E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.325

Research Article

Retinal Manifestations of Hematological Disorders: Clinical and Hematological Correlates in a Tertiary Eye Care Centre

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Orcid Id: [1]0009-0006-4742-7142, [2]0009-0002-2521-3515
Received: 23.06.26, Revised: 15.07.26, Accepted: 18.08.26

ABSTRACT
Purpose: To evaluate the demographic profile, clinical characteristics, hematological abnormalities, and retinal manifestations of patients with hematological disorders, with particular emphasis on the association between individual hematological parameters and anemic retinopathy/Roth spots.
Materials and Methods: A hospital-based observational cross-sectional study was conducted among 14 patients with hematological abnormalities. Demographic and clinical details, ophthalmic findings, and hematological parameters including hemoglobin, PCV, RBC count, MCV, MCH, MCHC, TLC, and platelet count were recorded. The association between individual hematological parameters and anemic retinopathy was assessed using appropriate statistical tests.
Results: A total of 14 patients were included, with a mean age of 44.3 ± 17.5 years; 8 (57.1%) were females and 6 (42.9%) were males. Anemia was the most common hematological abnormality, present in 12 (85.7%) patients, followed by pancytopenia in 3 (21.4%), thrombocytopenia in 2 (14.3%), and polycythemia in 2 (14.3%). Retinal abnormalities were documented in 4 (28.6%) patients, including anemic retinopathy with Roth spots in 2 (14.3%). One patient with Roth spots also had a pre-macular hemorrhage. Patients with anemic retinopathy had significantly lower median hemoglobin (3.80 vs. 8.35 g/dL; P=0.030) and PCV (12.75% vs. 26.80%; P=0.036) compared with those without retinal involvement. Hemoglobin and PCV demonstrated significant inverse correlations with anemic retinopathy (r=−0.648, P=0.023 and r=−0.671, P=0.024, respectively). Other hematological indices, including RBC count, MCV, MCH, MCHC, TLC, and platelet count, showed no significant association.
Conclusion: Severe anemia, particularly markedly reduced hemoglobin and PCV, was significantly associated with anemic retinopathy and Roth spots. Thrombocytopenia may contribute to the severity of associated retinal hemorrhage, particularly in profound anemia. Larger studies are required to validate these findings.

Keywords: Anemic Retinopathy, Roth Spots, Anemia, Hematological Abnormalities, Retinal Hemorrhage, Hemoglobin, PCV.

INTRODUCTION

Anemia is one of the most common hematological disorders and may produce a wide spectrum of systemic and ocular manifestations, particularly when severe. The retina is highly susceptible to abnormalities in oxygen delivery and microvascular integrity because of its high metabolic requirements. Reduced oxygen-carrying capacity, vascular fragility, altered blood rheology and impaired hemostasis may therefore result in retinal hemorrhages and other retinal abnormalities [1,2].

Anemic retinopathy refers to retinal abnormalities occurring in association with anemia and may include intraretinal hemorrhages, Roth spots, cotton-wool spots, retinal edema, vascular tortuosity and, in

severe cases, pre-retinal or vitreous hemorrhage [1,2]. The occurrence and severity of these changes appear to be influenced by the degree of anemia, although the exact hematological threshold at which retinal involvement develops remains incompletely defined.

Roth spots are white-centered retinal hemorrhages characterized by a pale central area within a retinal hemorrhage. Although historically considered characteristic of infective endocarditis, they are now recognized as nonspecific manifestations of retinal microvascular injury and may occur in anemia, leukemia, thrombocytopenia, diabetes mellitus, hypertension and other systemic disorders [3,4]. Histopathological studies have suggested that the pale center may represent fibrin-platelet aggregates and other components of the local hemostatic response rather than a specific infectious lesion [3].

The pathogenesis of anemic retinopathy is likely multifactorial. Severe anemia reduces oxygen delivery to the retinal tissue, potentially resulting in retinal hypoxia and endothelial dysfunction. At the same time, anemia may increase vascular susceptibility to rupture, while thrombocytopenia can impair platelet-mediated hemostasis and increase the tendency toward retinal hemorrhage [1,5]. The combination of anemia and thrombocytopenia may therefore produce more extensive hemorrhagic manifestations than either abnormality alone.

Retinal manifestations may also occur in a variety of hematological disorders, including pancytopenia, leukemia and myeloproliferative disorders. In these conditions, retinal injury may result from different mechanisms, including anemia, thrombocytopenia, leukostasis, hyperviscosity and direct vascular or tissue infiltration [6,7]. Consequently, the retinal phenotype may reflect the combined effect of several hematological abnormalities rather than a single laboratory abnormality.

