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# Ophthalmic Manifestations in Blood Dyscrasias - An Observational Study

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**Abstract**

**Aim:** The present study was conducted to study the spectrum of ophthalmic manifestations in blood dyscrasias and to assess the prevalence of ocular manifestations between acute and chronic blood malignancies.

**Material and Methods:** The Present observational study was conducted on a total of 200 patients diagnosed with blood dyscrasias at the Department of Ophthalmology, tertiary care hospital, Bhuj, during the study period of 2 years. Detailed history and examination were conducted, and findings were noted. All relevant haematological investigations were also done.

**Results:** Out of 200 patients, anemia was the most common diagnosis observed in 70 (35%) cases, followed by sickle cell anemia 54 (27%). Out of 70 patients with anemia, the majority of cases, i.e. 33, had iron deficiency anemia followed by 13 and 5 cases with megaloblastic and aplastic anemia, respectively. Retinal Veinous Tortuosity was the most common finding in Thalassemia. In contrast, Veinous Fullness and Tortuosity and sub - conjunctival bleeding were the most common finding in patients with leukemia and coagulation disorders, respectively.

**Conclusion:** The ocular changes of blood dyscrasias are not uncommon as is proved by various clinical and pathological studies. These changes in the eye are due to the hemorrhagic effect of the blood disorders or due to the infiltration of the ocular tissues by malignant cells. Ophthalmic manifestations are commonly observed in patients with blood dyscrasia.

**Keywords:** Anemia, Blood dyscrasias, Retinal Veinous Tortuosity, Sub - conjunctival bleeding

## Itroduction

The blood is common to every tissue, and its disorder can affect any part of the body. Anemia is the most common haematological disorder in India, which the pallor of palpebral conjunctiva can identify, although not a highly accurate index of severity of anemia. Damage by anemia can be an indicator for retinal damage manifesting as haemorrhage or pallor.[1] As the disease progresses, haemorrhages, exudates, distended tortuous retinal veins and ultimately even papilloedema may occur in the ocular fundus.[2]

The word dyscrasia comes from the Greek language and means"bad temperament". An increase or decrease in the total number of red cells in a given patient is referred as polycythaemia or anemia respectively.[3] A large population of atypical or neoplastic white blood cells within the blood constitutes leukemia. A subnormal number of platelets in the circulating blood or loss of normal platelet function can lead to bleeding disorders or coagulopathies.[4]

The ocular fundus examination offers a unique opportunity for direct observation of small blood vessels and vascular lesions. In any systemic condition, fundus examination helps in the diagnosis and/or prognosis of the condition.[5] Besides the skin

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and mucous membranes, where blood dyscrasias can sometimes produce visible symptoms, the retina presents our best early diagnostic opportunity. Indeed, significant ocular manifestations are not uncommon in these disorders and vision related issues may be the presenting symptom.[6] However, since patients may often present without symptoms, a review of retinal signs associated with blood dyscrasias is warranted.

Changes in the retina are the most common clinical manifestation of Leukemic involvement of the eye. These manifestations include vascular sheathing and tortuosity, pallor, haemorrhages and exudates, cotton wool spots and neovascularization at the periphery of the disc.[7] The presence of ocular involvement is associated with poor prognosis in acute childhood leukaemia.[8] Coagulative disorders such as Purpuras can present with haemorrhages involving the whole of the retina and vitreous in young girls, especially those who suffer from Idiopathic thrombocytopenic purpura.[9] Sickle cell disease can present with lid edema, conjunctival sickling sign, iris atrophy, and iris neovascularisation and angioid streaks. In the sickle cell, Thalassemia exudative and haemorrhagic changes have been found in the retina.[10] Notably, the incidence of proliferative retinopathy is highest in patients with HbSC or S-beta Thal, while patients with HbSS have a 3% incidence of proliferative retinopathy.[11]

Various reports indicate that there exists a link between haematological abnormality and ocular manifestations.[8] Ocular manifestations of thrombocytopenia included papilloedema, extraocular muscle palsies and visual field defects, which usually result in concomitant CNS findings. Retinal findings consist of hemorrhages, vascular occlusions and serous detachments.

The present study was conducted to study the spectrum of ophthalmic manifestations in blood dyscrasias and to assess the prevalence of ocular manifestations between acute and chronic blood malignancies. The study also aimed to correlate ophthalmic findings in anaemia, thalassaemia, leukaemia, lymphomas and other bleeding disorders.

**Material and Methods**

Patients with blood dyscrasias referred for complete ophthalmic examination from the Department of Medicine and Paediatrics to Department of Ophthalmology, Gujarat Adani Institute of Medical Science, Bhuj were included in the study for the duration of 2 years. Sample size was 200 patients diagnosed with blood dyscrasias.

Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants.

Inclusion criteria: All the patients diagnosed with blood dyscrasias, including anaemia, thalassaemia, leukaemia and bleeding disorders; belonging to an age group of fewer than 70 years and giving consent for the complete ophthalmic examination.

