

A study on ocular manifestations in patients with Diabetes mellitus

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Abstract

Background: Ocular complications other than Diabetic Retinopathy are frequent among diabetic population. This includes diseases causing reversible and irreversible visual loss. **Aim:** The aim of this study is to find out the frequency of occurrence of different ocular manifestation in patients with diabetes mellitus. **Design:** Hospital based cross – sectional study on diabetic patients visiting the outpatient department of ophthalmology. **Materials and methods:** A total number of 820 patients of non insulin dependent diabetes mellitus (NIDDM) and insulin dependent diabetes mellitus (IDDM) were included in this study. Ocular examination included oblique illumination study and slit lamp examination for all patients. Visual acuity was recorded using Snellen's chart and intraocular pressure was measured using Gold man applanation tonometer. A-Scan, fluorescein angiography and field charting using automated perimetry were done in selected cases. The results were recorded in a separate proforma for convenience of analysis. **Results and conclusion:** Our study showed cataract as the most common ocular manifestation in patients with diabetes mellitus (DM) followed by diabetic retinopathy. Development of diabetic retinopathy is directly proportional to the duration of the disease. The frequency of occurrence of various manifestations is similar to that of studies conducted worldwide.

Keywords: Diabetic papillopathy, Diabetic retinopathy (DR), Insulin dependent diabetes mellitus (IDDM), Non-insulin dependent diabetes mellitus (NIDDM), Ocular manifestations.

Introduction

A large share of the global diabetes mellitus cases is seen in India. Different studies have shown a steady increase in the prevalence of diabetes in the rural and urban population of India. The increase in the prevalence of the disease in the rural population may be the result of urbanization. Studies conducted in the urban and rural population show an increased conversion of impaired glucose tolerance to diabetes in south India. The prevalence of diabetes has reached approximately 20% in urban and 10% in rural populations [1].

In DM patients various ocular manifestations are seen of which few results in reversible blindness and few results in irreversible blindness.

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Follow up of DM patients are very often done by general physicians. However most of the physicians are unaware of these manifestations. Timely

reference to an ophthalmologist may prevent severe sight threatening diseases. Studies show that xanthelasma is widespread in DM patients. In a study conducted by A.

Jain et al. found that 42.4% of patients with xanthelasma had associated systemic diseases like hypertension, Coronary Artery Disease and DM [2]. It is sharply demarcated yellowish collections of cholesterol which is found under the skin on or around the lids. It is not harmful or painful and can be easily removed. Conjunctiva showed tortuous vessels in diabetic patients [3].

Diabetic neuropathy results in reduced corneal sensation [4]. Thus the chances of developing corneal

ulcer following trivial trauma is common in diabetes. Neovascularization around the pupillary margin is the most serious outcome of diabetes on the iris. It may involve the entire iris surface and angle of anterior chamber [5].

An association between idiopathic anterior uveitis and type 1 DM (63%) was observed by Rothova [5]. Positive associations between DM and primary open angle glaucoma (POAG) are reported [6].

Glaucoma occurs more often in patients with DM than in the general population. Therefore it is important to screen DM patients for POAG as this may be asymptomatic until reported for decreased vision and/or constricted visual fields.

A reduction in visual acuity in people with diabetes is mostly due to cataract, as shown by clinical epidemiological studies and basic science studies [7]. Asteroid hyalosis (AH) is a unilateral condition, where fat and calcium globules are formed in the vitreous. However this may not affect vision.

The study conducted by Akram et al. showed a significant association between diabetes and AH. [8]. An acute vascular condition like Non-Arteritic Anterior Ischemic Optic Neuropathy (NA-AION) is seen in patients with DM. Ischemia is due to diabetic microvascular disease involving the anterior part of the optic nerve. DM is found to be associated with increased risk of developing NA-AION [9].

An extraocular motility disorder is seen in patients with diabetes, involving the third, fourth and sixth cranial nerves. Simultaneous multiple extra ocular nerve palsies are seen, even though rarely. Diabetes is the underlying cause in 25–30% of patients above 45 years who develop acute extra-ocular muscle palsy [10].

Diabetic retinopathy and NA-AION [11] progresses rapidly in patients with diabetic papillopathy (DP) [12]. The significance of this condition is twofold. Primarily this may be misdiagnosed as papilledema. Secondly telangiectasia at the optic disc in DP may be mistaken as neovascularization in the optic disc as part of proliferative diabetic retinopathy.

DP spontaneously improves within a year, and visual prognosis is usually good. Diabetes is significantly related to retinal vein occlusion where increase in blood viscosity as well as turbulent flow leads to central retinal vein occlusion (CRVO) [13]. The signs of CRVO (e.g., hemorrhages or cotton wool spots) may “mimic” diabetic retinopathy. Hence in DM patients presenting with acute vision loss and unilateral diabetic retinopathy, CRVO should be ruled out.