Previous studies have established an association between the severity of anemia and retinal involvement, but the relationship between individual hematological indices and anemic retinopathy remains less clearly defined. In particular, it is uncertain whether hemoglobin concentration and PCV are more closely related to retinal involvement than RBC count, MCV, MCH, MCHC, TLC or platelet count. Determining which hematological parameters are associated with retinal manifestations may help identify patients who require closer ophthalmic evaluation [1,8].

The clinical significance of Roth spots also extends beyond their recognition as an ophthalmic finding. Because they may occur in several systemic diseases, their presence should be interpreted in conjunction with the patient's hematological profile and other systemic findings [3,4,10]. In patients with known hematological abnormalities, identifying a relationship between the severity or type of hematological disturbance and retinal involvement may provide additional insight into the systemic disease burden.

Despite the available literature, relatively few studies have evaluated multiple hematological parameters simultaneously in relation to anemic retinopathy. Much of the published literature consists of broader hematological cohorts, leukemia series or individual case reports, making it difficult to determine the relative contribution of individual blood parameters to retinal involvement [6,7,9].

Therefore, the present study was undertaken to evaluate retinal manifestations among patients with hematological abnormalities and to determine the association between individual hematological parameters and anemic retinopathy, particularly Roth spots. The study also aimed to compare hemoglobin, PCV, RBC count, red-cell indices, TLC and platelet count between patients with and without anemic retinopathy.

MATERIALS AND METHODS

This was a hospital-based observational cross-sectional study conducted at a tertiary eye care centre. A total of 14 patients with hematological abnormalities were included and evaluated for associated retinal manifestations.

Demographic and clinical details were recorded. Hematological parameters including hemoglobin (Hb), PCV, RBC count, MCV, MCH, MCHC, total leukocyte count (TLC), and platelet count were obtained from laboratory investigations. Hematological abnormalities were categorized as anemia, pancytopenia, thrombocytopenia, polycythemia, and other relevant abnormalities.

All patients underwent comprehensive ophthalmic examination, including visual acuity, anterior segment examination and dilated fundus examination. The fundus was assessed for retinal hemorrhages, Roth spots, cotton-wool spots, retinal edema, vascular abnormalities and pre-macular/pre-retinal hemorrhage. Roth spots were defined as retinal hemorrhages with a pale or white centre. Retinal findings attributable to other identifiable

causes, such as diabetic retinopathy, were recorded separately.

The primary outcome was the presence of anemic retinopathy/Roth spots. Hematological parameters were compared between patients with and without retinal involvement, and their association with anemic retinopathy was assessed.

Continuous variables were expressed as mean ± SD or median, and categorical variables as frequency and percentage. The Mann–Whitney U test was used for comparison of continuous variables, and Spearman correlation was used to assess associations between hematological parameters and anemic retinopathy. A P value <0.05 was considered statistically significant. Given the small sample size, the analysis was considered exploratory.

RESULTS

A total of 14 patients with hematological abnormalities were included in the study. The mean age of the study population was 44.3 ± 17.5 years, with 8 females (57.1%) and 6 males (42.9%). The demographic profile of the study population is presented in [Table 1].

Table 1: Demographic Profile of the Study Population (N=14)

Characteristic	Study population (N=14)
Mean age ± SD (years)	44.3 ± 17.5
Age range (years)	15–75
Female	8 (57.1%)
Male	6 (42.9%)

Hematological abnormalities

Anemia was the most common hematological abnormality, present in 12 of 14 patients (85.7%). Pancytopenia was present in 3 patients (21.4%), while thrombocytopenia was documented in 2 patients (14.3%). Polycythemia was identified in 2 patients (14.3%). As these hematological abnormalities could overlap, particularly because pancytopenia includes anemia and thrombocytopenia, the categories were not mutually exclusive. The overall distribution of hematological abnormalities is shown in [Table 2].

Table 2. Distribution of Hematological Abnormalities in the Study Population (N=14)

Hematological abnormality	n (%)
Anemia	12 (85.7)
Pancytopenia	3 (21.4)
Thrombocytopenia	2 (14.3)
Polycythemia	2 (14.3)

Type of anemia

Among the 12 patients with anemia, 5 (41.7%) had microcytic hypochromic anemia, 4 (33.3%) had normocytic normochromic anemia, while 3 (25.0%) had pancytopenia with associated anemia. Thus, microcytic hypochromic anemia was the most frequent anemia pattern in the study population. The distribution is presented in [Table 3].

