Current Indian Eye Research

- Ocular manifestations of SLE
- Ocular morbidity among street children
- Macular oedema after phacoemulsification without maculopathy
- Topical cyclosporine in dry eye
- Astigmatic changes after pterygium surgery
- Ocular involvement in AIDS
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Editorial

We are glad to come up with the June issue of Current Indian Eye Research. In this edition we have some interesting topics. Macular edema remains an important cause of loss of vision after an uncomplicated cataract surgery. Diabetics have increased incidence of macular edema. Banamali et al presented an interesting article comparing macular edema following uncomplicated phacoemulsifications in diabetic patients (without retinopathy) and normal population. Health of street children is of great concern to the UNICEF. Naiya BS came up with his work regarding ocular morbidity among urban (Kolkata area) street children. Systemic lupus erythematosus (SLE) is a multi system disorder involving the ocular structures as well. The review article and case series on ocular involvement of SLE by Mazumder AKM et al is a treat to read. With increasing use of electronic gazettes; incidence of dry eye disorders is on the rise. Mazumder M et al had written a fine article regarding topical cyclosporine A² in dry eye disorders. Refractive status is of paramount importance in modern ophthalmology. This is influenced by multitude of factors . Srivastava R et al revisited the outcome of pterygium surgery on refractive status of eye. AIDS is pandemic after it was first reported from African subcontinent. Dhali NN has presented an original article regarding ocular involvement of HIV in an eastern Indian perspective.

Somnath Mukhopadhyay
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Biopsy proven Systemic Lupus Erythematosus presenting as unilateral occlusive retinal vasculitis

Anindya K Majumder1, Sudha K Ganesh2, Sarah Kuruvilla3

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disorder involving any system of the body for example skin, heart, kidney, brain, eye, blood. In this autoimmune disease organs and cells undergo damage initially mediated by tissue-binding auto antibodies and immune complexes. It is a systemic disease with protean manifestation and not organ-specific. The average incidence of SLE in India is 1300 per 100,000 population and seen more frequently in the women1,2. On an average the prevalence values of SLE in Asia ranges between 30 and 50 per 100,000 population1. SLE has multifactorial causative factors. Genetic, hormonal, environmental influences are described in the literature. The genetic predisposition to SLE is a complex contribution of various factors as supported by various epidemiological studies3,4. Although the precise nature of these genetic factors and their exact role in the pathophysiology of the disease remains unknown. The lack of 100% concordance5 indicates a possible role of environmental factors inducing disease in genetically predisposed individuals.

The pathogenesis of SLE includes an autoimmune process in which body tissues are destroyed by auto antibodies against the components of the nuclei of a cell. Immune complex deposition mediated changes play a pivotal role in the pathogenesis of the disease process6,7,8,9. In most of the patients, auto antibodies are present for a few years before the first clinical symptom appears. Antibody-dependent cytotoxicity may cause retinal cell death and demyelination of the optic nerve. Ocular manifestations occur due to the immune complex deposition in the blood vessels of the conjunctiva, sclera, retina, choroid, ciliary body and the basement membranes of the ciliary body and cornea leading to vasculitis and thrombosis. Ocular manifestations include lid dermatitis, keratitis, scleritis, secondary Sjögren’s syndrome, dry eye, retinal and choroidal vascular lesions and neuro-ophthalmic complications.

Ocular manifestations, such as retinal vein or arterial occlusion is a potentially sight threatening condition and may be the first presenting feature of the disease9. Ocular involvement occurrence in up to one third of the patients with SLE7. Retinal involvement in SLE varies from 3% in well-controlled patients to 29% in patients with more active systemic disease10-12. In this review we are concentrating in salient feature of the disease and ocular manifestations in particular.

Epidemiology & Demography

The onset of disease is commonly found in the age group of 15 and 40 years13 and mostly affecting women in child bearing age group. Although it is a disease of the young adult mostly female, juvenile-onset SLE (J-SLE) represents 10-20% of all SLE cases14. Childhood-onset lupus has some differences in their disease profile compared with adult-onset disease and usually associated with rapidly progressive nature and severe disease activity14,15. SLE increases in women of childbearing age and then decreases after menopause. In male the incidence of SLE increases in the seventh decade or later in life. This could be probably due to the difference in hormonal influences in pre and post-menopausal female and in males13,14. Black females carry a higher risk, more associated with severe nephrological disease and higher mortality13,17.
Aetiopathogenesis

SLE is an autoimmune disease with protean manifestation and unknown aetiology. As discussed earlier SLE has multifactorial causation—genetic, environmental, hormonal. A definite genetic predisposition to SLE exists, although the precise role of the genetic factors in pathophysiology remained unknown. Familial studies\textsuperscript{5,13,17} have revealed a 15 to 20 fold increased risk for a sibling of an SLE patient to also develop the disease. SLE is a multigenic disease. There is definitive association of HLA-DR2 and HLA-DQ in patients with SLE\textsuperscript{18}. There is several associations between HLA-DQ alleles and specific autoantibodies\textsuperscript{13}. Apart from association with major histocompatibility complex region (multiple genes), well-established risk factors include alleles in the IRFS, ITGAM, STAT4, BLK, BANK1, PTPN22, TNFSF4, TNFAIP3, SPP1, some of the F\textsubscript{c}γ receptors, and deficiencies in several complement components, including C1q, C4 and C2\textsuperscript{19,20}. Recent genome wide association studies (GWAS) have identified and confirmed association of more than 25 gene variants (or gene complex) in SLE. Most of them are involved in immune complex processing, immune signal transduction in T, B lymphocytes, tissue damage, Toll-like receptor (TLR) function, or type I interferon (IFN) pathway\textsuperscript{21} and genetic polymorphism of certain cytokines, including tumor necrosis factor a, interleukin-10 and interleukin-6\textsuperscript{13}. Still the exact contribution of the various genetic factors is unknown. The lack of 100% concordance\textsuperscript{5} indicates a

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Prevalence (%)</th>
<th>Clinical Utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antinuclear antibodies</td>
<td>98</td>
<td>Best screening test; repeated negative tests rules out SLE</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>70</td>
<td>High titers are SLE-specific. Correlate with disease activity, nephritis, vasculitis</td>
</tr>
<tr>
<td>Anti-Sm</td>
<td>25</td>
<td>Specific for SLE. No definite clinical correlations, more common in blacks and Asians</td>
</tr>
<tr>
<td>Anti-RNP</td>
<td>40</td>
<td>Not specific for SLE. High titers associated with syndromes that have overlap features of several rheumatic syndromes</td>
</tr>
<tr>
<td>Anti-Ro (SS-A)</td>
<td>30</td>
<td>Not specific for SLE. Associated with sicca syndrome, predisposes to sub-acute cutaneous Lupus and neonatal lupus with congenital heart block</td>
</tr>
<tr>
<td>Anti-La (SS-B)</td>
<td>10</td>
<td>Usually associated with anti-Ro associated with decreased risk for nephritis</td>
</tr>
<tr>
<td>Antihistone</td>
<td>70</td>
<td>More frequent in drug-induced lupus</td>
</tr>
<tr>
<td>Antiphospholipid</td>
<td>50</td>
<td>Predisposes to clotting, fetal loss, thrombocytopenia</td>
</tr>
<tr>
<td>Antoerythrocyte</td>
<td>60</td>
<td>Measured as direct Coombs’ test; a small proportion develops overt hemolysis</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>30</td>
<td>Associated with thrombocytopenia, sensitivity and specificity are not good. Not used in clinical practice</td>
</tr>
<tr>
<td>Antineuronal (includes Anti-glutamate receptor)</td>
<td>60</td>
<td>In some series a positive test in CSF correlates with active CNS lupus</td>
</tr>
<tr>
<td>Antiribosomal P</td>
<td>20</td>
<td>In some series a positive test in serum correlates with depression or psychosis due to CNS lupus</td>
</tr>
</tbody>
</table>
possible role of environmental factors inducing disease in genetically predisposed individuals. Ultraviolet light and viral aetiology (EBV) described in literature\textsuperscript{20,21}. Animal models demonstrated possible role of estrogen in promoting auto antibodies and producing SLE like diseases\textsuperscript{16,22}. Conversely, testosterone suppresses the formation of immunoglobulins by human peripheral blood mononuclear cells, including autoantibodies in patients with SLE\textsuperscript{23}.

**Pathogenesis**

Autoimmune phenomena are the hallmark of SLE. SLE is a systemic disease with multisystem involving protean manifestation. In this disease process in body tissues of a genetically predisposed one are destroyed by auto antibodies against the different components of the nuclei of a cell. Auto antibodies against a number of nuclear and cytoplasmic constituents are present as a result of generalized polyclonal B cell hyperactivity. The antibody spectrum could be Autoantibodies play a central role in the pathogenesis of SLE. These IgG autoantibodies are produced by B cells with the help from CD4+ T cells.

Diverse T-cell dysfunctions, decreased numbers of CD8+ T cells and natural killer(NK) cells are also seen. The loss of feedback inhibition in B cells caused by abnormalities in the number and/or function of T cells, NK cells results ill the stimulation of forbidden B-cell clones to produce abnormal antibodies against the self antigen\textsuperscript{24,25}. These auto antibodies cause endorgan damages. Antibodies directed against cell surfaces are responsible for thrombocytopenia, hemolytic anemia, and diffuse CNS disease\textsuperscript{26}. Immune complex deposition mediated changes play a pivotal role in the pathogenesis of the disease process. The severe renal dysfunction and ocular affection in SLE, are related to immune-complex deposition\textsuperscript{27}. Once antibody adheres to a cell surface, or immune complexes form or are deposited in tissue, complement system comes into play via the classical pathway activation. Hereditary deficiencies of complement are associated with SLE for example C\textsubscript{2}. A possible mechanism could be a lack of these complement components results in deficient clearance of tissue debris, immune complexes, and other cellular waste, allowing exposure and sensitization of the immune system to these antigens for prolonged time.

**Pathology**

In SLE, biopsies of affected skin show deposition of Ig at the dermo-epidermal junction (DEJ), injury to basal keratinocytes, and T lymphocytes in the DEJ and around blood vessels and dermal appendages suggestive of inflammation. Clinically unaffected skin may also show immunoglobulin deposition at the DEJ.

In renal biopsies, the pattern and severity of injury are important in diagnosis and determining appropriate therapy. The International Society of Nephrology (ISN) and the Renal Pathology Society (RPS) have published a newer classification system for lupus nephropathy. ‘A’ denotes active , ‘C’ denotes chronic lesion. All the classification system focus mainly on glomerular disease, although the presence of tubular interstitial and vascular disease is important from prognostic point of view and clinical outcomes. The classification is as follows.

### Table 2: Lupus nephritis (International Society of Nephrology and Renal Pathology Society)\textsuperscript{28}

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Minimal Mesangial Lupus Nephritis</td>
</tr>
<tr>
<td>Class II</td>
<td>Mesangial Proliferative Lupus Nephritis</td>
</tr>
<tr>
<td>Class III</td>
<td>Focal Lupus Nephritis</td>
</tr>
<tr>
<td>Class IV</td>
<td>Diffuse Lupus Nephritis</td>
</tr>
<tr>
<td>Class V</td>
<td>Membranous Lupus Nephritis</td>
</tr>
<tr>
<td>Class VI</td>
<td>Advanced Sclerotic Lupus Nephritis</td>
</tr>
</tbody>
</table>

**Diagnosis**

The diagnosis of SLE is based on characteristic clinical features and detection of autoantibodies as discussed earlier. American College of Rheumatology\textsuperscript{29} set a criteria for diagnosing SLE. The diagnosis can be established if 4 of the 11 criteria are met. Although ocular disease is associated with SLE (it may be the first presenting symptom\textsuperscript{30}), ocular lesions are not included among the 11 diagnostic criteria. Patients with active SLE typically exhibit a decrease in the level of C3, C4, and total hemolytic complement.

