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ORIGINAL ARTICLE

OPHTHALMIC MANIFESTATIONS OF COMMON HAEMATOLOGICAL DISORDERS

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ABSTRACT: BACKGROUND AND OBJECTIVES: - To study complete clinical profile of ocular manifestations in haematological disorders **METHODS:** This was a prospective non-interventional study done on 60 cases admitted and diagnosed with various haematological disorders in Medicine, Paediatrics, Obstetrics and Gynaecology wards. Whenever general condition permitted, patients were examined in more details in the Ophthalmology O.P.D. For the record of visual acuity, a standard Snellen's chart was used. Dilated fundus examination was done in every case. Patients with diabetes, hypertension and dense cataracts were excluded. **RESULTS:** Out of total 60 cases, 39 cases of anaemia, 13 cases of leukaemia, 4 cases of haemorrhagic disorders and 4 cases of haemoglobinopathies were studied. Conjunctival pallor was observed in all cases (100%) of anaemia and fundal pallor in 38.46 % cases. Retinal haemorrhages were present in 57.14 % cases of megaloblastic anaemia, 50% cases of combined nutritional deficiency anaemia and 60% cases of aplastic anaemia, but absent in iron deficiency anaemia cases. Overall incidence of ocular manifestations in leukaemia was 69.23%. It was higher (87.5 %) in acute leukaemia as compared to chronic leukaemia (40%). Two cases of purpura with associated anaemia showed retinal flame shaped haemorrhages. Thalassemia major cases showed changes like conjunctival pallor and fundal pallor. **CONCLUSION:** It is essential to examine all patients' with haematological disorders for ocular manifestations as it helps in diagnosis and prognosis. Early recognition of the ocular manifestations is of great importance as early institution of treatment may prevent or alleviate both ocular and systemic complications.

KEYWORDS: Anaemia, haematological disorders, ocular manifestations.

INTRODUCTION: The blood is common to every tissue and its disease may be present in any part of body. The columns of arterial and venous blood lie exposed in the fundus of eye, so that they can be observed through the ophthalmoscope during any time of life. The ophthalmic symptoms may be initial mode of presentation so the ophthalmologist is often the first witness before the patient reaches the haematologist for final diagnosis.

Anaemias are most common haematological disorders in India. Pallor of palpebral conjunctiva is the constant ophthalmological finding in anaemia and inspection of this tissue has provided a time honored, although not highly accurate index of severity of anaemia. The retinal metabolism is unable to tolerate its deprivation of essential supplies falling prey to hypoxic damage in end. Anaemic damage can be thus an indicator for retinal damage manifesting as haemorrhage or pallor.[1]

With progression of the disease, haemorrhages, exudates, distended tortuous retinal veins and ultimately even papilledema may occur in ocular fundus.[2]

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Leukaemia while less prevalent may affect any ocular tissue either by direct infiltration of the leukemic cells or the secondary effect of the neoplasm. Retinal changes are most commonly seen clinical manifestation of Leukemic involvement of the eye.

They are nonspecific and generally due to combination of accompanying anaemia, thrombocytopenia and leukocytosis.[3]This manifestations include vascular sheathing and tortuosity, pallor, haemorrhages and exudates, cotton wool spots and neovascularization at the periphery of the disc.[4]

Haemorrhagic disorders such as Purpuras may present with haemorrhages involving whole of the retina and vitreous in young girls especially who suffer from Idiopathic thrombocytopenic purpura. Thrombocytopenic purpura should be included as one of risk factors of expulsive choroidal haemorrhage.[5]

Haemoglobinopathies such as Sickle cell disease which is an inherited blood disorder that affects red blood cells.It may present with lid oedema, conjunctival sickling sign, iris atrophy, and iris neovascularisation and angioid streaks. In sickle cell thalassemia exudative and haemorrhagic changes have been found in the retina.[6]

Ophthalmic manifestations in polycythemia are seen due to increase in blood viscosity with slowing of circulation and resulting hypoxia. The changes may be seen from dilated tortuous retinal veins, haemorrhages, papilledema to central retinal vein occlusion.[7]

Fundus changes in haematological disorders are studied in literature but ocular manifestations in haematological disorders as a whole are poorly studied, so we have tried to study above facts in detail.

