

Do Plasma Cells Affect Hemoglobin and Red Blood Cell Counts in Patients With and Without Myeloma?

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Abstract

Background: We undertook this study to evaluate if there is any significant correlation between hemoglobin levels, red blood cell (RBC) count, bone marrow normoblast percentage and marrow plasma cell percentage in patients with and without myeloma.

Methods: In this study, we compared hemoglobin level, red blood cell count and bone marrow normoblast percentage with plasma cell percent in 60 patients with and without myeloma (30 with and 30 without myeloma).

Results: There was significant negative correlation for all three in the myeloma group (P values of 0.03, 0.02 and < 0.0001 for hemoglobin, red cell count and normoblast percent respectively). In the non myeloma group significant negative correlation ($P = 0.02$) was seen only between normoblast and plasma cell percent. The students-t-test between the two groups revealed a significant difference between mean red cell count and normoblast percentage, however the mean hemoglobin was similar. We further sub classified the myeloma group based on hemoglobin level and found that the commonest subgroup had average hemoglobin of 84 g/L.

Conclusions: We conclude that in the non myeloma group there is possibility of plasma cells affecting bone marrow normoblast count. We have also raised the possibility of absence of ineffective erythropoiesis in the myeloma group.

Keywords: Myeloma; Pearsons correlarion; Students-t-test

Introduction

Anemia is seen in more than two thirds of patient with my-

eloma. The reasons for this are diverse, some of which include anemia of chronic disorders, reduced erythropoietin production, reduced sensitivity of erythroid precursors and myeloma cell mediated apoptosis of erythroid progenitors [1].

Reduced number of committed erythroid precursors and suppression of erythropoiesis by Interleukine-6 have been reported to be associated factors [2]. Crowding of marrow by plasma cells and replacement of marrow interferes with hematopoiesis and is also responsible for anemia. A severe normocytic normochromic anemia is seen in more than 20% of patients and is of anemia of chronic disorders type [3]. There is inappropriate erythropoietin secretion, moderate hypoferrremia with normal to increased iron stores and defective maturation of erythroid precursors [4]. There is an increase in levels of cytokines such as tumor necrosis factor- α , transforming growth factor- β , interferon- γ , and interleukins 8 and 11 which negatively regulate erythropoiesis by enhancing apoptogenic molecules on erythroid precursors.

We undertook this study to evaluate if there is any significant correlation between hemoglobin levels, red blood cell (RBC) count, bone marrow normoblast percentage and marrow plasma cell percentage in patients with and without myeloma (group 1 and 2) and we compared the two groups.

Fossi A and others reported a negative correlation between hemoglobin and CD-38 positive cells in S-phase ($P < 0.001$) in myeloma patients with moderate to severe anemia [5].

Materials and Methods

We compared 30 samples (FBC and marrow smears) from patients with myeloma- Group 1 (diagnosed between August 2011-May 2012 by biochemical, clinical, pathological evidence or combination) with 30 samples (FBC and marrow smears) collected from patients- Group 2 with no evidence or clinical suspicion of myeloma. This group included patients with unexplained anemias, anemia of chronic disorders, aplastic anemia, pancytopenia, autoimmune hemolytic anemias and lymphomas for staging. Group 1 patients included only patients who were newly diagnosed cases and

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Table 1. Summary Statistics of Hemoglobin, RBC Count, Plasma Cells and Normoblasts

Variable	Group 1	Group 2
Number	30	30
Hemoglobin (g/L)	42 - 139 Mean: 7.77 Standard deviation: 2.2	56 - 155 Mean: 8.8 Standard deviation: 2.53
RBC count $\times 10^{12}/L$	1.41 - 1.51 Mean: 2.5 Standard deviation: 0.67	1.73 - 5.99 Mean: 3.38 Standard deviation: 1.17
Plasma cells%	29 - 94 Mean: 55 Standard deviation: 16.89	0.5 - 13 Mean: 2.56 Standard deviation: 2.26
Normoblasts %	0.5 - 29 Mean: 11.75 Standard deviation: 7.42	2 - 74 Mean: 37.8 Standard deviation: 16.09

were not on chemotherapy.

The hemoglobin and RBC counts from both groups were estimated by Advia-2120(Siemens) and LH-750 (Beckman Coulter) analyzer.

Three Leishman stained bone marrow smears were evaluated and an average of three differentials from a 300 cell count was obtained.

Data analysis: Pearsons correlation and students-t-test (assuming unequal variance) was computed on Med Cal software (v12.2.1).

Observations

Statistical summary of patients in Group 1: The age range of these patients varied from 35 - 82 years with 20 male and ten female patients. The hemoglobin ranged from 42 - 139 g/L with a mean of 77g/L (normal: males-130 - 170 g/L, females-120 - 150 g/L). The RBC count varied from 1.41 -

$4.51 \times 10^{12}/L$ (normal: males, 4.5 - 5.5 $\times 1,012/L$, females, 3.8 - 4.8 $\times 10^{12}/L$ with an average of $2.5 \times 10^{12}/L$ (Table 1).

Bone marrow plasma cells varied from 29-94% (normal: 0-3.5%) with a mean of 55%. Bone marrow normoblasts varied from 0.5-29% (5-35%) with an average of 11.75% (Table 1).

The Pearsons coefficient correlation between hemoglobin and percentage of plasma cells was -0.39, between RBC count and plasma cells was -0.40 and between percentage of normoblasts and percentage of plasma cells was -0.75 (Table 2).