Ocular manifestation seen in more than 30% of the patients with SLE\textsuperscript{30}. Ocular manifestations can cause significant morbidity. It can be the first presenting feature of the disease entity as well as it can also reflect disease activity and acts as a prognostic indicator for long term survival of the patient\textsuperscript{30}. Nguyen and Foster\textsuperscript{31} suggested
Ocular manifestations of SLE

Ocular disease

Ocular manifestations of lupus are due to the deposition of immune complex in the blood vessels of the conjunctiva, retina, choroid, sclera, ciliary body, also in the basement membranes of the ciliary body and cornea, and in die peripheral nerves of the ciliary body and conjunctiva leading to vasculitis and thrombosis. This immune complexes along with complement system results in a cytotoxic reaction known as immune complex vasculitis. The retinal microangiopathy in SLE is a result from immune complex mediated vascular injury and micro vascular thrombosis. Antibody-dependent cytotoxicity results in retinal cell death and demyelination of the optic nerve. Similarly antibody complex along with complement centered on the lacrimal gland may result in secondary Sjogren syndrome with consequent dry eyes (keratoconjunctivitis sicca) due to inadequate tear production. The most common ocular manifestation of SLE is keratoconjunctivitis sicca, found in 25-30% of the patients with SLE. The decrease in aqueous tear production due to lacrimal gland affection results in decreased visual acuity, discomfort due to dryness and scarring of the ocular surface in severe disease. Malar rash may be seen in periocular skin, presence of scaly, pigmented eyelid lesions. Dermatitis, chronic blepharitis also seen. It may be combined results of immunoglulin deposition and hypertrophied meibomian glands. Orbital involvement has various manifestation. Orbital mass effect, periorbital edema, ocular ischemia secondary to orbital structure inflammation, posteriur scleritis all could be seen. Scleritis can reflect systemic disease activity. Scleritis could be of any type anterior, posterior, nodular, sectoral or diffuse and can be of any severity but usually of non necrotizing variety. Rest of the ocular surface structures like cornea, conjunctiva, episclera could also be involved. It may cause acute non granulomatous anterior uveitis too.

Posterol segment involvement in SLE are potentially
sight threatening. Any part of the posterior segment could be involved including the retina, choroid blood vessels and optic nerve. In literature it is well known that the presence of retinal manifestations parallels disease activity. The spectrum of posterior segment involvement could be cotton-wool spots, retinal haemorrhages, and vascular abnormalities other than vasculitis in the form of capillary and venous dilatation and tortuosity as well as arterial narrowing. Exudative macular edema, frosted branch angitis are also reported. The vascular changes contributed by disease process as well as systemic hypertension but lupus retinopathy can occur as an independent manifestation of the underlying disease process in the absence of hypertension. Pigment disturbances and pseudoretinitis pigmentosa has also been reported possibly secondary to vascular occlusions. Inflammatory vascular involvement and occlusive sequelae are known to have worst prognosis. Direct involvement of the optic nerve can also occur as acute retrobulbar neuritis, acute anterior optic neuritis, anterior ischemic optic neuropathy, or slowly progressive visual loss. Optic neuropathy as well as retinal occlusive disease can result in optic atrophy and poor visual prognosis. Immune complex vasculitis, lupus anticoagulant and related anti-phospholipid antibodies, and possibly anti-neuronal antibodies play a pathological role in neuro-ophthalmic complications. The possible differential diagnosis vasculitis seen is SLE could be Behcet’s disease, Wegener’s granulomatosis, sarcoidosis, syphilis, Lyme disease, HIV retinopathy, and viral retinitis. SLE is relatively a rare cause. Choroidopathy in SLE is relatively uncommon. It manifests as multifocal serous detachments of the retinal pigment epithelium and neurosensory retina.

Management

The management of SLE is therapy in combination. Detailed discussion is out of the scope of this review. Because of the protean manifestation, treatment of SLE requires multisystemic approach and wide range of therapeutics. Although SLE is a systemic disease, ocular manifestation could be the first presenting symptom. So systemic treatment approach by an experienced rheumatologist is of primary concern. Proper systemic control of the disease activity could control the ocular disease as well. Ophthalmologist could treat the ocular part and could work in conjugation with the rheumatologist to diagnose the severity and disease activity early as ocular manifestations are usually associated with severe disease activity. Keratoconjunctivitis sicca is treated with aqueous tear supplementation, tear preservation and topical cyclosporine. Episcleritis is relatively benign condition managed by aqueous tear with topical nonsteroidal anti-inflammatory (NSAIDS) agents. Topical steroid and cyclosporine are also described. In SLE-associated anterior uveitis, topical corticosteroids may be sufficient but in the presence of scleral, retinal, choroidal, neurological, or orbital involvement requires systemic therapy. Initial therapy is with pulse. oral prednisolone 1mg/kg body weight with or without intravenous methyl prednisolone (1 g/day, typically for three days) according to severity and dose and duration are determined according to the severity. In case of long term therapy (steroid therapy-3 months), patients require immuno-suppressive agents. A number of agents have been described such as cyclophosphamide, azathioprine, methotrexate, cyclosporine and mycophenolate mofetil. Other reagents include the antimalarial agents hydroxychloroquine, chloroquine are used for systemic condition and not usually for ocular disease. Antimalarials can cause macular toxicity. Hormonal therapies, Plasmapheresis, intravenous immunoglobulin are also described in the literature. Biologic therapy with monoclonal antibodies and Stem-cell transplantation are newer modalities.

In case of unilateral asymmetric involvement posterior sub-Tenon’s or retroseptal injection of triamcinolone acetonide is also described but not very popular option.

Here we are going to discuss a case of SLE with characteristic renal biopsy presented to us with combined retinal vascular occlusion.

Case Report

A 26 years old female presented to us with sudden painless severe visual loss in her right eye for four months. One year back she presented to an internist with low grade fever, multiple joint pain, loss of appetite with loss of weight and vomiting. Her review of system was normal. Complete hemogram revealed low haemoglobin (7.8 gm%), raised ESR (40mm 1st hr), borderline raised creatinin (1.2mg%) and special tests revealed raised antinuclear antibodies and anti double stranded DNA antibody. Her urine examination revealed proteinuria with cast formation and microscopic haematuria. A provisional diagnosis of systemic lupus erythematosus was made and renal biopsy
was done. Her renal biopsy section stained negative for IgA. Biopsy section showed 50% of the glomeruli were globally sclerotic. Some viable glomeruli showed ischemic changes with retracted capillary loops, wrinkled basement membrane and increase in urinary space. The remaining glomeruli showed mesangial hypercellularity along with mesangial matrix expansion. Interstitial fibrosis and tubular atrophy involved about 25% of the core with evidence of hyalinosis of the arterioles (Figure 1A, 1B, 1C, 1D). Renal biopsy confirmed lupus nephritis class II. She was diagnosed as systemic lupus erythematosus with class-II SLE nephropathy with severe disease activity and was put on intravenous cyclophosphamide, methylprednisolone and later maintained on oral hydroxychloroquine, corticosteroid and mycophenolate mofetil. She was advised to follow up regularly in the nephrologist clinic.

On ocular examination her right eye best corrected visual acuity was 3/60, less than N36 and 6/6, N6 in the left eye. Right eye had relative afferent pupillary defect, normal anterior segment and ocular adnexa, quiet anterior chamber, I ( ) mm of Hg intraocular pressure and a clear lens. Fundus examination revealed a clear vitreous, tortuous retinal veins, sclerosed branches of retinal veins and arteries, intraretinal haemorrhages, macular oedema and a pale disc (Figure 2A,2C). Fundus fluorescein angiography revealed delayed arterial filling, prolonged arteriovenous transit vascular staining macular non perfusion and very large area (more than 25 disc diameter) of capillary drop out affecting superior, inferior and temporal periphery (Figure 2B). Left eye was normal throughout. She underwent aggressive pan retinal photocoagulation of her right eye and advised close follow up.

Discussion:

SLE is a multisystem diseases having protean manifestation and can affect any organ/system of the body. Altered immune responses to auto antigens results

![Figure 1: Fig 1A: Hematoxylin and Eosin stain: Sections from renal biopsy showing glomerulus with increase in mesangial cellularity (black arrow) and slight increase in mesangial matrix. Fig 1B: PAS stain of renal biopsy showing increase in glomerular mesangial cellularity and mesangial matrix (black arrow). Interstitium shows small mononuclear cell collection (blue arrow). Fig 1C: Silver stain of renal biopsy showing glomerulus with focal increase in mesangial cellularity (blue arrow). Adjacent blood vessel showing mild thickening (yellow arrow). Focal tubular dropout and mild interstitial fibrosis present (black arrow). Fig 1D: Immunofluorescence showing C1q Positivity (+++) over mesangial region.](image1)

![Figure 2: Fig 2A: Colour fundus photograph of the right eye (pre treatment) showing retinal haemorrhages, sclerosed branches of central retinal vein, sclerosed branches of central retinal artery, retinal oedema with hard exudates surrounding macula and a pale disc. Fig 2B: Fluorescein angiography montage photo of the right eye in late AV phase showing macular non perfusion, vascular staining and gross capillary non perfusion areas. Fig 2C: Colour Fundus montage picture of the right eye (post treatment) showing sclerosed branches of retinal vein and retinal artery, pan retinal laser photocoagulation marks and a pale optic disc.](image2)
in pathologic autoantibody production, formation and deposition of antigen-antibody complexes, and propagation of a chronic inflammatory process that destroys organ parenchyma and results in end-age organ failure. Ocular manifestation seen in more than 30% of the patients with SLE. Ocular manifestation can cause significant morbidity. It can be the first presenting feature of the disease entity as well as it can also reflect disease activity and acts as a prognostic indicator for long term survival of the patient. The ocular manifestation of the disease occurs due to the immune complex deposition causing micro thromboembolism and occlusive vasculities as well as the cytotoxic effect of the auto antibodies causing damage to the retinal cells and demyelination of the nerve. In our case the patient is a young female and the incidence of SLE increases in women of childbearing age and then decreases after menopause. In male the incidence of SLE increases in the seventh decade or the later life. This could be probably due to the difference in hormonal influences in pre and post-menopausal female and in males.

Our patient had enaemia, elevated anti nuclear (ANAs) and anti bodies and nephropathy with biopsy proven evidences of SLE. Based on the widely accepted diagnostic criteria for SLE by American College of Rheumatology our patient was diagnosed SLE. Ocular features can be the presenting feature of SLE and the disease can involve any portion of the eye. Nguyen and Foster suggested inclusion of ocular disease among the diagnostic criteria for SLE as that could lead to earlier diagnosis and therapeutic intervention for the diseased.

Sero-diagnosis of systemic lupus is based on elevated antinuclear antibodies (ANAs) in 95% of patients with SLE. However, their absence does not rule out the dianosis. Anti ds DNA antibodies are one of the antinatives of ANAs and are very specific for diaiong the disease. Our patient had elevated serum levels of both the antibodies, ANAs as well as anti ds DNA.