Exclusion criteria: whereas pregnant females; patients with the known ocular disorder; with a history of any ocular trauma due to RTA/head injury/ocular injury and not giving consent for the study.

Detailed history regarding sociodemographic variables such as age, gender, socioeconomic status etc., was obtained and entered the questionnaire. Clinical history regarding the blood dyscrasias, presence of ocular symptoms, time since diagnosis, chemotherapy received, and other relevant information was obtained from all the study participants and documented. The examination of the eyes was carried out at the bedside or in the eye department. Visual acuity was recorded using Snellen charts, and refractive error was assessed. Anterior segment examination was done using a slitlamp. Intrao-ocular pressure was measured using schiotz tonometer and applanation tonometer. Fundus examination was done by slit-lamp biomicroscopy, binocular indirect ophthalmoscopy. Fundus Fluorescein angiography and fundus photography were done wherever indicated. Additional procedures including Fundus Fluorescein Angiography (FFA) and OCT, B- SCAN of the eyes, central nervous system examination was done in cases suggested.

Further, all relevant hematological investigations like Hb%, TLC, DLC, peripheral smear, reticulocyte count, serum iron studies, bleeding and coagulation profile, serum iron studies were done in all the cases. Other routine investigations like serum electrolytes, urine routine microscopy, blood sugar profiles were ordered wherever indicated. And appropriate hematological/ histopathological investigations like bone marrow studies were ordered whenever indicated.

## Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

## Results

Out of 200 patients, anemia was the most common diagnosis observed in 70 (35%) cases, followed by sickle cell anemia 54 (27%). Out of 70 patients with anemia, the majority of cases, i.e. 33, had iron deficiency anemia followed by 13 and 5 cases with megaloblastic and aplastic anemia, respectively. However, anemia secondary to other causes was observed in 19 cases. Out of 54 patients with sickle cell anemia, Sickle Cell Anaemia (Homozygous) Hb-SS was seen in 27 (50%), Sickle Cell Trait (SC-As) in 18, Sickle Cell Disease-Thalassemia (ScThal) in 7 and HbD (Punjab variant) were noted in 2 cases. Among 18 patients, AML, ALL, CML and CLL were observed in 5, 3, 9 and 1 cases, respectively.

The majority of cases were males in our study (52%). The mean age of patients was 27.8 years, and the majority of patients belonged 0 to 10 years (29%), followed by 30 to 40 years (22%). (Table 1)

In patients with anemia, 57.14% of cases had normal results, whereas 37.14% had conjunctival pallor. However, in sickle cell anemia, conjunctival pallor and comma sign was observed in 61.1% of cases each. Retinal Veinous Tortuosity was the most common finding in Thalassemia. In contrast, Veinous Fullness and Tortuosity, and subconjunctival hemorrhage were the most common findings in patients with leukemia and coagulation disorders, respectively. (Table 2)

The above table suggests that the most common findings in blood dyscrasias were pallor of the fundus and veinous tortuosity/ fullness. Both these findings were observed in maximum proportions of cases with anemia, sickle cell anemia and Thalassemia. However, retinal hemorrhages were the most common finding in leukemia, whereas Veinous Tortuosity/ Fullness were the most common finding in coagulation disorders.

**Table 1: Distribution of study participants according to sociodemographic variables**

| Variables | | Number | Percentage (%) |
|---|---|---|---|
| Gender | Male | 104 | 52 |
| | Female | 96 | 48 |
| Age (years) | 0-10 | 58 | 29 |
| | 11-20 | 44 | 22 |
| | 21-30 | 46 | 23 |
| | 31-40 | 44 | 22 |
| | 41-50 | 30 | 15 |
| | 51-60 | 6 | 3 |
| | >60 | 2 | 1 |

**Table 2: Ophthalmic manifestations in various blood dyscrasias**

| Blood dyscrasias | Ophthalmic finding | Number | Percentage (%) |
|---|---|---|---|
| Anemia (n=70) | Normal | 40 | 57.14 |
| | Conjunctival Pallor | 26 | 37.14 |
| | The pallor of fundus, Veinous Tortuosity/venous Fullness | 25 | 35.7 |
| | Flame Shaped Haemorrhages With White Centres | 20 | 28.5 |
| | Superficial Haemorrhages With Cotton Wool Spots | 7 | 10 |
| | Neo- Vascularisation | 4 | 5.71 |
| | Subhyaloid Haemorrhage | 3 | 4.2 |