Statistical summary of patients in Group 2: The age range of these patients varied from 25 - 77 years with 19 male and 11 female patients. The hemoglobin ranged from 56 - 155 g/L with a mean of 88 g/L. The RBC count varied from 1.73 - 5.99 $\times 10^{12}/L$ with a mean of $3.38 \times 10^{12}/L$ (Table 1).

Bone marrow plasma cells varied from 0.5-13% with a mean of 2.56%. Percentage of normoblasts varied from 2 -

Table 2. Pearsons Coefficient Correlation in Group 1 and Group 2

Variable	Group 1 Pearsons	Group 2 Pearsons
Hemoglobin and plasma cells	-0.39, P = 0.03	-0.02, P = 0.9012
RBC and plasma cells	-0.40, P = 0.02	-0.08, P = 0.655
Normoblasts and plasma cells	-0.752, P \leq 0.0001	-0.4139, P = 0.023

Table 3. Summary of t-Tests

Variable (Group1:Group 2)	Statistical significance (P-value)
Hemoglobin	0.09
RBC count	0.0016
Normoblasts	< 0.0001

74 with a mean of 37.8% (Table 1).

The Pearson's coefficient correlation between hemoglobin and plasma cells was -0.02, between RBC count and plasma cells was -0.08 and between percentage of normoblasts and plasma cells was -0.4139 (Table 2).

Students-t-test comparing Group 1 and Group 2: The t-test was conducted between hemoglobin levels between group 1 (mean: 7.77, standard deviation: 4.87) and group 2 (mean: 8.8, standard deviation: 2.53), RBC counts in group 1 (mean: 2.56, standard deviation: 0.67) and 2 (mean: 3.38, standard deviation: 1.17) and percentage of normoblasts in group 1 (mean: 11.75, standard deviation: 7.42) and group 2 (mean: 37.83, standard deviation: 16.09). The results of the t-test are summarized in Table 3.

Sub classification of Group 1: We could classify our patients in to four subgroups based on hemoglobin levels, subgroup a with hemoglobin 40 - 70 g/L, subgroup b with hemoglobin 71 - 101 g/L, subgroup c with hemoglobin of 102 - 132 g/L and subgroup d with hemoglobin more than 133 g/L. Seventeen patients belonged to subgroup b, 12 were grouped in to subgroup a and one each in c and d subgroups.

In subgroup a, the average hemoglobin was 57 g/L and mean plasma cell percentage was 62.54. In subgroup b mean hemoglobin was 84.4 g/L and mean plasma cell percentage was 51.82 (Table 4).

Applying Pearson's coefficient correlation it is seen that in both subgroups a strong negative correlation exists between percentage of normoblasts and plasma cells (Table 5). Both hemoglobin and RBC count have only a weak negative

correlation with plasma cells.

Discussion

There is extensive literature on the pathogenesis of anemia in myeloma [1-4]. We do not propose to deal with the pathogenesis in this study. We have attempted to study closely the relation between hemoglobin (RBC count and normoblasts) and plasma cell percentage in both patients with and without myeloma. Our findings of a statistically significant negative correlation between hemoglobin (and RBC count) and plasma cells in myeloma are not surprising and are probably due to the replacement of marrow by plasma cells with suppression of erythroid precursors.

However, it is surprising that in the non myeloma group there exists a statistically significant negative correlation ($P = 0.023$) between marrow normoblast and plasma cell percentage. We could not find a reason for this as none of these patients had evidence of myeloma. Only one of our patients in this group had elevated plasma cell percentage (13%). This was a patient with aplastic anemia. This raises an interesting question as to whether plasma cells affect normoblast percentage with subsequent effect on hemoglobin in both patients with and without myeloma. To answer this question we need to study groups with benign plasmacytosis. In our myeloma subgroups it is not surprising to note that mean plasma cells was higher in subgroup a than b and the mean RBC count and percentage of normoblasts was higher in subgroup b. The in-

Table 4. Variables in the Commonest Myeloma Subgroups

Variable	Subgroup a	Subgroup b
Age in years	35 - 65(50.63)	35 - 76 (58.7)
Hemoglobin g/L	4.3 - 7 (5.7)	7.4 - 9.9 (8.44)
RBC $\times 10^{12}/L$	1.67 - 2.31 (1.930)	2.36 - 3.4 (2.77)
Plasma cell %	48 - 94 (62.54)	30 - 84 (51.82)
Normoblast %	0.5 -29 (11.31)	1 - 29 (12.11)

Table 5. Pearsons Coefficient Correlation in Myeloma Subgroups

Variable	Subgroup a Pearsons	Subgroup b Pearsons
Hemoglobin and plasma cells	-0.141	-0.131
RBC and plasma cells	-0.351	-0.148
Normoblasts and plasma cells	-0.757	-0.852

interesting fact we noted here is that the mean age in subgroup a (50.63 yrs) was less than subgroup b (58.70). Does this imply that younger patients present with lower hemoglobin levels? Our study group is small to conclude this.

Finally, the students-t-test brings out the surprising finding that though the mean hemoglobin is similar in the myeloma and non myeloma group, there is significant difference between mean RBC counts and normoblast percentage. The average RBC count and normoblast percentage are higher in the non myeloma group and does not explain the reason for the mean hemoglobin being similar in both groups. One of the obvious reasons could be that group 2 includes patients with ineffective erythropoiesis accounting for low hemoglobin levels. This could indirectly imply that ineffective erythropoiesis is not a feature of the myeloma group.

Our study group is small and the groups are not fully sex and age matched to definitely conclude our findings. We need to study larger groups to see if the findings of this study are conclusive.

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