Our patient was normotensive, had occlusive retinal vasculities as well as biopsy proven evidence of severe disease activity. In literature retinal vascular changes are reported to correlate with the severity of systemic disease activity. Stafford-Brady and Gladman et al in their prospective study showed that 88% of patients with retinopathy had active systemic disease and 73% had active CNS involvement. In literature it is also described well that lupus retinopathy can occur as an independent manifestation of the underlying disease process in the absence of hypertension.

Our patient had severe renal disease with combined occlusive vasculitis of retinal vessels. Severe renal dysfunction that occurs in SLE is related to immune-complex deposition. Immune complexes deposition mediated pathogenesis are well documented in ocular disease. The exact pathophysiology is unknown. Antibodies play a dual role in the pathophysiology of lupus. Some causes direct toxic effect to the target tissues while others may form antigen-antibody complexes. These immune complexes, bound with complement, may induce a destructive inflammatory response, known as immune complex vasculitis.

Our patient had unilateral combined retinal vascular occlusion. In systemic lupus arterial occlusion are described more commonly than venous occlusion. Although retinal vascular complications are usually bilateral in lupus patients, it can present as unilateral or asymmetric disease. Combined vascular occlusion could lead to early proliferative changes in retina and lead to poor visual prognosis. We managed the patient with aggressive pan retinal photocoagulation of her right eye to manage the diffuse retinal ischemia produced by occlusive retinal vasculitis. It is well documented in the literature that retinal vasculitis in SLE carries poor prognosis in spite of aggressive management.

Acknowledgment: Mr Meenakshi Sundaram Krishna, Ophthalmic photographer, Medical Research Foundation, Chennai.

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A study of ocular morbidity and ocular surface status in street children of Kolkata and its suburbs

Briti Sundar Naiya

Abstract

Background: To report the ocular morbidity status among street children. Material and Method: 1000 street children from Kolkata and suburban areas were examined over a period of 1.5 years for vision, cycloplegic refraction, presence of squint, color vision, sodium fluorescense staining test and Schirmer’s test. Anterior segment evaluation was performed with a portable slit lamp biomicroscope. Posterior segment was evaluated by direct ophthalmoscope after papillary dilatations. Results: Majority of the street children were within 6-10 years age group (n = 440, 44%). 79.72% of street children were getting formal education. 48.1% were underweight. No association was found between dry eye and refractive error. Overall ocular morbidity was found among 29% children. Allergic conjunctivitis was the leading cause (16.3%) of ocular morbidity followed by refractive error (8.6%). Conclusion: Allergic conjunctivitis and refractive error are two important cause of ocular morbidity among street children from Kolkata.

Keywords: Ocular morbidity; Ocular surface; Street children.

The United Nations Children’s Fund (UNICEF) describes a street child as “any girl or boy who has not reached adulthood for whom the street (in the broadest sense of the word, including unoccupied dwellings, wasteland etc.) has become his or her habitual abode and/or source of livelihood, and who is inadequately protected, supervised or directed by responsible adults”1,2. UNICEF classifies street children into four categories: child of the street, child on the street, child of a street family and child in institutional care3. In 1989, UNICEF estimated that 100 million children were growing up on urban streets around the world4. Ocular morbidities mostly originate in childhood and if undetected it may cause serious ocular disabilities in the later part of the life. In case of school children it may early detected during the early years of school life but in case of street children it may remain undetected for a longer period due to lack of early schooling. The phenomenon of street children is rapidly becoming one of global epic proportions. Ten years ago, UNICEF estimated that over 30 million children worldwide work and/or live in the streets, for circumstances usually beyond their control, and often without family support.

The epidemic of street children is global issue. Global urbanisation is attributed to growing numbers of homeless children. Many children leave their homes in smaller towns to work in larger cities. Estimations on how many children are living on the street are between 10 million and 100 million globally. Street children move frequently and are often reluctant of adults. So information on the children is limited. Poverty, violence, lack of family support and hunger are some of the main reasons children choose to move to the street. Street children are typically between the ages of 6 and 16 years old and live without adult support. Africa, Asia and Latin America have the highest number of street children. Almost all countries have children who are homeless and living in the streets. In developing countries like India, street children comprise of a large proportion of child population. With this background, it was envisaged to estimate the prevalence of ocular morbidity amongst street children in Kolkata and its suburbs treat the treatable to prevent ocular morbidity and to study the socio-demographic factors responsible for the causes of Ocular morbidity in the street children.

Materials and Methods:

This is a cross-sectional community-based study (duration 1.5 years) conducted among street children (n=1000) aged younger than 16 years in the Kolkata and...
its suburbs for a period of one and half years. This study had been conducted under street children programs, from Regional Institute of Ophthalmology (Kolkata). Prior to this study ethical committee clearance was taken from Medical College and Hospital (Kolkata). Other variables studied were age (as per the parent’s information), sex, religion, BMI (Body Mass Index) calculated as weight (Kg) / Height (mt)$^2$, parental occupation and socio-economic status. Children without legal guardians were excluded from this study.

Various points of Kolkata where street children live were visited for collection of data for this study. A vehicle with all the necessary ophthalmological equipment was granted by XOVA for the street children programme. The history was taken and then the children were examined as per aforesaid questionnaire format. A proforma was filled in to collect the data about their parents’ educational status, profession and approximate monthly income. Visual Acuity, for distant vision was tested at a distance of six meters under adequate illumination with Snellen’s chart (provided with the vehicle); each eye was tested separately. Near vision was tested by Jaeger’s chart, keeping at a distance of 25-30 cm from both the eyes of the subject. Pinhole vision was tested to differentiate refractive error from posterior pole pathology in cases of low visual acuity (less than 6/9). Objective refraction was performed with retinoscope which was followed by subjective refraction till the best corrected visual acuity was achieved. Mydriatics (cyclopentolate, tropicamide) were used prior to streak retinoscopy in street children with visual acuity less than 6/6. Finally, spectacle power was prescribed after testing acceptance. Children already wearing spectacles were also examined and change in refractive error was noted. The visual acuity was tested with appropriate lenses. Each eye was tested separately. All children with refractive error were provided with spectacles free of cost. Cover/uncover test was done to detect phoria/tropia.

Color vision testing was done by Ishihara’s pseudo-isochromatic plates. Anterior segment and posterior segment examination was done. Detailed anterior segment evaluation was done by a portable slit lamp. Posterior segment evaluation was done by direct ophthalmoscope. Fundus evaluation under mydriasis was carried out with 0.5% tropicamide with cases with media opacities. Schirmer’s test & sodium fluorescene staining test to measure the tear film break up time was done.

Anthropometric measurements were taken by weighing machine and measuring tape. Weight was on flat surface, measurement to be taken without shoes, measurement to be accurate to nearest 100grams. Height was measured on flat surface, standing against the wall, without wearing shoes, calibration to be accurate to nearest 0.5cm. Statistical Analyses were performed using IBM SPSS statistics 19.0.0 version software. Master chart was prepared by Microsoft excel and then loaded onto the SPSS software.

Results:

This study was a cross-sectional, observational study to detect the ocular morbidity and ocular surface status in street children in Kolkata and its suburbs. The study was conducted from January 2015 to August 2016 in 1000 children in various streets of Kolkata. Majority of the street children were within 6-10 years age group (n=440, 44%). And also the number of street children in 0-5 age group (29.1%) was 291 and in 11-16 age groups (26.9%) was 269. Among the street children the number of males (50.2%) were 502 and the rest (n=498, 49.8%) were females. Religion wise; Hindus (n=554, 55.4%) were higher than Muslims (n=398, 39.8%) and percentage of other religion (n=48, 4.8%) were less. Based on BMI, total street children were divided in four groups (underweight, normal, overweight, and obese). The number of underweight street children (n=481, 48.1%) was maximum, followed by normal (n=443, 44.3%), overweight (n=75, 7.5%) respectively. Only one child was obese.

In the present study, Out of 1000 street children 661 were getting education (66.10%). Out of those 661 street children 134 were getting non formal education (NFE) (20.27%). And 527 street children were getting formal education (79.72%). Among the total students in the formal education group, children of class 1(n=115) and class 2(n=123) were more in comparison to other classes. No association was found between dry eye and refractive error. Out of 837 emmetropic street children; 74 were found having dry eye (8.84%), 3 out of 57 myopic street children were found having dry eye (5.26%). No dry eye was found in hypermetropia and astigmatism. No sex predominance was found in the context of dry eye. 39 out of 502 males were found as dry eye (7.76%), 38 out of 498 females were found as dry eye (7.63%).

In the present study the myopic street children were divided into three age groups 0-5 years, 6-10 years, and 11-16 years. 14 out of 57 myopic street children was in the group.
of 0-5 years age (24.56%) , 16 out of 57 myopic street children were in the 6-10 years group (28.07%) and in the last group there were 27 street children (47.36%). Majority of these myopic street children were corrected by lens with d" - 1.50D. Only a few children (n=3) required greater than -1.50D lens. In case of hypermetropia the children were divided in the same manner as previous. 4 out of 14 hypermetropic street children were in the age group of 0-5 years(28.57%) , 9 out of 14 hypermetropic street children were in the age group of 6-10 years(64.28%) and only 1 out of 14 was found as hypermetropic in the last age group of 11-16 years (7.14%). 1 out of 15 street children with astigmatism was found in between 0-5 years (6.66%), 8 out of 15 street children with astigmatism were found in between 6-10 years age group (53.33%), 6 out of those 15 street children with astigmatism were found in between 11-16 years (40%).

Discussion:

Overall ocular morbidity in our study was 29%. A similar from Kathmandu valley reported ocular morbidity rate as 31.6%.

This study reported highest ocular morbidity in greater than 15 years age group as compared to 6-10 years age group in our study. We reported allergic conjunctivitis as most common cause of ocular morbidity followed by myopia. The study from Nepal found conjunctivitis as the prime cause followed by refractive error. In another study from Kathmandu by Ghising et al; we found simple hyperopia followed by myopia and astigmatism as the prime refractive errors in mentally retarded children. Shrestha et al. working on the children staying in different orphanages in Kathmandu valley reported 17.9% prevalence of ocular morbidity. They reported refractive error as the prime cause of ocular morbidity as compared to allergic conjunctivitis in our study. Prevalence of ocular morbidity in a similar study from Shimla among urban school children (both government and private schools) was 31.6% as compared to 29% in our study. Like the similar studies from Nepal; they also reported refractive error as the prime cause of ocular morbidity. But a low prevalence of refractive error (3.3%) had been reported among urban non-school going slum children in Ahmedabad.

The major volume of ocular morbidity in this study is contributed by allergic conjunctivitis and refractive error. In the present study the overall amount of allergic conjunctivitis and refractive error were 16.3% and 8.6% respectively. This may be due to the dusty and polluted environment of the street where the eyes of the children are exposed to various obnoxious gases and particles. Kumar et al and Bagchi et al had reported a low prevalence of ocular morbidity (5.4% and 4.03% respectively) in their study from Delhi and Bankura. A study conducted by Das et al on school children of Kolkata found a prevalence of 25.11% refractive error in 5-10 years of age group with increasing proportion of cases in higher age group, a similar trend has also been noted in the context of street children in the present study. Alam et al in their study of Urdu speaking children of Karachi found a prevalence of refractive error 8.9% which is very similar to the present study of street children of Kolkata (8.6%). In the present study on street children myopia was the most common refractive error. Das et al, Bagchi et al and Mondal et al also found myopia as a leading cause of refractive error in their study on students also.