Table 3. Distribution of Anemia Patterns among Patients with Anemia (N=12)

Type of anemia/hematological pattern	N (%)
Microcytic hypochromic anemia	5 (41.7)
Normocytic normochromic anemia	4 (33.3)
Pancytopenia	3 (25.0)

Retinal manifestations

Retinal abnormalities were documented in 4 of the 14 patients (28.6%). Two patients had retinal manifestations considered to be associated with their hematological abnormalities, while two patients had diabetic retinopathy that was considered to have an independent etiology. Among the hematology-associated retinal manifestations, Roth spots were identified in 2 patients (14.3%); one of these patients additionally had a pre-macular hemorrhage. The overall distribution of retinal findings is summarized in [Table 4].

Table 4. Retinal Manifestations in the Study Population (N=14)

Retinal finding	n (%)
Normal fundus	10 (71.4)
Anemic retinopathy	2 (14.3)
Diabetic retinopathy	2 (14.3)

Thrombocytopenia and retinal manifestations

Among the patients with thrombocytopenia, no retinal manifestation was documented when thrombocytopenia occurred as an isolated hematological abnormality. However, one patient with severe pancytopenia, profound anemia and marked thrombocytopenia demonstrated Roth spots associated with a pre-macular hemorrhage. This patient had a hemoglobin concentration of 2.2 g/dL, PCV of 7.0%, and platelet count of 0.27 lakh/cumm. In contrast, the second patient with Roth spots had a platelet count of 3.44 lakh/cumm, indicating that Roth spots were not consistently associated with thrombocytopenia. Thus, thrombocytopenia may have contributed to the severity of hemorrhagic retinal involvement in the patient with pancytopenia, but did not demonstrate an apparent association with Roth spots in this cohort.

Pancytopenia and retinal manifestations

Three patients (21.4%) had pancytopenia. Their hemoglobin concentrations ranged from 2.2 to 10.2 g/dL. Retinal involvement was observed in only one patient, who had profound anemia with hemoglobin of 2.2 g/dL and PCV of 7.0%. This patient demonstrated Roth spots with a pre-macular hemorrhage and had severe thrombocytopenia. The remaining two patients with pancytopenia, whose hemoglobin concentrations were substantially higher, had no documented retinal abnormality. These findings suggest that within pancytopenia, the severity of anemia may be more important for retinal involvement than pancytopenia itself.

Polycythemia and retinal manifestations

Two patients (14.3%) had polycythemia. Their hemoglobin concentrations were 19.6 and 18.4 g/dL, with PCV values of 57.5% and 53.9%, respectively. One patient had associated severe thrombocytopenia, while the other had leukocytosis. Neither patient demonstrated a documented retinal abnormality attributable to polycythemia.

Comparison of Hemoglobin in patients with anemic retinopathy

A clear descriptive gradient was observed between hemoglobin concentration and retinal involvement. Among patients with hemoglobin <5 g/dL, the only patient in this category had Roth spots with pre-macular hemorrhage. Among those with hemoglobin 5–7.9 g/dL, one of four patients had Roth spots. No Roth spots were documented among patients with hemoglobin concentrations of ≥8 g/dL. Thus, both patients with anemic retinopathy had hemoglobin concentrations below 6 g/dL. The distribution of Roth spots according to hemoglobin severity is presented in [Table 5].

Table 5. Distribution of Anemic Retinopathy According To Hemoglobin Concentration

Hemoglobin category	Anemic patients, n	Roth spots/anemic retinopathy, n (%)
<5 g/dL	1	**1 (100)**
5–7.9 g/dL	4	**1 (25.0)**
8–9.9 g/dL	2	0
≥10 g/dL	5	0
Total	12	2 (16.7)

Comparison of hematological indices in patients with anemic retinopathy

When the 12 anemic patients were compared according to the presence or absence of Roth spots, patients with Roth spots had substantially lower hemoglobin and PCV values. The median hemoglobin concentration was 3.8 g/dL in patients with Roth spots compared with 8.35 g/dL in those without Roth spots (P=0.030). Similarly, median PCV was 12.75% versus 26.8% (P=0.036), respectively. RBC count was also lower in the Roth-spot group, although this difference did not reach statistical significance. In contrast, MCV, MCH and MCHC did not demonstrate a significant association with Roth spots. These findings indicate that the severity of anemia, particularly hemoglobin and PCV reduction, showed a stronger relationship with retinal involvement than the morphological indices of anemia. [Table 6]