Various reports[8,9] also indicate that their indeed exist a link between haematological abnormality and ocular manifestations.

AIMS AND OBJECTIVES:

1. To find out incidence of ocular manifestations in haematological disorders.
2. To study clinical presentation of ocular manifestations of haematological disorders.

MATERIALS AND METHODS: This prospective non-interventional study was undertaken in the department of ophthalmology for period of 24 months.

60 cases admitted and diagnosed with various haematological disorders were studied for ocular manifestations related to it. All the cases were examined for ocular manifestations in the respective wards, where the patients were admitted.

Exclusion criterion was diabetes, hypertension, and media opacities. Whenever general condition permitted, patients were examined in more details in the Ophthalmology O.P.D with detailed anterior and posterior segment evaluation. For the record of visual acuity, a standard Snellen's chart was used.

Detailed fundus examination was done in every case after full mydriasis. Fundus photography and Fundus Fluorescein Angiography was done in selected cases showing posterior segment lesions. Ultrasonography study (A-scan, B-scan) was done in selected cases.

When patients were called by respective departments for review, simultaneous ophthalmic examination and evaluation was done in the cases which presented with ocular symptoms and signs.

DOI: 10.14260/jemds/2014/3370

All patients were subjected to detailed history, thorough clinical examination, routine and specific lab investigations bone marrow study and lymph node biopsy.

The details of the patients and of examination findings along with ocular examination and investigations were recorded in proforma.

RESULTS: Out of total 60 cases, 39 cases (65%) were of anaemia, 13 cases (21.66%) of leukaemia, 4 cases (6.66%) of haemorrhagic disorders and 4 cases (6.66%) of haemoglobinopathies. We got maximum number of patients in age group below 10 years (36.6 %). The next group of patients comprising 20 % was between 21 to 30 years and 31 to 40 years (13.33 %), 11 to 20 years (8.33 %), 41 to 50 years (10 %), 51 to 60 years (5 %) and above 60 years (6.66%).32 (53.33 %) patients were females and 28 (46.66 %) cases were males.

Anaemia-Out of 39 cases of anaemia included in study, maximum number of cases were of iron deficiency anaemia (43.58%). 17.94% cases were of megaloblastic anaemia, 25.64% of combined nutritional deficiency anaemia and 12.82% cases of aplastic anaemia (Table 1).

Type of anaemia	No. of cases	Percentage
Iron deficiency anaemia	17	43.58 %
Megaloblastic anaemia	7	17.94%
Combined nutritional deficiency anaemia	10	25.64 %
Aplastic anaemia	5	12.82 %
Total	**39**	**100 %**

Table 1: Distribution of cases according to type of anaemia

All cases of anaemia (100%) showed conjunctival pallor.

In our study none of the case of iron deficiency anaemia showed retinal haemorrhages but various types of retinal haemorrhages were present in megaloblasticanaemias (4 out of 7 cases 57.14 %), combined nutritional deficiency anaemias (5 out of 10 cases i.e., 50%) and aplastic anaemias (3 out of 5 cases i.e., 60%).

Ocular Manifestations	Iron deficiency anaemia (17 cases)	Megalobiastic anaemia (7 cases)	Nutritional deficiency anaemia (10 cases)	Aplastic anaemia (5 cases)	Total (39 cases)	Percentage
Diminution of Vision	--	2	5	2	9	23.07%
Lid oedema	1	--	--	--	1	2.56%
Conjunctival pallor	17	7	10	5	39	100%
Subconjunctival haemorrhage	--	--	1	--	1	2.56%
Fundal pallor	4	5	5	1	15	38.46%
Papilledema	--	--	--	2	2	5.12%
Venous dilatation & tortuosity	--	1	--	1	2	5.12%
Retinal oedema	--	1	--	2	3	7.69%