Amongst other causes of ocular morbidity, squint, and color blindness were prominent. Over all number of squint was 3 (0.003%) and total number of color blindness was 9 (0.009%). Gupta et al reported a prevalence rate of 2.3% in school children of Shimla. Desai et al in their study on school children of Jodhpur found a prevalence of 2.8%. Kumar et al reported 1% prevalence in school children of Delhi. But no data on the prevalence of color blindness in street children was found. The present study however recorded 9 cases out of total number of street children of Kolkata (0.90%). A study on the Brazilian preschool children for the detection of vitamin A deficiency. They concluded that elevated proportions of vitamin A deficiency in its subclinical form were observed in that study population. But no case of xerophthalmia was observed during the present study. This could be due to the vitamin A prophylaxis being given along with the successfully running National Immunization Program and food fortification. Xerophthalmia cases have become rare finding in street children of Kolkata nowadays.

The limitation of the study was lack of exact enumeration of street children, making determination of sample size difficult; so randomization was lacking. Detailed history related to use of drugs, vulnerability of abuses, social context, belief, cultural practices, awareness related to health, psychological perspectives and detailed educational status could not be assessed.

References:


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The occurrence of macular edema after phacoemulsification in diabetic patients without retinopathy and normal patients

Bonomali Roy

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Corresponding Author: Dr. Bonomali Roy.
Received on: 08/05/2017, Revision accepted on: 22/05/2017
Conflict of Interest: None, Financial Disclosure: None

Abstract

Background: To compare the central retinal thickness (CRT) after uncomplicated phacoemulsification cataract surgery in diabetic patients without clinically diagnosed retinopathy changes and non diabetic patients. Material and Method: Serial optical coherence tomography (OCT) was done (macular scan) preoperatively and postoperatively at 1st post operative day, 1st Week, 2nd Week and 4th Week in 50 consecutive patients having diabetes mellitus without clinically detectable retinopathy who underwent phacoemulsification by a single surgeon. The results were compared with 50 control patients (non-diabetic). Result: In the non-diabetic group, there was a statistically significant increase in CRT at postoperative Week 1, Week 2, and postoperative Week 4 (p < 0.0001). In the diabetic without retinopathy group, the CRT at postoperative Week 1, Week 2, and Week 4 increased significantly compared to the baseline value (p < 0.0001). There were no significant differences in mean CRT between the groups preoperatively (p = 0.58) and at postoperative day 1 (p = 0.82) Week 1 (p = 0.68), Week 2 (p = 0.11), and Week 4 (p = 0.07). Conclusion: The short-term post-cataract surgery visual recovery in diabetic patients without retinopathy may not be different from the non diabetic group.

Keyword: Macular oedema; Diabetic macular oedema; Diabetic retinopathy; Cystoid macular oedema.

Macular edema is a well-known complication after cataract surgery. Even uncomplicated cataract surgery may induce postsurgical inflammation and vitreous instability that may subsequently cause postoperative macular edema in normal individuals. When the post cataract macular edema is associated with a decrease in visual acuity, it can be categorized as clinical pseudophakic cystoid macular edema. It usually appears as a petaloid pattern of leakage in fluorescein angiography, and has been referred to as Irvine–Gass syndrome. Clinical cystoid macular edema (CME) is not frequently encountered with a reported incidence after phacoemulsification of 0.1-2% in healthy participants. However, angiographic macular leakage is more commonly detected in patients who do not have visual impairment. This is referred to as subclinical macular edema, with a reported incidence of 9-19% after uncomplicated phacoemulsification.

Diabetic retinopathy has long been implicated as a risk factor for more prominent postoperative macular edema and poorer visual outcomes. In eyes with diabetic retinopathy, the blood–retina barrier is often impaired to a variable degree, which may cause the eyes to be more prone to develop postoperative macular edema. In the present study, we evaluated changes in CRT and visual outcomes in diabetic patients without retinopathy and in nondiabetic controls at the preoperative examination and Day 1, 1st Week, 2nd Week, and 4th Week of phacoemulsification surgery using OCT as study tool.

Material and Method:

This is a prospective comparative study of assessment of central retinal thickness after uncomplicated phacoemulsification surgery in diabetic patients without retinopathy and nondiabetic patients. The study was conducted in 100 eyes at the Regional Institute of Ophthalmology, Kolkata from January 2015 to August 2016.

50 consecutive patients having diabetes mellitus without clinically detectable retinopathy presenting in Institutional out patient department were selected from June 2015 to December 2016. All of them underwent uneventful phacoemulsification at the Institute by a single surgeon.
Patients having documented diabetic retinopathy, preoperative macular edema, previous intraocular surgery, any other ocular diseases such as macular hole, epiretinal membrane, retinal detachment, retinal vein occlusion, retinal artery occlusion, age-related macular degeneration, optic neuritis, and other macular diseases were excluded from the study. Each of the patients underwent proper history taking, visual acuity testing and slit lamp biomicroscopy with 78D lens. Ocular coherence tomography (Stratus; Carl Zeiss, Germany) was performed during each visit. CRT was obtained using six diagonal, 6-mm radial line scans, with the manufacturer's macular thickness map software (version 4.0). The mean retinal thickness of the central 1-mm-diameter area was recorded for analysis. OCT was performed preoperatively and on day 1, week 1, week 2 and on week 4 postoperatively. The results were compared with 50 control patients (non-diabetic). Written informed consent was taken from each of the participants. Institutional ethical committee was obtained before start of trial.

Statistical Analyses were performed using IBM SPSS statistics 19.0.0 version software. Master chart was prepared by Microsoft excel and then loaded onto the SPSS software. LogMAR was used to compare the BCVA between two groups by the MannWhitney U test. The pre- and postoperative intraindividual differences were analyzed with the paired sample t test, and the independent t test was used when comparing central retinal thickness between the groups. Statistical significance was defined as p < 0.05.

Results:

Majority of the patients in the diabetic group were 51-60 years of age group (32%). Majority of the study population (non diabetic) were 51-60 years of age group (44%). Total 32 male (diabetic group) and 36 male (non-diabetic group) participated in this study. Majority of the study population in the diabetic group were male (64%). Majority of the study population in the non diabetic group were from rural area (52%). NS GRADE 2 was the predominant presentation among diabetic group (44%) while only 4% had NS grade 2 with PSC. Majority of the study population in the nondiabetic group were of NS GRADE 3 (40%) followed by NS grade 3 in 34%. Only 10% had NS grade 2 with PSC. There is statistically significant increase in CRT at different post operative periods (p<0.0001) non diabetic group (Table 2).

There is no significance difference in mean CRT between the groups pre operatively (p=0.58), at post operative day 1 (0.82), Week 1 (p=0.68), Week 2 (p=0.11), Week 4 (p=0.20) (Table 3). There was no significant difference in median BCVA (Best corrected visual acuity) between the groups pre operatively (p=0.06), post operatively Day 1 (p=0.71), Week 1 (p=0.12), Week 2 (p=0.13), Week 4 (p=0.24) (Mann-Whitney U test) (Table 4). There is no significant correlation between the CRT and BCVA in pre operative and post operative periods in diabetic patients without retinopathy group (p>0.05) (Table 5). There is no

<table>
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<td>Mean</td>
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<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>Pair 1 Pre op 210.28</td>
</tr>
<tr>
<td>Day 1 214.96</td>
</tr>
<tr>
<td>Pair 2 Pre op 210.28</td>
</tr>
<tr>
<td>Week 1 222.04</td>
</tr>
<tr>
<td>Pair 3 Pre op 210.28</td>
</tr>
<tr>
<td>Week 2 229.90</td>
</tr>
<tr>
<td>Pair 4 Pre op 210.28</td>
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<td>Week 4 234.80</td>
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<tr>
<td>Pair 1 Pre op and Day1</td>
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<tr>
<td>Pair 2 Pre op and week1</td>
</tr>
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<td>Pair 3 Pre op and week2</td>
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<td>Pair 4 Pre op and week4</td>
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in CRT at different post operative periods (p<0.0001) non diabetic group (Table 2).

Table 1: Paired t test of central retinal thickness of study population diabetic without retinopathy (n=50)
significant correlation between the CRT and BCVA in preoperative and postoperative periods in non diabetic patients (p>0.05) (Table 6). Linear regression shows no statistically significant correlation between BCVA in LogMAR and Fasting blood sugar pre operatively (p=0.06), Day 1 (p=0.24), Week 1 (p=0.94), Week 2 (p=0.27), Week 4 (p=0.99).

Discussion:

Kim et al reported that both postoperative macular edema and visual outcomes were significantly worse in the diabetic retinopathy group than in the non diabetic retinopathy group after cataract surgery\textsuperscript{16}. Similar to our study, they found that the mean central foveal thickness of diabetic eyes without retinopathy increased by only a very small amount in the short-term postoperative periods (18 mm and 14 mm at 1 month and 3 months after phacoemulsification, respectively).

Degenering et al conducted a study similar to ours, and compared the post phacoemulsification macular changes and visual outcomes between diabetic and non diabetic eyes for 4 weeks after cataract surgery\textsuperscript{17}. Although they did not find a significant difference in macular thickness on OCT between the groups preoperatively and all time points postoperatively.

Eriksson et al reported eyes with diabetic retinopathy, the OCT finding of macular change and the inferiority of visual outcome may only be transient in the short-term (6 weeks) post phacoemulsification period\textsuperscript{18}.

In our study in the nondiabetic group, there was a statistically significant increase in CRT at postoperative Week 1, Week 2, and postoperative Week 4 (p < 0.0001). In the diabetic without retinopathy group, the CRT at postoperative Week 1, Week 2, and Week 4 increased significantly compared to the baseline value (p < 0.0001). The comparison of pre- and postoperative CRT between both groups. There were no significant differences in mean CRT between the groups preoperatively (p=0.58) and at postoperative day 1 (p=0.82) Week 1 (p=0.68), Week 2 (p=0.11), and Week 4 (p=0.07).

Kim et al reported that there seemed to be a threshold of post cataract surgery macular thickening associated with clinically impaired visual outcomes\textsuperscript{16}. An increase of 40% or more in macular thickness or a morphological Irvine-Gass pattern of cystic changes as detected by OCT could be regarded as a threshold for reporting clinical vision-relevant post cataract macular edema. In our study, there was no difference in median macular thickness between the groups, and no cases in either group had an increase in macular thickness to reach this threshold. The increases in macular thickness in all of our cases could only be regarded as subclinical changes. In our study there was no significant difference in median BCVA between the groups postoperatively (p=0.06) and at postoperative day 1 (p=0.71) Week 1 (p=0.12), Week 2 (p=0.13) and Week 4 (p=0.24).