| Blood dyscrasias | Ophthalmic finding | Number | Percentage (%) |
|---|---|---|---|
| Sickle cell anemia (n=54) | Conjunctival Pallor | 33 | 61.1 |
| | Conjunctival Sign (Comma Sign) | 33 | 61.1 |
| | Normal | 20 | 37.03 |
| | The pallor of fundus, Veinous Tortuosity/venous Fullness | 32 | 59.25 |
| | Flame Shaped Haemorrhages With White Centers | 26 | 48.1 |
| | Cotton Wool Spots | 15 | 27.7 |
| | Retinitis Proliferans with Neovascularisation | 3 | 5.5 |
| | Black Sunburst Sign | 1 | 1.85 |
| | Vitreous Haemorrhage | 3 | 5.55 |
| Thalessemia (n=40) | Normal | 19 | 47.5 |
| | Dry eye | 4 | 10 |
| | Lenticular Opacities | 3 | 7.5 |
| | Retinal Veinous Tortuosity | 13 | 32.5 |
| | Retinal Pigment Epithelium Changes(Degeneration/ Mottling) | 11 | 27.5 |
| | Defective Color Vision | 3 | 7.5 |
| | Defective Visual Field | 2 | 5 |
| Leukemia (n=18) | Normal | 5 | 27.7 |
| | Orbital Involvement | 1 | 5.5 |
| | Sub-Conjunctival Haemorrhage | 1 | 5.5 |
| | Veinous Fullness and Tortousity | 13 | 72.2 |
| | Flame Shaped Haemorrhage with White Centers | 9 | 50 |
| | Cotton Wool Spots | 3 | 16.6 |
| | Pre-Retinal Haemorrhage | 5 | 18 |
| | Papilloedema with Neo-Vascularisation Over Disc | 3 | 16.6 |

## Discussion

Many studies and case reports highlighting the ocular manifestations of different blood dyscrasias are present in the literature. However, the results shown by them are not uniform and the significance of these changes and their relationship with hematological parameters has been reported differently by various studies.[9-11] There are, however, certain common denominations in these diseases which predispose to the formation of retinal lesion.[12]

The maximum number of patients had iron deficiency anemia which is a common factor in our country. Anemia was observed in patients with a mean age of 27.8 years with a slightly high male: female ratio. In our study, around 39% of cases with anemia had retinopathy. Similarly, 28.35% and 22.5% of patients had retinopathy in a survey by Rubenstein et al.[12] and Merin et al[13], respectively. The subsequent common finding comprised of flame-shaped haemorrhages and haemorrhages with central pallor suggestive of Roth spots. It has been documented in the literature that fundus findings have been associated with a profound fall of haemoglobin, and a critical level of 50% fall has been described by Ballantyne et al.[14]

Out of 54 patients with sickle cell anemia, 33(61.1%) patients had conjunctival sign positive in them, and 20 of them belonged to SS, had AS, and 5 were cases of sickle- thalassemia trait. Cordon et al [15] reported corkscrew-like dilated conjunctival vessels in 74 out of 76 SS patients. They correlated this finding with irreversibly sickled cells.

The authors described retinitis proliferans to be common in HbC (SC) and auto- infarction in homozygous (SS) disease. Meurs et al[16] observed proliferative retinopathy in 2% of SS patients and 50% of SC patients. It led to vitreous hemorrhage in 18% and RD in 8% of cases.

In this study, 18 cases with leukaemia were enrolled, of which chronic leukaemia was found more in number than acute leukaemia. About 75% of subjects had venous fullness and tortuosity, 50% of patients had flame-shaped hemorrhage with white centres, however, 16.6% had neovascularisation on the disc and cotton wool spots in the general fundus, and 16.6% had bilateral papilloedema. Retinopathy in leukemia was observed in 56% of Kataria et al[17] and 44% cases by Holt et al[18]. The wide variation in incidence of ocular involvement in these studies may be ascribed to majority of them being pathological studies whereas ours was a clinical study. The figures of retinal hemorrhages in all types of leukemia are 43% by various studies.[19-21]

Most common ocular finding in patients with Thalassemia was retinal veinous tortuosity followed by retinal pigment epithelium changes. Similar findings were observed by Jafari et al.[22]in which ocular findings such as the dry eye, cataract, retinal pigment epithelium degeneration, colour vision deficiency and visual field defects were detected in 69% of the thalassemic group. Barteselli et al.[23] reported ocular fundus abnormalities characteristic of pseudoxanthoma elasticum (PXE) in 70 of 255 patients (27.8%) with Thalassemia. These findings were supported by Sodhi et al[24], in which the authors stress subconjunctival bleeding as the first presenting clinical feature in ITP. Retinal hemorrhages were noted in around 44 % of the cases in our study. This was in agreement with several studies. [11,25]

## Conclusion

The ocular changes of blood dyscrasias are not uncommon as is proved by various clinical and pathological studies. These changes in the eye are due to the hemorrhagic effect of the blood disorders or due to the infiltration of the ocular tissues by malignant cells. Ophthalmic manifestations are commonly observed in patients with blood dyscrasia. The routine ocular examination must be conducted in blood dyscrasias; especially posterior segment evaluation should be mandatory in severe anaemia/ sickle cell haemoglobinopathy and leukaemia, which is both diagnostic and prognostic of the severity of this disease. Also, there is a need to develop a standard referral protocol between the haematology clinic and the eye clinic so that blood dyscrasia patients can have periodic evaluations.

**Ethical approval was taken from the institutional ethical committee and written**

**Informed consent was taken from all the participants.**

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