Considering the ocular complications in diabetes the present study was designed to find out the frequency of its occurrence in diabetes mellitus and the relationship between various risk factors and development of diabetic retinopathy (DR).

Materials and Methods

Patients included in this study were mainly referred from diabetic clinic (95%) and others (5%) with ocular manifestations suggestive of DM from the outpatient department of Ophthalmology of a medical college. Diagnosis was done by blood sugar tests.

In each case after recording the detailed history including family history, general and ocular examinations were carried out. Ocular examination included oblique illumination study, slit lamp bio microscopic examination, measurement of visual acuity using Snellen's chart, Intraocular pressure measured using Goldman Aplanation tonometer and visual fields assessed using automated perimetry.

Pupils were dilated with Tropicamide eye drops for retinoscopy and fundus examination. A scan was done for cases with refractive error.

Fundus examination was done using direct ophthalmoscope and indirect ophthalmoscope. Necessary fundus diagrams were drawn in the case sheet. Fluorescein angiography was done in few cases.

The three types of diabetic retinopathy are pre-proliferative diabetic retinopathy (PPDR), proliferative diabetic retinopathy (PDR) and diabetic retinopathy with or without macular edema. For further analysis findings of each patient (n 820) were recorded in separate proforma. MS Excel and SPSSII version were used for data analysis.

Results

The details of patients included in the study are given below.

Type	Total	Age	Male	Female
NIDDM	810	31-87	345	465
IDDM	10	11-30	8	2
Total	820	--	353	467

Patients were referred mainly from diabetology clinic (95%). The remaining 5% had ocular manifestations as presenting symptoms of diabetes. The remaining group included 6 with recurrent chalazion, 26 with cataract and 9 with refractive errors. The result of total study is given in Table 1, 2 & 3.

Table 1: Results of Anterior segment manifestations observed in this study

No:	Ocular manifestations	Male	Female	TOTAL	%
1	Lids xanthelasma	4	10	14	1.7
	Recurrent chalazion	14	10	24	2.9
2	Tortuous conjunctival blood vessel	2	6	8	1
3	Corneal ulcer	6	10	16	2
4	Iridocyclitis	9	6	15	1.8
	Rubeosis Irides	3	5	8	1
5	Primary open angle glaucoma	18	37	55	6.7
	Primary angle closure glaucoma.	2	7	9	1.1
	Secondary glaucoma-neovascular	4	6	10	1.2
6	Cataract	217	259	476	58
7	Change in refractive error	60	38	98	12

The most common ocular manifestation is cataract.

Table 2: Posterior segment manifestations observed in this study

No:	Ocular manifestations	Male	Female	Total	%
1	Vitreous Haemorrhage	10	6	16	2
	Asteroid hyalosis	2	6	8	1
2	Retinopathy				
	PPDR	126	170	296	36.1
	PDR	12	20	32	4
	Maculopathy ± retinopathies	97	76	173	21.1
3	Optic disc-AION	5	0	5	0.6

4	Mono neuropathies				
	3 rd N	2	0	8	1
	6 th N	5	1		
5	Diabetic papillopathy	0	7	7	0.9
6	CRVO	2	10	12	1.5

Diabetic retinopathy is the most common posterior segment manifestation.

Table 3: Duration of diabetes Vs diabetic retinopathy observed in this study

Duration in years	No: of patients	Diabetic retinopathy	%
0-4	492	141	28.7
5-9	180	96	53.3
10-14	107	77	72
> 15 yrs	41	30	73.2

Incidence of diabetic retinopathy is directly proportional to the duration of DM

Discussion

Physician awareness is essential in reducing the incidence of visual loss in patients with DM. A range of Ocular manifestations leading to visual loss is associated with diabetes. However, some of these ocular conditions may not be familiar to the general physicians. In this study, incidence of xanthelasma is 1.7% (Table 1). Several structural changes in the conjunctival blood vessels are seen in diabetic patients [3]. Our study showed tortuous conjunctivitis in 1% cases (Table 1). Assessment of corneal sensitivity using the Cochet-Bonnet aesthesiometer (C-BA) showed significant reduction in DM [14]. This may result in developing corneal ulcer secondary to trivial trauma. Present study showed 1% of corneal ulcer. Rubeosis Irides was present in 1%. In the current study we observed 2 % cases with iridocyclitis (Table1) where as one report showed 63% cases of idiopathic anterior uveitis [5]. Prevalence of POAG was 1.6 – 4.7 times more in patients with diabetes than in non diabetic individuals [15]. In the present study POAG is seen in 6.7% and PACG in 1.2 % (Table 1). Other studies showed cataract as the major cause for defective vision [13]. In the present study also the most common ocular manifestation causing defective vision is cataract (58%). Cataract occurred at a younger age and progressed more rapidly in diabetic patients, resulting in cataract surgery at a young age [16]. We observed the mean age of cataract patients as 55.6 years. In the past, it was suggested that Asteroid Hyalosis (AH) was more prevalent in diabetics [17]. Though recent elaborate studies have not shown a major association between AH and diabetes [18], in the present study, we observed 1 % cases of AH. Earlier studies suggested that up to 25% of patients with NA-AION had a history of diabetes [19]. In our study 0.6% showed NA-AION.