Nicholas S et al 2006 also showed significant correlation between macular thickness and visual acuity after cataract surgery\textsuperscript{18}. They showed that significant correlation between logarithmic visual acuity and foveal minimal

| Table 2: Paired t test of central retinal thickness of study population non diabetic (n=50) |

<table>
<thead>
<tr>
<th>Paired samples statistics</th>
<th>Mean</th>
<th>No. of patients</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
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<td>Pair 1 Pre op Day 1</td>
<td>211.84</td>
<td>50</td>
<td>12.464</td>
<td>1.762</td>
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<tr>
<td>Pair 2 Pre op Week 1</td>
<td>211.84</td>
<td>50</td>
<td>12.464</td>
<td>1.762</td>
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<tr>
<td>Pair 3 Pre op Week 2</td>
<td>211.84</td>
<td>50</td>
<td>12.464</td>
<td>1.762</td>
</tr>
<tr>
<td>Pair 4 Pre op Week 4</td>
<td>211.84</td>
<td>50</td>
<td>12.464</td>
<td>1.762</td>
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<table>
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<th>Paired samples correlation</th>
<th>No. of patients</th>
<th>correlation</th>
<th>Significance</th>
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</thead>
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<tr>
<td>Pair 1 Pre op and Day 1</td>
<td>50</td>
<td>0.788</td>
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<tr>
<td>Pair 2 Pre op and Week 1</td>
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<td>0.459</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Pair 3 Pre op and Week 2</td>
<td>50</td>
<td>0.416</td>
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<tr>
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<td>50</td>
<td>0.253</td>
<td>P&lt;0.0001</td>
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</table>
thickness on day one and 6 week follow up. Our findings are different from those finding. Chang B et al 2002 showed that the best corrected visual acuity after surgery had a negative correlation with retinal thickness. Our study found no correlation 19.

The limitations of this study include the smaller number of patients in the diabetic without retinopathy group. Follow up of our study is only 4 Weeks. The use of time domain OCT instead of the more recent spectral domain of OCT is also a drawback, because a detailed morphological analysis may therefore not be possible. Fluorescein angiography was not done in any case which is a gold standard till now. We might have missed some cases of CME as we have not done fluorescein angiography study in this series. Another major limitation

Table 3: Comparison of pre operative and post operative central retinal thickness between diabetic and non diabetic group.

<table>
<thead>
<tr>
<th></th>
<th>Non diabetic (n=50)</th>
<th>Diabetic without Retinopathy (n=50)</th>
<th>Significance</th>
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</thead>
<tbody>
<tr>
<td>Pre operative</td>
<td>211.84±12.46</td>
<td>210.28±14.80</td>
<td>P=0.58</td>
</tr>
<tr>
<td>Post op Day 1</td>
<td>214.52±12.87</td>
<td>214.96±16.70</td>
<td>P=0.82</td>
</tr>
<tr>
<td>Post op Week 1</td>
<td>220.52±17.02</td>
<td>222.04±17.36</td>
<td>P=0.68</td>
</tr>
<tr>
<td>Post op Week 2</td>
<td>224.74±13.09</td>
<td>229.90±15.80</td>
<td>P=0.11</td>
</tr>
<tr>
<td>Post op Week 4</td>
<td>228.48±13.73</td>
<td>234.80±17.45</td>
<td>P=0.07</td>
</tr>
</tbody>
</table>

Data presented as mean±SD

Table 4: Comparison of median BCVA in LogMAR in in diabetic group and non diabetic group pre operatively and post operatively.

<table>
<thead>
<tr>
<th></th>
<th>Non diabetic (n=50)</th>
<th>Diabetic without Retinopathy (n=50)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Pre operative</td>
<td>3.0</td>
<td>3.0</td>
<td>P=0.06</td>
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<tr>
<td>Post op Day 1</td>
<td>1.0</td>
<td>1.0</td>
<td>P=0.71</td>
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<tr>
<td>Post op Week 1</td>
<td>1.0</td>
<td>1.0</td>
<td>P=0.12</td>
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<tr>
<td>Post op Week 2</td>
<td>1.0</td>
<td>1.0</td>
<td>P=0.13</td>
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<tr>
<td>Post op Week 4</td>
<td>1.0</td>
<td>1.0</td>
<td>P=0.24</td>
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</table>

Table 5: Correlation between central retinal thickness and Best corrected visual acuity in pre operative and post operative periods in diabetic without retinopathy group (n=50)

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Correlation coefficient</th>
<th>Significance</th>
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<tbody>
<tr>
<td>Pre operative</td>
<td>50</td>
<td>0.135</td>
<td>P=0.35</td>
</tr>
<tr>
<td>Post op Day 1</td>
<td>50</td>
<td>0.067</td>
<td>P=0.64</td>
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<tr>
<td>Post op Week 1</td>
<td>50</td>
<td>0.082</td>
<td>P=0.56</td>
</tr>
<tr>
<td>Post op Week 2</td>
<td>50</td>
<td>0.184</td>
<td>P=0.20</td>
</tr>
<tr>
<td>Post op Week 4</td>
<td>50</td>
<td>0.191</td>
<td>P=0.18</td>
</tr>
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</table>

Table 6: Correlation between central retinal thickness and Best corrected visual acuity in pre operative and post operative periods in non diabetic group (n=50)

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Correlation coefficient</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre operative</td>
<td>50</td>
<td>0.035</td>
<td>P=0.80</td>
</tr>
<tr>
<td>Post Day 1</td>
<td>50</td>
<td>0.033</td>
<td>P=0.81</td>
</tr>
<tr>
<td>Post op Week 1</td>
<td>50</td>
<td>0.172</td>
<td>P=0.23</td>
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<tr>
<td>Post op Week 2</td>
<td>50</td>
<td>0.289</td>
<td>P=0.16</td>
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<tr>
<td>Post op Week 4</td>
<td>50</td>
<td>0.256</td>
<td>P=0.07</td>
</tr>
</tbody>
</table>

thickness on day one and 6 week follow up. Our findings are different from those finding. Chang B et al 2002 showed that the best corrected visual acuity after surgery had a negative correlation with retinal thickness. Our study found no correlation 19.

The limitations of this study include the smaller number of patients in the diabetic without retinopathy group. Follow up of our study is only 4 Weeks. The use of time domain OCT instead of the more recent spectral domain of OCT is also a drawback, because a detailed morphological analysis may therefore not be possible. Fluorescein angiography was not done in any case which is a gold standard till now. We might have missed some cases of CME as we have not done fluorescein angiography study in this series. Another major limitation
is that we did not investigate the long term macular changes and the visual results. As mentioned above, there is some controversy over the duration of the macular changes between diabetic without retinopathy eyes and nondiabetic eyes. There is a need for long term study to verify this question.

References:
Effect of topical cyclosporine A (0.05%) in dry eye disorders

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Abstract

Introduction: To report effects of topical cyclosporine A (0.05%) on dry eye. Material methods: 63 consecutive dry eye patients underwent Monnies questionnaire review, Fluorescein tear break up time, Fluorescein staining of the cornea and conjunctiva, Schirmer I test (without anaesthetic), Rose B-Engal staining of the cornea and conjunctiva and Conjunctival impression cytology. Subsequently they were prescribed Cyclosporine eye drop 0.05% was instilled in the right eye (A) and artificial tears was instilled in the left eye (B) twice daily for nine months. Results were compared and presented. Results: In eyes with Cyclosporine treatment, the percentage improvement of all the above parameters of examination was greater than the eyes treated with artificial tears. This was of statistical significance. Visual acuity improvement was much better than those treated with artificial tears. The percentage of eyes showing normal cytology was higher in the Cyclosporine treated eyes than those treated with artificial tears. This was also of statistical significance. Conclusion: Topical cyclosporine (0.05%) causes significant betterment in dry eye cases.

Keywords: Dry eye; Medical management; Immunomodulators; Cyclosporine A.

Dry eye is a generic term for a group of conditions characterized by irritated, gritty, burning eyes and clinically by alteration in the tear film and the anterior surface of the eye. Lemp (1995) described it as “a disorder of the tear film due to tear deficiency or excess tear evaporation which causes damage to the interpalpebral ocular surface, and is associated with symptoms of ocular discomfort”. Dry eye is a common condition seen with increased prevalence in patients with autoimmune disease, post-menopausal women, and the elderly. Epidemiological studies have reported that more than 6% of the population over the age of 40 suffers from dry eye, with the prevalence increasing to 15% of the population over the age of 65.

There is increasing evidence that decreased tear secretion, decreased tear turn over, and desiccation promote inflammation on the ocular surface. An increase in soluble mediators (cytokines and proteases) in the tear fluid, adhesion molecules expression by the conjunctival epithelium and T-cell infiltration of the conjunctiva have been noticed in dry eye patients. Interestingly, a novel therapy for dry eye disease holds promise for treating both arms of the dry eye classification; aqueous deficiency and evaporative loss. This is accomplished by immunomodulation therapy. Clinical improvement of Keratoconjunctivitis Sicca (KCS) has been noted after therapy with anti-inflammatory agents including corticosteroids, Cyclosporine and Doxycycline. Cyclosporine An emulsion was approved by food and drug administration (FDA) of USA as therapy for dry eye. This study is undertaken to report effects of topical cyclosporine A (0.05%) in dry eye disorders.

Materials and Methods:
The study was conducted with consecutive 63 patients with dry eye who attended the out patient department of a teaching institution in Kolkata, during the period from August 2005 to July 2008 and was analyzed at three months, six months and nine months intervals.

To each of these patients Cyclosporine eye drop 0.05% was instilled in the right eye (A) and artificial tears was instilled in the left eye (B) twice daily for nine months. The patients were selected by screening procedures at the OPD after the following examinations- Subjective interview of symptoms (Mc Monnies questionnaire), Medical and contact lens history, Slit lamp examination.
including lids, lashes and Meibomian glands, Fluorescein tear break-up time, Fluorescein staining of the cornea and conjunctiva, Schirmer I test (without anesthetic), Rose Bengal staining of the cornea and conjunctiva and Conjunctival impression cytology. All the symptomatic dry eye cases having Schirmer I test <5mm, Corneal and interpalpebral staining, Normal lid anatomy/returning function and Visual acuity-Snellen >=6/24; were included in this study. Patients having Severe dryness: Schirmer test (nasal stimulation) <3 mm, permanent goblet cell loss/scarring, acute ocular infection, ocular rosacea, contact lens wear during study, severe blepharitis and history of punctal occlusion within 3 months were excluded from the study. These were followed up monthly for a period of nine months for improvements of all the criteria mentioned above. The improvements were compared with previous results.

Mc Monnies questionnaire (Mc Monnies 1986) is a well balanced focused simple test that allows the patient to think about when the symptoms occur. If symptoms occur occasionally, the questionnaire allows us to pinpoint the source of provoked symptoms. The questionnaire has been designed to determine if the symptoms are constant or occasional; and if the symptoms are related to external environmental factors or genuine intrinsic systemic factors. Mc Monnies questionnaire has a simple scoring system based on the patient’s answers, the higher the score the worse the condition. If a treatment is effective, at a later date the symptom scores should reduce and this indicates numerically the subjective value of the treatment regimen. The index score can range from 0 to 45, where higher scores are considered more indicative of dry eye syndrome. A cut point of greater than 14.5 is recommended for a dry eye diagnosis.

**Schirmer Test**

The patient was seated in a temperate room comfortably and the electric fan was switched off. No-41 Whatman filter paper 35 mm × 5 mm was folded 5 mm from one end and inserted at the lower fornix at the junction of middle third and outer third of lower eyelid taking care not to touch the cornea. The patient was asked to keep the eyes open and to blink normally. After 5 minutes the filter paper was removed and the amount of wetting measured in mm. This test was performed without anaesthesia (Schirmer test II), and was thus a measure of both basal and reflex tearing.

**Measurement of Tear Stability and Break-up Time**

This test was done by observing the cornea using a slit lamp biomicroscope, with a broad beam cobalt-blue light source. To view the tear film, fluorescein dye was instilled, by wetting a dry fluorescein impregnated paper strip with a drop of saline and placing on the bulbar conjunctiva for a brief moment. The patient was asked to refrain from blinking, and in most cases within 60 seconds dark spots or streaks were found within the tear film. The time elapsing between a complete blink, and the appearance of the first ‘dark spot or streak’ was measured, and taken to be the ‘break-up time’. Five successive measures were routinely taken, and the mean value was calculated.