Table 6. Comparison of Hematological Parameters between Patients with and Without Anemic Retinopathy

Hematological parameter	Roth spots present (n=2), Median	Roth spots absent (n=10), Median	P value
Hemoglobin (g/dL)	3.80	8.35	0.030
RBC (million/cumm)	1.67	3.80	0.145
PCV (%)	12.75	26.80	0.036
MCV (fL)	96.90	77.20	0.909
MCH (pg)	29.75	25.90	1.000
MCHC (g/dL)	30.35	32.40	0.097
TLC (cells/cumm)	6230	8429.5	0.606
Platelet count (lakh/cumm)	1.86	1.14	0.909

Correlation of hematological parameters with anemic retinopathy

Exploratory correlation analysis demonstrated an inverse correlation between hemoglobin concentration and Roth spots (r = −0.648, P=0.023). PCV showed a similarly strong inverse correlation (r = −0.671, P=0.024). RBC count showed an inverse trend but did not reach statistical significance (r = −0.522, P=0.100). No significant correlation was observed for MCV, MCH, MCHC, TLC or platelet count. Thus, among the hematological parameters evaluated, hemoglobin and PCV demonstrated the strongest association with anemic retinopathy, whereas platelet count and red-cell indices did not show a consistent relationship. The complete correlation analysis is presented in [Table 7].

Table 7. Correlation between Hematological Parameters and Anemic Retinopathy

Parameter	Spearman r	P value
Hemoglobin	-0.648	0.023
PCV	-0.671	0.024
RBC count	-0.522	0.100
MCV	0.075	0.828
MCH	0.000	1.000
MCHC	-0.562	0.072
TLC	-0.194	0.545
Platelet count	0.075	0.828

Overall, the results demonstrate that severe reduction in hemoglobin and PCV was the principal hematological feature associated with Roth spots in this cohort. Both patients with anemic retinopathy had hemoglobin levels below 6 g/dL, while no Roth spots were observed at higher hemoglobin concentrations. The absence of a consistent association with MCV, MCH, MCHC or platelet count suggests that the severity of anemia rather than the morphological type of anemia or thrombocytopenia alone may be the major determinant of retinal involvement. However, only two patients demonstrated Roth spots; therefore, these findings should be considered exploratory and hypothesis-generating rather than definitive. [Tables 5–7]

DISCUSSION

The present study found retinal abnormalities in 4 of 14 patients (28.6%), with 2 patients (14.3%) demonstrating retinal findings considered attributable to their hematological abnormalities. Both hematology-associated cases had Roth spots, and one also had a pre-macular hemorrhage. This frequency of retinal involvement is comparable with previous observations in patients with hematological disease, although direct comparison is limited by differences in study populations and definitions of retinal involvement.

The principal finding of this study was the relationship between severity of anemia and anemic retinopathy. Both patients with anemic retinopathy had hemoglobin concentrations below 6 g/dL, whereas no Roth spots were observed at hemoglobin concentrations ≥8 g/dL. Patients with Roth spots had a significantly lower median hemoglobin than those without retinal involvement (3.80 vs. 8.35 g/dL; P=0.030), and hemoglobin demonstrated a significant inverse correlation with anemic retinopathy (r=−0.648, P=0.023).

This finding is consistent with the study by Carraro et al., which evaluated 226 patients

with anemia and/or thrombocytopenia and found retinopathy in 28.3% of patients. Retinal lesions were closely associated with severe anemia, defined as hemoglobin <8 g/dL, as well as severe thrombocytopenia [11]. The similar relationship observed in our cohort, despite the much smaller sample, supports the importance of the degree of anemia in the development of retinal abnormalities.

A similar association was reported by Venkatesh et al., who studied 70 patients with anemia and found anemic retinopathy in 29.6%. Patients with retinopathy had significantly lower hemoglobin and hematocrit values than those without retinopathy. Their study also found that hemoglobin and hematocrit were important hematological determinants of anemic retinopathy [12]. Our findings are concordant, with both hemoglobin and PCV demonstrating statistically significant associations with retinal involvement.

The relationship with PCV was particularly notable in our study. The median PCV was 12.75% in patients with Roth spots compared with 26.80% in those without retinal involvement (P=0.036), and PCV showed a significant inverse correlation with anemic retinopathy (r=−0.671, P=0.024). The parallel behavior of hemoglobin and PCV suggests that the degree of reduction in circulating red-cell mass and oxygen-carrying capacity may be more important than the morphological type of anemia.