We observed 1% cases with mononeuropathy (Table 2). Similar observation is reported by Watanabe et al.(1990) [20] where 1% patients with DM had cranial nerve palsies, where as only 0.13% of control subjects had cranial nerve palsies. Of these cases, 41% had a third nerve palsy. In another study, patients with sixth cranial nerve palsy were more likely to have diabetes [10]. Diabetic papillopathy is a rare optic nerve condition where acute disc edema and mild vision loss are seen [11]. In the present study 0.9 percent had diabetic papillopathy (Table 2).

Country	Percentage
Nepal[23]	44.7
Tehran[24]	37
Yemen[25]	55
China[26]	43
Present study	42

The most consistent risk factor for the development and severity of retinopathy is duration of diabetes [21, 22]. The present study conducted also showed an increase in the incidence of diabetic retinopathy as the duration of diabetes increases (Table 3). Prevalence of diabetic retinopathy reported by different authors is shown above with our observations.

Conclusion

A wide spectrum of ocular conditions other than diabetic retinopathy is seen in diabetes. Some of these conditions appear to be casually linked to hyperglycemia and diabetes, whereas diabetes may be only one of many risk factors for other conditions. In addition, there are a range of retinal conditions that mimic common diabetic retinopathy signs. The management of ocular manifestations in DM is mainly preventive.

A regular examination of the eye and timely reference to an ophthalmology unit reduces the risk of diabetes induced visual loss. Most of the cases present as gradual loss of vision; however in some cases, where visual loss is sudden an acute surgical or laser interventions may be required.

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Flow immunophenotyping features of crisis phase of chronic myeloid leukemia in childhood: do we really care?

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Abstract

Objective: Chronic leukemias are rare in childhood & CML is extremely rare in children. Immunophenotypic studies have a limited role in the diagnosis of CML but are increasingly being used in CML blast transformation. Purpose of the study was determine the clinical and laboratory and Flow immunophenotyping (FIC) features with Mutational analysis of blast transformation of CML in children. **Methods:** 11 years analysis was done 187 cases of suspected CML were studied in children and adolescents. Patients were evaluated at KMIO between 2004 to 2015. 97 cases had Bone marrow diagnosis of CML. 22 cases peripheral smear was suggestive of blastic phase CML (20 %) were chosen for the study. Bone marrow confirmation was available in all the cases. Cytogenetics and Molecular confirmation was also available in all cases. FIC was done in 8/22(36%) cases. Mutations were studied in 7 cases. **Results:** The disease predominantly affected older children more than 10 years 16/22(72 %). Male sex predilection was seen. Gender ratio was 1.4: 1. Most predominant clinical sign was splenomegaly. Leucocyte count >100X10⁹/L was seen in all cases. Peripherals smear suggested CML in all 22cases and bone marrow aspiration confirmed the diagnosis. 17 Cases were at diagnosis. 5 Cases progressed to blastic phase from chronic phase. Median year of transformation was 4 years. In 22 cases Phildelphia chromosome was noted and 5 cases revealed additional markers PCR revealed p210 transcript in all cases. In 8 cases in the blastic phase Flow cytometry immunophenotype was done. 5 cases were myeloid blastic phase, single case was mixed phenotype, 2 cases were lymphoid blastic phase. **Conclusion:** Imatinib highly effective in children with advanced phase of CML. This is the largest, exclusive first reported series of blastic phase of CML in children from a single center. Only 5 cases received Imatinib, All 5cases attained remission; Cases are on follow up and continue to be in remission after a mean of 6 months.

Key words: CML: chronic myeloid leukemia, childhood, polymerase chain reaction. FCI: Flowcytometry immunophenotyping, Blastic phase

Introduction

Chronic Myeloid Leukemia (CML) is a stem cell disorder and is clonal. Balanced translocation between the long arm of chromosome [9] and 22,t(9:22)(q34;q11) also called the Phildelphia chromosome is the hallmark of this disease [1]. CML are rare in children, constitutes around 3% of

leukemias in children [2,3]. Usual initial presentation is chronic phase [4]. Blastic phase (BC) as initial presentation of CML accounts for only 10% of all cases [5]. We studied laboratory features including the clinical features of blastic phase of CML in children. PS, BMA, Cytogenetics, flow cytometry Immunophenotype (FCI) were studied in detail with the special note on molecular methods, including BCR-ABL transcripts and mutation analysis. Present study is the first exclusive and largest

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