**Ocular Surface Staining**

The extent of ocular surface damage was assessed by instilling a small amount of Rose-Bengal or Fluorescein onto the ocular surface. Fluorescein sodium in the form of sterile filter paper strips impregnated with fluorescein was applied to the lower conjunctival sac. It stained areas of epithelial cell loss when viewed by slit lamp, using a cobalt blue filter. Rose Bengal was also applied to the conjunctival sac by sterile filter paper strips. It stained dead and devitalized epithelial cells and mucus. Van Bijsterveld’s scoring system (1969) can be used to quantify the level of staining observed (with scores ranging from 0 to 9). The visible area of the eye was divided into three zones, formed by imaginary vertical lines at either side of the limbus. Each zone was given a score depending upon the degree of staining contained, from 0 for no staining, through 1 for mild staining and 2 for moderate staining to 3 for severe staining. A total score was calculated by adding the scores for the 3 zones of the ocular surface.

**Conjunctival Impression Cytology**

Specimen collection: After one drop of topical anaesthetic to each eye excessive tear fluids was wiped and the filter paper was applied to the desired area using a pair of smooth and flat ended forceps. Filter paper was placed on four quadrants at the limbus and two on the upper fornix and lower fornix. The filter paper was removed by picking up the tip of the filter paper with the forceps. The
filter paper was dropped into sample bottle, which contains the fixative solution, containing glacial acetic acid 5 ml, 37% formaldehyde 5 ml and 70% ethyl alcohol 100 ml in a sample holder. Sheets of impression cytology specimen information was labeled accordingly, by entering the date of sample collection, patient’s name, medical record number, which eye, which area of the conjunctiva or cornea where the sample.

Findings were plotted according to following parameters-staining characteristics and NC ratio, goblet cell density, squamous metaplasia and mucin aggregates. Staging of CIC findings on the basis of epithelial cell morphology goblet cell density, presence of mucin granules has been done by Nelson6.

In the present study, the CIC specimens were examined and staged according to the degree of squamous metaplasia as described by Wittppen – normal, borderline normal, borderline abnormal, abnormal. The characteristic features of each of this group as described by Wittppen are as follows. In the normal group, the predominant cells were small epithelial cells found in sheets together with presence of goblet cells and mucin spots. The goblet cells showed a tendency to aggregate into groups. In those having abnormal cytology, the predominant cells were large discrete epithelial cells with rare or no goblet cells and mucin spots. The borderline abnormal showed cytology similar to abnormal, except that few goblet cells can be seen and in borderline normal, the picture was similar to normal, with the exception of the epithelial cells, which were abnormal.

Results:

In the study group of 63 patients who were treated with Cyclosporine eye drops in the right eye and artificial tears in the left eye, 61 (96.82%) patients treated with Cyclosporine in right eye showed normal TBUT as compared to only 10 (15.87%) patients treated with artificial tears in the left eye. This improvement on treatment with Cyclosporine in the right eye was found to be statistically significant (Table 1).

<table>
<thead>
<tr>
<th>TBUT</th>
<th>After treatment with cyclosporine (n=63)</th>
<th>After treatment with artificial tears (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&gt;10 sec)</td>
<td>61 (96.82%)</td>
<td>10 (15.87%)</td>
</tr>
<tr>
<td>Abnormal (&lt;10 sec)</td>
<td>2 (3.17%)</td>
<td>53 (84.12%)</td>
</tr>
</tbody>
</table>

Chi Square = 83.92, p Value = < 0.001, dF1

improvement was found in 2 (3.17%) patients. On treatment with artificial tears no patient showed >15mm or normal wetting , 4 (6.39%) patients showed low normal 10-15 mm wetting , 50 (79.36%) showed borderline 5-9 mm and 9 (14.28%) showed abnormal values (Table 2).

Table 2: Table showing the results of Schirmer test in Cyclosporine treated and those treated with artificial tears.

<table>
<thead>
<tr>
<th>Schirmer reading</th>
<th>After treatment with cyclosporine (n=63)</th>
<th>After treatment with artificial tears (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&gt;15mm)</td>
<td>23 (36.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Low Normal (10-15mm)</td>
<td>35 (55.55%)</td>
<td>4 (6.39%)</td>
</tr>
<tr>
<td>Borderline (5-9mm)</td>
<td>3 (4.76%)</td>
<td>50 (79.36%)</td>
</tr>
<tr>
<td>Abnormal (&lt;5mm)</td>
<td>2 (3.17%)</td>
<td>9 (14.28%)</td>
</tr>
</tbody>
</table>

Chi Square = 93.77, p Value = < 0.001, dF3

The staining score improved in 56 (88.88%) patients treated with Cyclosporine as compared to 40 (63.49%) patients treated with artificial tears in the left eye (Table 3).

In the present study of 63 patients Mc Monnies score improved in 52 (82.53%) patients treated with Cyclosporine in the right eye as compared to only 8 (12.69%) patients treated with artificial tears in the left eye. (Table 4)
In the study group of 63 patients with right eyes treated with Cyclosporine and left eyes treated with artificial tears for 6 months it was found that in Cyclosporine treated eyes, 18 (28.57%) patients had normal CIC, 29 (46.03%) had borderline normal CIC, 16 (25.39%) had borderline abnormal CIC and no patient had abnormal CIC on treatment, while in artificial tears treated group no patient had normal CIC, 14 (22.22%) patients had borderline normal CIC, 41 (65.07%) had borderline abnormal CIC and 8 (12.69%) had abnormal CIC which showed that treatment with Cyclosporine in the right eye was statistically significant (Table 6).

**Discussion:**

Several recent publications have suggested that dry eye disease is the result of complex inflammatory processes and suggest that the immuno modulatory drug Cyclosporine may have potential as a novel therapeutic treatment for moderate to severe dry eye. The epidemiological studies have reported that more than 6% of the population over the age of 40 suffers from dry eye, with the prevalence increasing to 15% of the population over the age of 3, 4, 5.

Most dry eye symptoms result from an abnormal, non lubricating ocular surface that increases shear forces under the eye lids and diminishes the ability of the ocular surface to respond to environmental challenges. This ocular surface dysfunction may result from immuno compromise due to systemic auto immune disease or...
may locally occur from a decrease in systemic androgen support to the lacrimal gland as seen in aging, most frequently in the post menopausal women.

Components of the ocular surface (cornea, conjunctiva, accessory lacrimal glands), the main lacrimal gland, and inter connecting innervations act as a functional unit. When one portion is compromised, normal lacrimal support of the ocular surface is impaired. Resulting immune based inflammation can lead to lacrimal gland and neural dysfunction. Restoration of lacrimal function involves resolution of lymphocytic activation and inflammation. The efficacy of Cyclosporine may be due to its immuno modulatory and anti inflammatory functions on the ocular surface resulting in a normalization of nerve traffic. Evidence linking this disease to T-cell mediated inflammatory processes lays the foundation for understanding the clinical benefits of topical Cyclosporine, and immuno modulatory and anti inflammatory agent.

After analysis of the results of Schirmer test in the present study it was found that statistically significant improvement with Cyclosporine treatment, as was intended for the study. In the present study there was statistically significant improvements of TBUT in Cyclosporine treated eyes as compared to artificial tears. After analysis of the results of TBUT, 61 (96.82) patients had normal values on treatment with Cyclosporine in the right eyes and 10 (15.87%) patients treated with artificial tears in the right eye.

In the present study, conjunctival impression cytology was used to evaluate the ocular surface changes. Wittpenn grading system was used, as it simple and easy to work with. In the present study it was found that in Cyclosporine treated eyes, 18 (28.57%) patients had normal CIC, 29 (46.03%) patients had borderline normal, 16 (25.39%) patients had border line abnormal CIC & no patient had abnormal CIC. The improvements were found to be statistically significant when compared with eyes treated with artificial tears in which no patients had borderline normal CIC, 14 (22.22%) patients had borderline normal CIC, 41 (65.07%) had borderline abnormal CIC and 8 (12.69%) patients had abnormal CIC. In the study conducted by Kenneth Sall in 2000, density of conjunctival goblet cells was observed to be significantly greater after 6 month of treatment with Cyclosporine than had been seen at baseline. Our study results were similar to those found by other workers.

Major limitation of our study was short period of followup. Immunomodulatory effects of topical cyclosporine A usually appear slowly. Number of recruited eyes is second limitation of this study. Greater number of eyes being followed up for longer duration should definitely yield better results specially using a comparative model of different concentrations of topical cyclosporine A preparations.

References:


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Visual acuity and astigmatic changes after pterygium excision with limbal stem cell grafting - a prospective analysis

Richa Shrivastava², Debjani Mishra², Surpriya Hawaibam³

Abstract

**Objectives:** The aim of this study was to assess if there is any significant reduction in astigmatism and thus improvement in visual acuity after pterygium excision with limbal stem cell grafting. **Methods:** In this prospective study, patients with primary pterygium were included. Preoperative and postoperative corneal astigmatism, refractive astigmatism and visual acuity were analyzed. All patients underwent pterygium excision with limbal stem cell grafting. **Results:** Mean improvement in visual acuity of 0.09 log MAR units was observed (p < 0.0001, statistically significant). Mean corneal astigmatism for grade I, II and III was found to be 1.03 ± 0.68D, 1.69 ± 0.80D and 2.90 ± 1.06D respectively. Mean corneal astigmatism decreased by 1.29D (p < 0.0001, statistically significant). A decrease of 0.77D in cylindrical power required was found after surgery (p < 0.0001, statistically significant). **Conclusions:** there is a significant reduction in pterygium induced astigmatism and improvement in visual acuity on surgical removal of the pterygium.

Keywords: Pterygium, corneal astigmatism, limbal stem cell grafting

The term pterygium is derived from Greek word ‘pteron’ meaning wing. Pterygium is a triangular shaped growth onto cornea, usually nasally, of fibrovascular tissue that is continuous with conjunctiva. It occurs in interpalpebral fissure area, more often nasally than temporally. When present on both the sides it is called as double pterygium. It is a degenerative lesion and is associated with ultraviolet light exposure. Incidence is more in tropical areas near equator. Pterygium is made up of cap (avascular halo like subepithelial gray zone at advancing edge), head, neck and body¹. Pterygium can be classified into type one, two and three depending upon extent of cornea involvement. Type 1 extends less than 2mm from limbus onto cornea. Type 2 involves up to 4mm of cornea from limbus. Type 3 involves more than 4mm of cornea from limbus and may involve visual axis. Histology shows elastotic degeneration in vascularized subepithelial stromal collagen. It occurs at highest prevalence and most severely in tropical areas near the equator²³. Pterygia warrant treatment when they encroach upon the visual axis, induce significant regular or irregular astigmatism, or become cosmetically bothersome. Aggressive or recurrent pterygia may also cause restrictive strabismus and distortion of the eyelids.

The exact mechanism of flattening in horizontal meridian is not clear. It is thought to be caused by formation of tear meniscus between the corneal apex and the elevated pterygium, causing an apparent flattening of the normal corneal curvature or tractional flattening of horizontal meridian⁴. Treatment of pterygium is mainly surgical. Post-operative refractive error gets stabilized usually after one month. A variety of surgical techniques has been developed. Currently, the most widely used techniques are conjunctival autografting, mitomycin C application and human amniotic membrane grafts⁵.