In contrast, RBC count, MCV, MCH and MCHC did not demonstrate significant associations with anemic retinopathy. Although RBC count showed an inverse trend, the difference was not statistically significant. This finding is consistent with the study by Venkatesh et al., in which the red-cell indices did not demonstrate significant differences between patients with and without anemic retinopathy [12]. Thus, the severity of anemia appears to be more relevant than whether the anemia is microcytic, normocytic or macrocytic.

The association with thrombocytopenia was less consistent. One patient with severe pancytopenia, profound anemia and marked thrombocytopenia had Roth spots with a pre-macular hemorrhage, whereas the second patient with Roth spots had a platelet count of 3.44 lakh/cumm. Therefore, thrombocytopenia was not consistently present in patients with Roth spots. Carraro et al. reported a higher prevalence of retinopathy when severe anemia and thrombocytopenia occurred together, with retinal hemorrhages occurring particularly frequently in this combination [11]. Our findings similarly suggest that thrombocytopenia may contribute to the hemorrhagic severity of retinal involvement but may not be necessary for the development of Roth spots.

The findings of Guyer et al. provide further context for this observation. In their study of 117 patients with acute leukemia, intraretinal hemorrhages were associated with thrombocytopenia, while white-centered hemorrhages were associated with anemia in patients with acute nonlymphocytic leukemia. Patients with intraretinal hemorrhages also had lower hematocrit levels in acute lymphocytic leukemia [13]. These observations support the possibility that anemia and thrombocytopenia may have complementary roles in retinal hemorrhagic manifestations.

Among our three patients with pancytopenia, retinal involvement occurred in only one. Importantly, this patient had a hemoglobin concentration of 2.2 g/dL, while the other two patients with pancytopenia had substantially higher hemoglobin levels and no retinal abnormality. This again suggests that profound anemia may be a more important component of retinal involvement than pancytopenia itself.

A recent report by Gupta et al. described a patient with severe megaloblastic anemia and pancytopenia who had multiple Roth spots and retinal hemorrhages at a hemoglobin concentration of 2.3 g/dL. Following correction of the anemia, the retinal hemorrhages and Roth spots showed marked resolution [14]. The similarity between this case and our patient with hemoglobin 2.2 g/dL and Roth spots with pre-macular hemorrhage further supports the association between profound anemia and hemorrhagic retinal manifestations.

Neither of our two patients with polycythemia demonstrated retinal abnormalities attributable to the hematological disorder. Although increased red-cell mass may theoretically affect retinal microcirculation through hyperviscosity, the very small number of patients with polycythemia in our study prevents any meaningful conclusion regarding this association.

TLC did not demonstrate a significant relationship with anemic retinopathy in our cohort. This finding is supported by the South Indian leukemia study by Soman et al., in which white blood cell count was not independently associated with ophthalmic manifestations after adjustment for other hematological parameters [15]. Their study, however, involved patients

with leukemia, where additional mechanisms such as leukostasis and abnormal blood rheology may contribute to retinal disease. Therefore, the absence of an association with TLC in our heterogeneous cohort should be interpreted cautiously.

Taken together, our findings indicate that hemoglobin and PCV were the hematological parameters most strongly associated with anemic retinopathy, while RBC count, MCV, MCH, MCHC, TLC and platelet count did not demonstrate significant correlations. The direction and magnitude of the Hb and PCV associations suggest that the severity of reduction in oxygen-carrying capacity may be more relevant to retinal involvement than the morphological subtype of anemia.

The study has important limitations. The sample size was small, with only 14 patients and two cases of anemic retinopathy, which limits statistical power and prevents reliable multivariable analysis. The hematological abnormalities were also heterogeneous. Consequently, the findings regarding thrombocytopenia, pancytopenia and polycythemia should be considered exploratory. Larger prospective studies with a greater number of patients with retinal involvement are required to establish clinically useful hematological thresholds for predicting anemic retinopathy.

In conclusion, marked reduction in hemoglobin and PCV was the hematological feature most closely associated with anemic retinopathy in our cohort. Thrombocytopenia may contribute to the severity of associated hemorrhage when accompanied by profound anemia, but it was not consistently present in patients with Roth spots. Given the small sample size, these findings should be considered hypothesis-generating and require confirmation in larger studies.

CONCLUSION

Severe anemia, particularly markedly reduced hemoglobin and PCV, was significantly associated with anemic retinopathy and Roth spots. Other hematological indices showed no significant association. Thrombocytopenia may contribute to the severity of retinal hemorrhage when associated with profound anemia. Larger studies are required to confirm these findings.

Source of Funding

None

Conflict of Interest

None

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