DOI: 10.14260/jemds/2014/3370

Flame shaped Haemorrhage	--	4	5	3	12	30.76%
White centered Haemmorage	--	2	3	--	5	12.82%
Vitreous/ Sub-hyaloidhaemorrhage	--	2	2	2	6	15.38%
Cotton wool spots	1	--	3	--	4	10.25 %
Macular star	--	--	1	1	2	5.12 %

TABLE 2: Distribution of ocular manifestations in anaemia cases

Table 3 shows relationship of retinal haemorrhages with haemoglobin level in anaemia cases. In our study all cases of anaemia with haemorrhages in the fundus were with haemoglobin level less than 5 gm%.The incidence of retinopathy increases with profundity of theanaemia.

Haemoglobin Level (gm %)	No. of cases of anaemia studied	No. of cases with retinal haemorrhages
1-1.9	3	2
2-2.9	13	6
3-3.9	6	1
4-4.9	9	3
5-5.9	5	0
6-6.9	3	0
Total	**39**	**12**

Table 3: Relationship of retinal haemorrhages with haemoglobin level

Fig. 1: Fundus photo of a case of combined nutritional deficiency anemia showing flame shaped haemmorhage, white centered haemmorhages and subhyaloid haemmorhage.

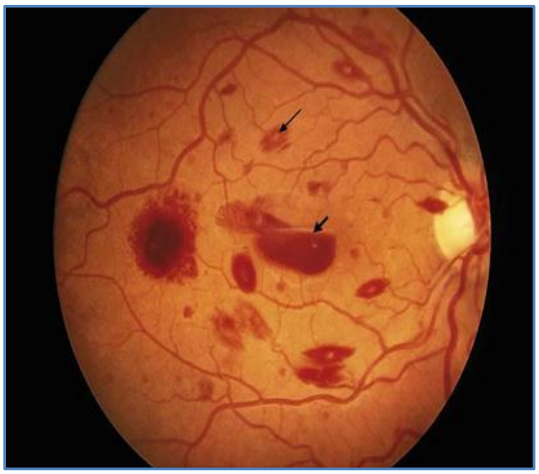

Fig. 1

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Leukaemia: In this study, we studied total 13 cases of leukaemia.

Out of which 8 cases (61.53 %) were of acute leukaemia4 cases of acute myeloid leukaemia (AML) and 4 cases of acute lymphoblastic leukaemia (ALL).

5 cases (38.46%) were of chronic leukaemia.3 cases of chronic myeloid leukaemia (CML) and 2 case of chronic lymphocytic leukaemia (CLL)

Out of 13 cases of leukaemia, ocular manifestations were present in 9 cases (69.23%).

Leukaemia	No. of cases	No. of cases with ocular manifestations	Percentage
All leukaemia	**13**	**9**	69.23 %
Acute leukaemia	**8**	**7**	87.5 %
Chronicleukaemia	**5**	**2**	40%

Table 4: Percentage of leukaemia cases with ocular manifestations

Out of 13 cases, flame shaped haemorrhages were present in 9 cases (69.23%), white centered haemorrhages in 4 cases (30.76%), sub hyaloid haemorrhages in 2 cases (15.38%).Cotton wool spots were observed in 3 cases (23.07%). Cotton wool spots are a prominent feature of leukemic retinopathy.

Haemorrhagic disorders: We studied 2 cases of idiopathic thrombocytopenic purpura and 2 case of Henoch-Schonleinpurpura. Out of these 4 cases, flame shaped haemorrhages were present in 2 cases (50%), papilloedema and dilated tortuous vessels in 1 case (25%) and subconjuctival haemorrhage was present in 1 case (25%) Thus ocular manifestations were present in 3 out of 4 cases (75%) of purpura.

Haemoglobinopathies: We studied 3 cases of thalassemia major and 1 case of sickle cell disease.