Recently extensive work has been done on limbal stem cell dysfunction in pterygium and barrier role that limbal stem cells play against conjunctival overgrowth on cornea. Their deficiency at limbus allows conjunctivalization of corneal epithelium with fibrovascular tissue overgrowth. Limbal stem cell grafting prevents recurrences⁶.

Materials and Methods:

A hospital based prospective and interventional study was conducted from 1st April 2013 till 31st March 2014 and 100 newly diagnosed patients having primary pterygium were
included in the study after proper informed written consent. The tenets of Helsinki were followed. Institutional review board approval was obtained. The size of the pterygium was recorded in mm by projecting a horizontal slit-lamp beam from the limbus to the apex. Grade I included pterygium extending up to 2mm on the cornea from limbus. Grade II included pterygium extending more than 2mm but less then 4mm from limbus. Grade III included pterygium encroaching onto cornea more than 4mm. Grade III primary pterygium crossing center of the pupil were not included in the study. Patients with recurrent or atrophic pterygium and patients with history of any ocular surface disorder or trauma were excluded out of the study.

Assessment of preoperative astigmatism was done by standard method of refraction and keratometry. All patients underwent Pterygium surgery with limbal stem cell grafting under peribulbar anaesthesia (Lignocaine 2% with adrenaline mixed with Bupivacaine in 1:1 ratio). After proper anaesthesia, 0.5cc of lignocaine was injected under the pterygium to elevate it. Corneal epithelium 2mm ahead of head of pterygium was scraped off by a no. 15 blade. A superficial delineating keratectomy was done at leading edge of pterygium. Careful superficial lamellar dissection, from leading apex of pterygium towards limbus was done. This freed apex of pterygium from cornea. Now body of pterygium was separated from underlying sclera. This exposes bare sclera. Size of graft needed was measured using calipers. A conjunctival graft at superotemporal limbus, measuring 1mm more than bare sclera was harvested. While dissecting limbal part of graft dissection was continued upto 0.5mm into clear cornea to harvest limbal stem cells into the graft. Graft was placed over bare sclera so that limbal side of graft is placed on limbal side of bare sclera. Graft was then sutured using 10-0 monofilament nylon suture. Antibiotic eye ointment and dressing was done. Patients were followed up at one week, two week and one month after surgery.

Comparison of preoperative and postoperative astigmatism was done after one month of pterygium surgery. Visual acuity assessment, keratometry and refractions were done on the day of admission and on 30th postoperative day. Data was analyzed by using Graph pad quick calcs software. Paired t test was used to compare preoperative and postoperative results. A p value (one tailed) of < 0.05 was defined as statistically significant.

Results:

The average age of the patient was 47.19 ± 9.77 years. Age ranged from 21 years to 80 years. 50% of patients were between 40 and 54 years of age. Out of hundred patients analyzed 52 (52%) were males and 48 (48%) were females. It was found that 34% (34 in number) patients were from urban background and 66% (66 in numbers) patients were from rural background. Of the 100 cases of pterygium examined 17% were in grade I, 52% were grade II and remaining 31% were graded as III. No case of temporal pterygium or double pterygium was found in the duration of this study.

Preoperative visual acuity ranged from 0.00 to 1.48 (log MAR units). Mean preoperative visual acuity was 0.52 ± 0.32. Postoperative visual acuity at one month ranged from 0.00 to 1.08. Mean postoperative visual acuity was 0.43±0.29. Improvement in visual acuity was mainly

Table 1: Preoperative and postoperative visual acuities as log Mar values (Mean ±SD)

<table>
<thead>
<tr>
<th></th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative</td>
<td>0.26±0.15</td>
<td>0.39±0.17</td>
<td>0.89±0.27</td>
<td>0.52 ± 0.32</td>
</tr>
<tr>
<td>Post-operative</td>
<td>0.22±0.14</td>
<td>0.31±0.17</td>
<td>0.76±0.23</td>
<td>0.43±0.29</td>
</tr>
</tbody>
</table>

p<0.0001 (df=99)
attributed to stabilization of corneal astigmatism. Mean improvement in visual acuity of 0.09 log MAR units was observed ($p <0.0001$, statistically significant) (Table 1).

Corneal astigmatism was measured by manual keratometry (Reichert type Bausch and Lomb keratometer). Mean preoperative corneal astigmatism was $1.96 \pm 1.1$ Diopters (D). Fifty percent of cases had corneal astigmatism from $1.25D$ to $2.25D$. Mean corneal astigmatism for grade I, II and III was found to be $1.03 \pm 0.68D$, $1.69 \pm 0.80D$ and $2.90 \pm 1.06D$. Mean corneal astigmatism increased with increasing grade of pterygium. Mean postoperative corneal astigmatism was $0.67D \pm 0.57D$. Mean corneal astigmatism for grade I, II and III was found to be $0.44D \pm 0.38D$, $0.54D \pm 0.49D$ and $0.98D \pm 0.69D$ respectively. Mean corneal astigmatism decreased by $1.29D$ ($p <0.0001$, statistically significant). In one case WTR astigmatism changed to ‘against the rule’ (ATR) astigmatism (Table 2).

Table 2: Preoperative and postoperative corneal astigmatism in diopters (D)

<table>
<thead>
<tr>
<th></th>
<th>Mean±SD (Pre-op)</th>
<th>Mean±SD (Post-op)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>$1.03\pm0.68D$</td>
<td>$0.44\pm0.38D$</td>
</tr>
<tr>
<td>Grade II</td>
<td>$1.69\pm0.8D$</td>
<td>$0.54\pm0.49D$</td>
</tr>
<tr>
<td>Grade III</td>
<td>$2.90\pm1.06D$</td>
<td>$0.98\pm0.69D$</td>
</tr>
<tr>
<td>Total</td>
<td>$1.96\pm1.1D$</td>
<td>$0.67\pm0.57D$</td>
</tr>
</tbody>
</table>

$p\text{ value}< 0.0001$ (df 99)

Mean preoperative refractive cylinder was $1.54 \pm 0.86D$. Cylindrical power determined by refraction ranged from $0.25D$ to $4.25D$. 75% of patients had refractive cylinder of more than $0.75$. Mean astigmatism for grade I, II and III was $0.97D \pm 0.56D$, $0.30D \pm 0.69D$ and $2.26D \pm 0.83D$ respectively. Mean postoperative refractive cylinder was $0.77 \pm 0.55D$. Fifty percent of cases had postoperative cylindrical power between $0.5D$ to $1.0D$. Mean refractive cylindrical power for grade I, II and III was $0.51 \pm 0.41D$, $0.67 \pm 0.50D$ and $0.04 \pm 0.59D$ respectively. Single case of WTR astigmatism changed to ATR astigmatism. A decrease of $0.77D$ in cylindrical power required was found after surgery ($p <0.0001$, statistically significant) (Table 3).

Table 3: Preoperative and postoperative refractive cylinder in diopters (D)

<table>
<thead>
<tr>
<th></th>
<th>Mean±SD (Pre-op)</th>
<th>Mean±SD (Post-op)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>$0.97\pm0.56D$</td>
<td>$0.51\pm0.41D$</td>
</tr>
<tr>
<td>Grade II</td>
<td>$1.30\pm0.69D$</td>
<td>$0.67\pm0.50D$</td>
</tr>
<tr>
<td>Grade III</td>
<td>$0.26\pm0.83D$</td>
<td>$0.04\pm0.59D$</td>
</tr>
<tr>
<td>Total</td>
<td>$1.54\pm0.86D$</td>
<td>$0.77\pm0.55D$</td>
</tr>
</tbody>
</table>

$p\text{ value}< 0.0000$ (df 99)

Improvement in visual acuity and astigmatism is more in grade III than grade II and in grade II than I. This is due to worsening of visual acuity and more induced astigmatism as pterygium increases in size. Preoperative astigmatism by keratometry was found to be more than astigmatism by refraction. Two cases (2%) showed recurrence during the one year period of the study.
Discussion:
The pterygium has been reported to have highest incidence in fourth decade. In a study conducted by Marmamula S et al. in Andra Pradesh, mean age of patients was very similar to present study (47.5±13 years) . A study by Salagar KM in Karnataka showed 73% of cases were above age of 40 . Another study conducted by Rao SK et al. showed that 56.98% of cases were above the age of 40 years. In present study 78% of patients were above 40 years of age.

While most studies demonstrated an increased risk of pterygium among men compared with women, this study found only slight difference in sex distribution of pterygium (51% males, 48% females). Studies in India, including the study by Salagar KM et al and Asokan R et al found a similar prevalence in both the sexes. Similar to other studies; we found a significantly higher prevalence of pterygium in the rural population (66%).

Pterygium induces refractive changes leading to visual impairment. There was poor correlation between the magnitude of refractive astigmatism and keratometric astigmatism. This can be due to the hemi-astigmatic nature of the induced changes. During manifest refraction patient deals with two images, one from the more spherical temporal cornea and one from the flatter nasal cornea. The patient preferentially views the more spherical image and therefore the corneal changes are incompletely reflected in the refraction. Similar discrepancy has been shown by various other studies.

Keratometry measures only the central cornea and peripheral cornea is ignored and hence astigmatism calculated by keratometry is less than that measured by other topographical methods. The exact mechanism of flattening in horizontal meridian is not clear. It is thought to be caused by the formation of tear meniscus between the corneal apex and the elevated pterygium, causing an apparent flattening of the normal corneal curvature or tractional flattening of horizontal meridian.

Various studies have shown increasing size of pterygium causing increasing astigmatism. Lin and Stern found pterygium to induce significant degrees of astigmatism once it exceeded >45% of the radius. Tomidokoro et al. evaluated the percentage extension of pterygium on cornea and found larger pterygia to adversely affect astigmatism. Avisar et al in 2000 found that pterygia more than 1.1 mm from limbus produce increasing astigmatism of 1D or more. Lindsay RG et al found pterygium causes with-the-rule astigmatism and found a significant correlation between the extension of the pterygium onto the cornea and the amount of induced astigmatism. In our study mean astigmatism increased with increasing size of pterygium. Corneal astigmatism recorded in grade I, II and III was 1.03 ± 0.68D, 1.69 ± 0.80D and 2.90 ± 1.06D respectively.

Mean corneal astigmatism in the present study, decreased from 1.96D to 0.67D after excision of pterygium, a difference of 1.29 D (p<0.0001). Several previous studies by different researchers including Cinal A et al, Maheshwari S, Stern and Lin, Tomidokoro et al. and Yagmur and et al have also reported a significant decrease in corneal astigmatism following surgical removal of pterygium. Khan FA et al recently did a study based on automated keratometry. In the study median pre-operative astigmatism of 2.25D reduced significantly to median postoperative astigmatism of 1.30D.

In the present study mean refractive cylindrical power for grade I, II and III was 0.97D ± 0.56D, 0.30D ± 0.69D and 2.26D ± 0.83D respectively. This showed worsening of refractive cylindrical power with increasing encroachment of cornea by pterygium. According to the study by Maheshwari S the refractive cylinder reduced from 1.94±2.24D to 0.78±1.07D. Another study by Maheshwari S. reported the preoperative refractive cylinder improved from 4.60 ± 2 D to 2.20 ± 2.04 D postoperatively. In our study a reduction of 0.77D (p<0.0001) in refractive cylinder was found.

In the present study, mean visual acuity had an improvement of 0.09 log MAR units (p<0.0001). Similar improvement in visual acuity has been shown by other studies. Study by Maheshwari S. showed a mean visual acuity pre-operatively of 0.53 ± 0.35 D which improved to 0.68 ± 0.34 D (p = 0.001) postoperatively (snellen’s fraction). Yagmur M et al in 2005 evaluated visual acuities and observed significant improvement in mean uncorrected visual acuity postoperatively.

