.79% (Nepal et al 2004). The higher prevalence of uveitis in our study may be attributed to a more detailed evaluation and inclusion of subtle features suggestive of uveitis. Lower intraocular pressure has been reported in patients of leprosy as a result of plastic iridocylcitis (Karacorlu, 1991) or autonomic dysfunction (Hussain et al 1990). This study, however, did not find any decrease in IOP in patients with ocular complications.

Visual disability was seen exclusively in patients with corneal disease in our series. None of the eyes with uveitis had vision of <6/18. A shorter disease duration may be responsible for the lower prevalence of uveitis-related visual impairment.

Patients without ocular complications were found to have higher Schirmer values. Lower Schirmer values reflect poor aqueous production, which is a result of autonomic dysfunction and is commonly observed in multi-bacillary disease (Courtright and Lewallen, 1998; Koshi et al 2001).

Conclusion

Corneal complication is the most common cause of blindness among the patients with leprosy in eastern Nepal. The prevalence of complications is high in patients released from treatment for leprosy. The determinants for ocular complications of leprosy are longer disease duration, high bacillary index, decreased corneal sensation and lower Schirmer values.

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