Out of these 4 cases, conjunctival pallor was observed in 3 cases and fundal pallor in 2 cases. Thus out of 4 cases, 3 cases (75%) showed ocular manifestations.

DISCUSSION: Haematological diseases encompass a wide spectrum of disorders ranging from benign to malignant conditions that can present with ocular involvement. The ocular manifestations may be the initial indication of an underlying haematological disorder, which often requires a laboratory work-up to arrive at a final diagnosis.

The ocular manifestation is often asymptomatic. Common manifestations include conjunctival pallor and haemorrhages, intraretinal haemorrhages and cotton wool spots. Retinal infiltrates, bleeding manifestations of anterior segment, eye lid, orbit, optic nerve are rare.

Anaemias are the most common haematological disorders in India and iron deficiency anaemia is the commonest type of anaemia.

Among 39 patients of anaemia, maximum number of cases were of iron deficiency anaemia (43.58%). It was observed that decreased amount of Haemoglobin in blood lead to subjective impression of pallor and critical level was 5 gm % which was consistent with other studies.[10]

All cases of anaemia (100%) showed conjunctival pallor. Flame shaped haemorrhages were present in 12 cases (30.76%), subhyaloid haemorrhage in 6 cases (15.38%), white centered haemorrhages in 5 cases (12.82%). There was no evidence of vitreous haemorrhage in our study.

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Foster Moore (1925),[11] well' known for his painstaking clinical observations, stated that "few, if any, patients die of leukaemia, whether lymphocytic or myelogenous, acute or chronic, without at some time showing ocular manifestations. "Estimates of the occurrence of ophthalmic manifestations of leukaemia are varied.

Out of 13 cases of leukaemia, venous dilatation was seen in all cases of acute leukemia. Literature documents venous dilatation and tortuosity as initial retinal changes in leukemia.[12] Flame shaped haemorrhages were present in 9 cases (69.23%), white centered haemorrhages in 4 cases (30.76%), and sub hyaloid haemorrhages in 2 cases (15.38%).

Retinal haemorrhages are extremely common in leukemic fundus particularly in the acute type of the disease and indeed they may be the only and most frequent and serious ocular complication. Cotton wool spots were observed in 3 cases (23.07%). Cotton wool spots are a prominent feature of leukemic retinopathy.

Pathologic studies, such as those of Allen and Straatsma (1961)[13] have quoted an ocular involvement in 50% of cases. 80% of these changes were in cases of acute leukaemia, whereas only 20% were associated with chronic leukaemia.

In haemorrhagic disorders ocular manifestations were present in 3 out of 4 cases (75%) of purpura.

Rubenstein et al (1968)[14] found in their study that in thrombocytopenia with associated anaemia, the incidence of ocular haemorrhages is as high as 70% if both are severe. In thrombocytopenia alone it was 0%. (They studied 6 cases) and in anaemia alone 10% in their study.
2 cases (50%) which showed haemorrhages in our study were having associated anaemia, one with haemoglobin level 7 gm% and other with 10.8 gm%.

Out of 4 cases of Haemoglobinopathies, 3 cases of thalassemia major and 1 case of sickle cell disease, 3 cases (75%) showed ocular manifestations. These changes perhaps are not specific of thalassemia major and depend more on the degree of anaemia.

None of these patients showed retinal haemorrhages. These patients were all previously diagnosed cases of thalassemia major and had reported to the hospital for blood transfusions. This indicates that the disease was not freshly diagnosed and other retinal findings, if any, may have regressed.

The limitation of our study was that detail response to treatment could not be documented as it was one time analysis and patients were referred to us by concerned experts.

CONCLUSION: To conclude Haematological disorders affect millions worldwide, with the potential for significant morbidity and mortality. The ocular manifestations may be the initial indication of the underlying haematological disease.

Because prompt diagnosis and treatment is critical in management of these disorders, it is essential to be aware of these changes as well as the important clinical findings associated with haematological disorders.

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