Hence, it was found that induced astigmatism increases with increasing encroachment of pterygium onto cornea. This can be corrected effectively by pterygium surgery with limbal stem cell grafting.

Pterygium is more common in rural population and males, due to more exposure to sunlight (ultraviolet radiation). Mean age at presentation is 47.19 years. Magnitude of induced astigmatism increases and hence visual acuity...
decreases with increasing encroachment of pterygium on the cornea. There is a significant reduction in the induced astigmatism on pterygium excision with limbal stem cell autografting.

References:


Cite this article as:
Ophthalmic manifestations of acquired immune deficiency syndrome (AIDS)

Narendranath Dhali

Abstract

Introduction: To report the nature and extent of ocular involvement of AIDS. Material and Method: 280 consecutive seropositive patients attending HIV/AIDS clinic and admitted in-house between April 2005 to July 2008 were evaluated and extent of ocular manifestations were noted and documented. Result: Among 280 cases; 231 were adult male. 81% of male were in 20-40 year age group. Heterosexual contact was commonest risk factor of transmission. Tuberculosis was most common systemic opportunistic infection. Prevalence of ocular involvement was 32%; most common being HIV retinopathy (11%). CMV retinitis was commonest ocular opportunistic infection (9.2%). Conclusion: AIDS mainly involves posterior segment of eye ball. Proper diagnosis and prompt institution of appropriate therapy will help to reduce ocular morbidity.

Keywords: AIDS; Ophthalmic AIDS; HIV vasculopathy.

Acquired immune deficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) is a serious disorder of immune system. Normal defense of human body against various diseases breaks down; leaving it vulnerable to a host of life threatening infections and unusual malignancies. Since first official in June 1981 in centre for disease control (CDC) USA; it has emerged as global pandemic. In India; the first official case was reported from Chennai in 1986. Since then the disease has spread to most of the states due to poor literacy level, interstate migration of working class, potential high risk behavior and presence of sexually transmitted diseases (STD). According to national AIDS control organization (NACO) New Delhi; about 5.1 million Indians are suffering from AIDS with clustering of cases from north-eastern states. The organism multiplies in all human cells but CD4+ lymphocytes are most vulnerable. With introduction of highly active antiretroviral therapy (HAART) since 1996; morbidity from this deadly disease has been reduced drastically.

Ocular involvement of AIDS is very common; involves all parts of the eye, multifocal and bilateral in extent. The disease involves 30-70% of people worldwide but after autopsy the rate can touch up to 90%\(^a\),\(^b\). Since the first description of ocular manifestation of AIDS in 1996; many studies had been conducted\(^c\). Our study was conducted to report the extent of ocular involvement of AIDS in an eastern Indian perspective.

Material and method:

The study comprised of 280 consecutive HIV cases that were undergoing treatment at School of Tropical diseases (STM), Kolkata. They were either admitted or attended out patient department of STM. The study was conducted between April 2005 to July 2008. The sero positivity of all the patients were established by enzyme linked immunosorbent assay (ELISA) for HIV-1 and HIV-2 by the department of Virology, STM Kolkata as per guidelines by NACO, New Delhi. Systemic evaluations of these cases were done by physicians (STM) which included detailed history, counseling, investigations. The history included demographic data, occupation and detection of HIV transmission risk factor. Investigations included haemogram (hemoglobin percentage, total count of WBC, CD4+ lymphocyte count, CD8+ lymphocyte count and ESR), liver function tests and blood sugar level estimation. All the patients were screened for pulmonary tuberculosis (mantoux test, chest x-ray and sputum for acid fast bacillus). They were screened for syphilis, toxoplasmosis and Cryptococcus when indicated. Findings of ultrasound examination and other imaging like CT scan and MRI scan were recorded and documented. Ophthalmic evaluation included vision, anterior segment evaluation by slit lamp biomicroscopy, applanation tonometry and dilated fundoscopy by indirect ophthalmoscope. Fundus photographs were taken as indicated in ambulatory patients.
### Results:

The other common systemic opportunistic infection in our study was oropharyngeal and esophageal candidiasis (30.7%), cryptosporidial and other worm induced diarrhea (16.7%), cryptococcal meningitis (6.4%), toxoplasmosis (6.07%), Herpes simplex and zoster infection (4.64%), hepatitis (3.1%), Syphilis (1%) and histoplasmosis (1%). We found 8 cases of lymphoma but not a single case of Kaposi sarcoma in contrast to the USA based studies (10% by Holland et al.). Holland found 9 cases of Kaposi sarcoma in a small series of 27 AIDS cases. The lower prevalence in our study is mostly attributed to lower proportion of cases having homosexual orientation. Recently DNA sequences of human herpes virus 8 had been detected in Kaposi sarcoma patients with or without HIV infection. The low prevalence of human herpes virus 8 in India may explain this low frequency of Kaposi sarcoma.

The most common ocular manifestation of AIDS in our study was HIV microvasculopathy just like other Western and African studies. The prevalence is 11 % (31 out of 280) in our study in the form of cotton wool spots and/or intraretinal hemorrhages without any vasculopathy. Number of cotton wool spots and hemorrhages varied and they were restricted to the posterior pole. Twenty patients (64.5%) had unilateral and the rest had bilateral lesions. Six patients had CMV retinitis with reduced vision. One patient had lateral rectus paresis.

Among HIV retinopathy cases; CD4† lymphocyte count below 50 was noted in 65.3 % (n=17), between 51-100 in 34.7 % (n=9). In 5 cases the CD4 count was not available. None had CD4† T cell count above 100/µl.

The most common ophthalmic opportunistic infection noted in this study was CMV retinitis. The prevalence was 9.2% (95 percent confidence interval 5.8-12.6%). CMV retinitis was present in 33 eyes of total 26 out of 280 patients. Three of them were female and the rest were male. Unilateral lesions were noted in 19 cases and bilateral in 7 cases (27%). There were mainly two clinical forms of CMV retinitis in this study. Most patients were of fulminant or hemorrhagic variety characterized by confluent retinal necrosis with haemorrhage in posterior pole. Six eyes had indolent or granular type with mild haemorrhage and little necrosis along the vascular arcade in the periphery. They had mild visual impairment (<6/18) and two (6.6%) had no perception of light. 23 eyes (73.7%) had vision ranged from 6/24 to hand movement.

In this study; CD4† count was available in 192 cases ranging from 3 to 759. Among which 83 patients had count between 51-199cells/µl, 78 patients had 1-50 cells/µl and only 4 had cells above 500/µl. Among 78 patients (1-50 cells/µl) 38(48.7%) had ocular involvement and among 83 patients (cells 51-199/µl) ocular involvement was noted in 27(32.5%). In 200-500cell group; only 4 out of 27(14.8%) had ocular involvement. None had ocular involvement with cell count above 500/µl.

Among 21 patients whose cell count was available; 15(71%) had count below 50/µl, 5 patients (25%) had 50-200 cells/µl. This difference was statistically significant (p<0.005). Only one case had cell count of 255/µl. 96 out of 280 patients were on HAART. Among them; 31 had ocular involvement. Six out of 26 patients (23%) of CMV retinitis were on HAART and 20 cases were not on HAART. 11 out of 31 patients (35.5%) were on HAART.

Non specific chorioretinitis was found in 2 patients. One case of tubercular meningitis had multiple hypopigmented spots in the posterior pole (presumed tubercular choroiditis) despite 118 patients who had systemic tuberculosis in our study. One case had toxoplasma chorioretinitis and one case had acute retinal necrosis. Though this series had 3 systemic syphilis; ocular involvement was found in one case only. Vitritis was found in 2 cases (0.7%). Three cases had dry eye (1%); out of which one had toxic epidermal necrolysis. Similarly; herpes zoster ophthalmicus was noted in 1%. Prevalence of anterior uveitis was 2.5 % (n=7, 95 percent confidence interval 1.8-4.2%). Out of seven cases; two had complicated cataract, one had dry eye with retinopathy and rest four cases had only uveitis. Total 4 cases (1.4%) had cataract and 1 % (n=3) had unilateral subconjunctival hemorrhage. One case had molluscum contagiosum (0.4%) with cell count dropping to 48/µl. One critically ill patient had orbital cellulitis. Neuro ophthalmic manifestations were noted in 18 cases (6.4%). Three cases had papilitis (1%), 4 patients had papilloedema (1.4%) and 7 cases had optic atrophy (2.5%). Four cases (1.4%) had cranial nerve paresis, one had HIV encephalopathy. Among 3 cases of papilitis; 2 were with CMV retinitis and the rest was with toxoplasmosis.

### Discussion:

Our study was conducted to report prevalence of ocular manifestations of AIDS in an eastern Indian perspective. Demographic patterns noted in our study were similar to other Indian studies as reported by NACO. Out of 233 people; 82% were male in our study as compared to 79% by NACO and 78% by Biswas et al16, 232 patients (81.89%) were in 20-40 years age group and 87% (41 out of 47) in 20-40 year age group. This is analogous to national statistics where majority of patients (89%) were in 15-44 years age group. This is the most affected group of people affected around the world because they are sexually most active, economically productive and vulnerable to HIV transmission. A large number of people in our study were migrant workers, truck drivers and transport workers. In the present study; heterosexual route of transmission through exposure to commercial sex
workers was the most common risk factor for transmission (87.6%) whereas the National figure was 85%. The next common factor was via blood and blood product transmission in our study (3.9%) which was much reduced (12%) from the study by Biswas et al. This reduction may be due to advancement of blood transfusion service in all facets of donor management, storage of blood, grouping and cross matching and testing blood transmissible diseases. In our series; intravenous drug abusers comprised of 2.85% as compared to 2% in other study. Men having sex with men (MSM) and bisexual accounted for only 1.4% cases in our study but 5% in other study. This is in sharp contrast in USA where the same rate was as high as 47%. Ocular involvement in our study was in 90 out of 280 cases (32.1%) which was lower than other Indian studies (40-45.7%). However Sahu et al reported 100% ocular involvement. Ocular involvement in AIDS was higher in USA (76%) by Freeman et al and 63% by Holland et al. In sub-Saharan African region the rate was 55% by Kestelyn et al and 27% by Lewallen et al. Only 6 out of 26 patients were receiving HAART in our study. There is a less chance of development of CMV retinitis in cases receiving HAART. As most of the patients participating in our study belonged to poor socioeconomic status; they could not afford HAART. Hence, the role of HAART on decreasing visual acuity by retinitis and retinal detachment in our study could not be elicited though other trials claim it to be 30%. The most common systemic infection was tuberculosis in our study which tallies with other national and African studies. Out of 280 patients, we found tuberculosis among 113 patients; 33 of which had extra pulmonary TB. Out of 90 patients who had ocular manifestations in our series; 53 patients (58%) had systemic tuberculosis. The prevalence of HIV positivity is also increasing among tuberculosis patients in this country. Prevalence of HIV among patients with bacteriological or radiological confirmation of tuberculosis in India ranges from 2.8% to 9.4%. Although most of our patients had systemic tuberculosis; only one case had presumed choroidal tuberculosis and one case had choroidal granuloma. It correlates with the fact that although extra-pulmonary TB had been reported in many distant organs; eye is rarely affected. This correlates well with the study done by Lewallen et al who found only one case of presumed choroidal TB.

References:

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